SUPPLEMENTARY MATERIAL

Title: Biomarkers of ambient air pollution and lung cancer: strength of evidence

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Table 1 – Prospective study results on the relationship between exposure to air pollution and lung cancer incidence and/or mortality, listed by study or cohort

First Author, Year	Area/ Country	Exposure‡	Outcome	Controlled Confounders	Number of Subjects	RR†	CI†
AMERICAN STUDIES							
American Legion Study							
Buell, 1967	USA	>10 yrs in LAcounty vs.other counties	Lung Cancer Mortality	Age, sex, smoking, size of birthplace	336,571 person-yrs	2.5	*not reported
		>10yrs vs. <10yrs in LA county	Lung Cancer Mortality	Age, sex, smoking, size of birthplace		1.26	*not reported
ASHMOG Study							
Mills, 1991	USA	Total Suspended Particulate (exceedance frequency of 200µg/m3)	Cancer in females incidence	Age, sex, education, ex-smoking, ETS†, and occupational exposure	6,000	1.72	0.81-3.65
		Ozone (exceedance frequency of 10pphm)	Lung Cancer incidence	Age, sex, education, ex-smoking, ETS, and occupational exposure		2.25	0.96-5.31
Beeson, 1998	California, USA	Ozone (100ppb increase)	Lung Cancer incidence - males	Pack-years of past cigarette smoking, educational level, and current alcohol use	6,338	3.56	1.35-9.42
		PM10† (IQR increase)	Lung Cancer Incidence - males	Pack-years of past cigarette smoking, educational level, and current alcohol use		5.21	1.96-13.99
		SO_2 (IQR increases)	Lung Cancer Incidence - males	Pack-years of past cigarette smoking, educational level, and current alcohol use		2.66	1.62-4.39
		PM10 exceedance frequencies of 50 microg/m3 (IQR increase)	Lung Cancer Incidence - females	Smoking, Age		1.21	0.55-2.66
		PM10 exceedance frequencies of 60 microg/m3 (IQR increase)	Lung Cancer Incidence - females	Smoking, Age		1.25	0.57-2.71
		SO_2 (IQR increases)	Lung Cancer Incidence - females	Smoking, Age		2.14	1.36-3.37
Abbey, 1999	USA	PM10 (IQR increase in mean conc.)	Lung Cancer Mortality in males	Years of education, pack-years of ex smoking, alcohol use	6,338	3.36	1.57-7.19
		PM10 (IQR increase in mean conc.)	Lung Cancer Mortality in females	Years of education and pack-years of past smoking		1.33	0.60-1.96

		Ozone (IQR increase in mean conc.)	Lung Cancer Mortality in males	Years of education, pack-years of ex smoking, alcohol use		2.10	0.99-4.44
		Ozone (IQR increase in mean conc.)	Lung Cancer Mortality in females	Years of education and pack-years of past smoking		0.77	0.37-1.61
		SO_2 (IQR increase in mean conc.)	Lung Cancer Mortality in males	Years of education, pack-years of ex smoking, alcohol use		1.99	1.24-3.20
		SO_2 (IQR increase in mean conc.)	Lung Cancer Mortality in females	Years of education and pack-years of past smoking		3.01	1.88-4.84
		NO_2 (IQR increase in mean conc.)	Lung Cancer Mortality in males	Years of education, pack-years of ex smoking, alcohol use		1.82	0.93-3.57
		NO_2 (IQR increase in mean conc.)	Lung Cancer Mortality in females	Years of education and pack-years of past smoking		2.81	1.15-6.89
McDonnell, 2000	USA	PM2.5† (IQR increase = 24.3 μg/m3),	Lung Cancer Mortality		6,338	2.23	0.56-8.94
		PM2.5-10 (IQR increase = 9.7 μg/m3)	Lung Cancer Mortality			1.25	0.63-2.49
		PM10 (IQR increase = 29.5μg/m3)	Lung Cancer Mortality			1.84	0.59-5.67
American Cancer Prevention Study II							
Pope, 2002	USA	NO_2 (10 microg/m3 increase)	Lung Cancer Mortality	Age, sex, race, smoking, education, marital status, body mass, alcohol comsumption, occupation, and diet	409-493 thousand	1.14	1.04-1.23
Jerrett, 2005	USA	PM10 (10 microg/m3 increase)	Lung Cancer Mortality	Age, sex, race, education, smoking, marital status, BMI, alcohol consumption, occupational exposure, diet, and other ecological variables	22,905	1.2	0.79-1.82
		Ozone (10 microg/m3 increase)	Lung Cancer Mortality	Age, sex, race, education, smoking, marital status, BMI, alcohol consumption, occupational exposure, diet, and other ecological variables		0.99	0.91-1.07
		Distance to freeways (<500m vs. >500m)	Lung Cancer Mortality	Age, sex, race, education, smoking, marital status, BMI, alcohol consumption, occupational exposure, diet, and other ecological variables		1.44	0.94-2.21
Turner, 2011	USA	PM2.5 (10 microg/m3 increase) ACP	Lung Cancer Mortality	Age, sex, smoking, educational attainment, BMI, chronic lung disease	188,699	NA	1.15-1.27
Pope, 2011	USA	PM2.5 (10 microg/m3 increase)	Lung Cancer Mortality	Age, sex, education, marital status, body mass, alcohol consumption, occupational exposures, smoking duration, and diet	1.2million	1.14	1.04-1.23
Harvard Six Cities Study							
Dockery, 1993	USA	Inhalable particles:	Lung Cancer	Age, sex, smoking, education, and BMI		1.27	1.08-1.48

		Most polluted vs. Least polluted city	mortality				
					8,111		
		Fine particles: Most polluted vs. Least polluted city	Lung Cancer mortality	Age, sex, smoking, education, and BMI		1.26	1.08-1.47
		Sulphate particles: Most polluted vs. Least polluted city	Lung Cancer mortality	Age, sex, smoking, education, and BMI		1.26	1.08-1.47
Krewski, 2005	USA	PM2.5 (most vs. least polluted city = 18.6 microg/m3 increase)	Lung Cancer Mortality	Age, sex, smoking, education, BMI, diabetes, occupational exposure to dust, gases or fumes	8,111	1.43	0.85-2.41
Laden, 2006	USA	PM2.5	Lung Cancer mortality	Age, sex, smoking, education, and BMI	8,096	1.27	0.96-1.69
EUROPEAN STUDIES							
Cohort of Oslo men							
Nafstad, 2003	Norway	NO(x) (per 10 μg/m3 - home address)	Lung Cancer incidence	Age, smoking habits, and length of education	16,209	1.08	1.02-1.15
		SO_2 (per 10 μg/m3)	Lung Cancer incidence	Age, smoking habits, and length of education		1.01	0.94-1.08
French PAARC Study							
Filleul, 2005	France	Total Suspended Particulate (exceedance frequency of 200 μg/m3)	Lung Cancer Mortality	Age, sex, BMI, smoking, occupational exposure, education	14,284	0.97	0.94-1.01
		Black Smoke (for 10 μg/m^3)	Lung Cancer Mortality	Age, sex, BMI, smoking, occupational exposure, education		0.97	0.93-1.01
		NO (for 10 μg/m^3)	Lung Cancer Mortality	Age, sex, BMI, smoking, occupational exposure, education		0.97	0.94-1.01
		NO_2 (for 10 μg/m^3)	Lung Cancer Mortality	Age, sex, BMI, smoking, occupational exposure, education		0.97	0.85-1.10
		SO_2 (for 10 μg/m^3)	Lung Cancer Mortality	Age, sex, BMI, smoking, occupational exposure, education		0.99	0.92-1.07
GENAIR Cohort Study							
Vineis, 2006	Ten European Countries	PM10 (10 microg/m3 increase)	Lung Cancer Incidence	Age, BMI, education, gender, smoking, alcohol use, intake of meat, intake of fruit and vegetables, time since recruitment,	197 cases	0.91	0.70-1.18

				country, occupational index and cotinine	556 controls		
		NO_2 (10 microg/m3 increase)	Lung Cancer Incidence	Age, BMI, education, gender, smoking, alcohol use, intake of meat, intake of fruit and vegetables, time since recruitment, country, occupational index and cotinine		1.14	0.78-1.67
		SO_2 (10 microg/m3 increase)	Lung Cancer Incidence	Age, BMI, education, gender, smoking, alcohol use, intake of meat, intake of fruit and vegetables, time since recruitment, country, occupational index and cotinine		1.08	0.89-1.30
		Proximity of residence to major road (exposed vs. nonexposed)	Lung Cancer Incidence	Age, BMI, education, gender, smoking, alcohol use, intake of meat, intake of fruit and vegetables, time since recruitment, country, occupational index and cotinine		1.31	0.82-2.09
Netherlands Cohort Study on Diet and Cancer							
Beelen, 2008	Netherlands	Black smoke concentration	Lung Cancer incidence	Age, sex, smoking status, area-level socioeconomic status	40,114	1.47	1.01-2.16
		Traffic intensity on nearest road	Lung Cancer incidence	Age, sex, smoking status, area-level socioeconomic status		1.11	0.88-1.41
		Living near a major road	Lung Cancer incidence	Age, sex, smoking status, area-level socioeconomic status		1.55	0.98-2.43
Brunekreef, 2009	Netherlands	Black smoke (per 10 μg/m3)	Lung Cancer Mortality	Age, sex, smoking status, area-level socioeconomic status	120,000	1.03	0.88-1.20
		Traffic intensity (increase of 10,000 motor vehicles/day)	Lung Cancer Mortality	Age, sex, smoking status, area-level socioeconomic status		1.07	0.96-1.19
		Black smoke (per 10 μg/m3)	Lung Cancer Incidence	Age, sex, smoking status, area-level socioeconomic status		1.47	1.01-2.16
Diet, Cancer and Health cohort study							
Raaschou-Nielsen, 2011	Denmark	**NO_x** at **residence** (per 100 μg/m3 increase)	Lung Cancer Incidence	Age, smoking, ETS, length of school attendance, fruit intake, and employment	52,970	1.09	0.79-1.51
		Traffic load at residence (per 10^4 vehicle km/day)	Lung Cancer Incidence	Age, smoking, ETS, length of school attendance, fruit intake, and employment	52,970	1.03	0.90-1.19
Three Prospective Cohorts							
Raaschou-Nielsen, 2010	Denmark	NOx[∫] (30-72 μg/m3 vs. <30 μg/m3)	Lung Cancer Incidence	Smoking (status, duration, and intensity), educational level, body mass index, and alcohol consumption.	679 cases 3481 controls	1.30	1.07-1.57
		NOx (>72 μg/m3 vs. <30 μg/m3)	Lung Cancer Incidence	Smoking (status, duration, and intensity), educational level, body mass index, and alcohol consumption.		1.45	1.12-1.88

OTHER STUDIES							
Pope, 1995	USA	Most vs. Least polluted: Sulphates	Lung Cancer mortality	Smoking	552,138	1.15	1.09-1.22
		Most vs. Least polluted: Fine particles	Lung Cancer mortality	Smoking		1.17	1.09-1.26
Yorifuji, 2010	Japan	NO_2 (10 microg/m3 increase)	Lung Cancer mortality - non smokers	Smoking	14,001	1.3	0.85-1.93
Katanoda, 2011	Japan	PM2.5 (10 microg/m3 increase)	Lung Cancer mortality	Sex, age, smoking status, pack-years, smoking status of family members living together, daily green and yellow vegetable consumption, daily fruit consumption, and use of indoor charcoal or briquette braziers for heating	63,520	1.24	1.12-1.37
		NO2 (10 microg/m3 increase)	Lung Cancer mortality	Sex, age, smoking status, pack-years, smoking status of family members living together, daily green and yellow vegetable consumption, daily fruit consumption, and use of indoor charcoal or briquette braziers for heating	63,520	1.26	1.07-1.48
		SO2 (10 microg/m3 increase)	Lung Cancer mortality	Sex, age, smoking status, pack-years, smoking status of family members living together, daily green and yellow vegetable consumption, daily fruit consumption, and use of indoor charcoal or briquette braziers for heating	63,520	1.17	1.10-1.26
Hales, 2011	New Zealand	PM10(1microg/m3 increase)	Lung Cancer mortality	Age, sex, ethnicity	1 050 222	1.015	0.004-1.026

Table 2 – Results on the association between air pollution and 1-OHP in the urine of exposed individuals: linear regression, logistic regression, and correlation analyses.

First author, Year	Area/ Country	Exposure	Controlled Confounders	Effect Measure≠	Sample Size (Total: 541)	Subject desription	P
Castaño-Vinyals, 2004	Review	B[a]P	Not applicable	r: 0.76	17	Pairs of data - log transformed means - from different studies	0.038
Hansen, 2004	Copenhagen, Denmark	B[a]P†		r: 0.83		personal sampling of B(a)P: mean values	0.04
		Environmental pollution	Job, gender, NAT2 phenotype, age, vehicle exhaust, cooked food mutagens, physical exercise	OR†: 1.51 (male) / 1.38 (female)	60 88	bus drivers mail carriers	0.08
Hansen, 2005	Denmark	Residence in urban vs. rural areas	Gender, time spent outside	OR: 1.29	102 100	children in Copenhagen children from rural residences	0.03
		One additional hour spent outside/day	Gender, residence	OR: 1.58	102 100	children in Copenhagen children from rural residences	<0.001
Freire, 2009	Granada, Spain	NO_2 (predicted)	Exposure to ETS† and cooking appliance	β: 0.401	93 81	children with predicted exposure to $NO_2 \geq 22.50$ $\mu g,m^{-3}$ / children with predicted exposure to $NO_2 < 22.50$ $\mu g,m^{-3}$	0.006
Hu, 2011	Taiwan	Residence near a coal fired power plant (PAH in air)	Age, gender, ETS, dietary exposure, and traffic	OR: 1.85 95%CI(1.43, 2.40)	146	Children in high exposure community 1 vs, Low exposure community 1	
				OR: 1.65 95%CI(1.30, 2.09)	88	Children in high exposure community 2 vs, Low exposure community 1	NA

≠ r = correlation coefficient; β = =linear regression coefficient (change in 1-OHP levels (7icromole/mol) for every unit change in exposure); OR = logistic regression odds ratio

† B[a]P Benzo [a] Pyrene; OR odds ratio; ETS environmental tobacco smoke.

Table 3 – Results on the association between air pollution and 1-OHP in the urine of exposed individuals: comparison of means analysis.

First author, Year	Area/ Country	Exposure	Controlled Confounders	Groups Sample Size (Total: 742)	Mean (micromol/mol) ± SD (unless otherwise stated)	P
Ruchirawa, 2002	Bangkok, Thailand	Environmental air pollution	Smoking	Traffic policemen 41 Office policemen 40	0.181±0.078 0.173±0.151	0.044
Hansen, 2004	Copenhagen, Denmark	Environmental pollution	Job, gender, NAT2 phenotype, age, vehicle exhaust, cooked food mutagens, physical exercise	Bus drivers – all 117samples Mail Carriers – all 93samples	0.19 (Range: 0.05-1.60) 0.11 (Range: 0.02-0.75)	<0.001
			Job, gender, NAT2 phenotype, age, vehicle exhaust, cooked food mutagens, physical exercise	Mail carriers Working outdoors 56samples Mail Carriers Working indoors 37samples	0.14 (Range: 0.02-0.75) 0.08 (Range: 0.02-0.57)	<0.001
Tuntawiroon, 2007	Bangkok and Chonburi, Thailand	PAH† from traffic related sources	Age and lifestyle (i.e. ETS†,diet, transportation, medication etc.)	Bangkok schoolchildren 115 Group matched provincial school children – Day 0 69	0.18±0.01 0.1±0.01	<0.0001
				Bangkok schoolchildren Day 1 115 Group matched provincial school children – Day 1 69	0.22±0.02 0.12±0.01	<0.0001
Freire, 2009	Granada, Spain	Residence in urban vs. rural areas	Exposure to ETS† and cooking appliance	4yr old children living in urban 118 4yr old children living in rural areas 56	0.060 ± 0.040 0.054 ± 0.055	0.20
Martinez-Salinas, 2010	Mexico	Traffic related air pollution	NA	Children in area with low vehicular traffic 39 Children in area with high vehicular traffic 17 Children in all communities of the study 258	0.8 ± 0.2 0.2 ± 0.2	<0.05 >0.05 *P-values compared to children from all communities
Hu, 2011	Taiwan	Residence near a coal fired power plant (PAH in air)	NA	High Exposure Community -1 146 High Exposure Community -2 88 Low Exposure Community -1 86 Low Exposure Community -2 49	0.186 ± 0.148 0.194 ± 0.143 0.113 ± 0.082 0.122 ±0.089	NA

† PAH polycyclic aromatic hydrocarbons; ETS environmental tobacco smoke.

Table 4 – Results on the association between air pollution and DNA adducts in exposed individuals; linear regression, logistic regression and correlation analyses

First author, Year	Area/ Country	Exposure	Controlled Confounders	Effect Measure≠	Sample Size (Total: 1787)	Subject desription	P
Binkova, 1995	Czech Republic	Outdoor air pollution – individual PAH†	Age, active and passive smoking, consumption of fried or smoked food, job category	r: 0.541	21	Non smoking women working outdoors up to 8 hours – gardeners or postal workers	0.016
Whyatt, 1998	Krakow, Poland	Ambient pollution at mother's place of residence	Smoking, dietary PAH, use of coal stoves, home or occupational exposures to PAH & other organics	β: 1.77	19	mothers not employed away from home	0.05
		Ambient pollution at place of residence	Smoking, dietary PAH, use of coal stoves, home or occupational exposures to PAH and other organics.	β: 1.73	23	newborns of mothers (high pollution / low pollution group)	0.03
Sørensen, 2003	Copenhagen	Personal PM2.5	Smoking, diet, season	ß=-0.0035	75	Students monitored 4 seasons of a year	0.31
Castaño-Vinyals, 2004	Review	B[a]P† (stationary meas.)	Not applicable	r: 0.6	12	pairs of data	0.038
Peluso, 2005	10 European countries	O_3† levels	Age, gender, educational level, country and batch	β: 0.066	564	EPIC cohort subjects	0.0095
Neri, 2006	Review	Environmental pollutants (including ETS† exposure)	Not applicable	Not applicable	178	Newborns – 17yr olds 2 studies in total – 2 with statistically significant results	Not applicable
Pavanello, 2006	North-East Italy	B[a]P indoor exposure	Smoking, diet, area of residence, traffic near house, outdoor exposure	β: 0.973	457	municipal workers (non smoking)	0.012
Palli, 2008	Florence City, Italy	PM10† (from high traffic stations)	Smoking	r: 0.562	16	traffic exposed workers	0.02
Peluso, 2008	Thailand	Industrial estate residence	Smoking habits, age, gender	OR†: 1.65	72 50	Industrial estate residents control district residents	<0.05
			Smoking habits, age, gender	OR: 1.44	64 72	PAH exposed workers industrial estate residents	<0.05
Pavanello, 2009	Poland	1-pyrenol	NA†	r: 0.67	92	coke oven workers and controls	<0.0001
Pedersen, 2009	Copenhagen, Denmark	Residential traffic density	ETS†, use of open fireplace, pre-pregnancy weight, folate levels, vitamin B12 levels, maternal education and season of delivery	β: 0.6 / 0.7	75 /69	Women /umbilical cords	<0.01
Garcia-Suastegui, 2011	Mexico City, Mexico	PM2.5	Various risk alleles	r: NR	92	Young adults living in Mexico City	0.013
		PM10	Various risk alleles	r: NR	92	Young adults living in Mexico City	0.035
Herbstman, 2012	USA	PAH exposure – measured in both air and urine	NA	r: NR	NR	152 participants – prenatal exposure, DNA adducts in cord blood	Not significant

≠ r = correlation coefficient; β =linear regression coefficient (change in DNA adduct levels (adducts/10^8 nucleotides) for every unit change in exposure); OR = logistic regression odds ratio
† PAH polycyclic aromatic hydrocarbons, PM10 particulate matter of diameter less than 10 microns; B[a]P Benzo [a] Pyrene; O_3 ozone; NA not available; ETS environmental tobacco smoke; OR odds ratio

Table 5 – Results on the association between air pollution and DNA adducts in exposed individuals; comparison of means analysis.

First author, Year	Area/ Country	Exposure	Controlled Confounders	Groups Sample Size (Total: 1044)	Mean adducts/ 10^8 nucleotides ± SD (unless otherwise stated)	P
Perera, 1991	Poland	Environmental air pollution	NA†	Residents in industrial area 20	30.4±13.5	
				Rural controls 21	11.01±22.6	<0.05
Hemminki, 1994	Stockholm, Sweeden	Traffic related air pollution	Age, smoking	Bus drivers – urban routes 26	0.9 ± 0.35	Non sig.
				Bus drivers – sub urban routes 23	1.4 ± 0.48	<0.001
				Taxi drivers – mixed routes 19	1.6 ± 0.91	<0.010
				Controls 22	1.0 ± 0.32	
Nielsen, 1996	Denmark	Environmental air pollution	Smoking, PAH† rich diet	Bus drivers in Central Copenhagen 49	Median: 1.214 Range: 0.142-22.24	
				Rural controls 60	Median: 0.074 Range: 0.003-8.876	0.001
Nielsen, 1996 (2)	Denmark and Greece	Environmental air pollution	Smoking, sex	Students in urban universities 74	Median: 0.205	
				Students in agricultural colleges 29	Median: 0.152	0.02
Yang 1996	Milan, Italy	Traffic related air pollution	Sex, age, smoking habits	News stand workers at high traffic areas 31	2.2 ± 1.0	
				News stand workers at low traffic areas 22	2.2 ± 1.2	0.27
Topinka, 1997	Teplice & Prachatice, N&S Bohemia	Residence in Industrial area	NA†	Placenta samples- industrial polluted area (winter): GSTM− genotype 15	1.49 ± 0.70	
				Placenta samples –agricultural area (winter): GSTM− genotype 17	0.96 ± 0.55	0.027
Merlo, 1997	Genova, Italy	Ambient PAH concentrations	NA†	Traffic police workers 94	1.48 ± 1.35	
				Urban residents 52	1.01 ± 0.63	0.007
Ruchirawa, 2002	Bangkok, Thailand	Environmental air pollution	Smoking, sex	Traffic Policemen 41	1.6±0.9	
				Office duty policemen 40	1.2±1.0	0.03
Marczynski, 2005	Germany	PAH in air (ambient and personal monitoring)	NA†	Samples from 16 workers(increased PAH exposure)	Range: 0.5 – 1.19Range: <0.5 –	
				Samples from 16 workers¥ (reduced PAH exposure)	0.09	<0.0001
Topinka, 2007	Prague, Czech Republic	c-PAH† (personal exposure)	Smoking, ocuupational duration	109 policemen – January (highest exposure)	2.08±1.60	
				109 policemen – March	1.66±0.65	<0.0001
Tuntawiroon, 2007	Bangkok and Chonburi, Thailand	c-PAH and B[a]P†	Age and lifestyle (i.e. ETS†, transportation, medication, diet etc.)	Bangkok schoolchildren 115	0.45±0.03	
				Provincial school children (group matching) 69	0.09±0.00	<0.0001
Fanou, 2011	Cotonou, Benin	Environmental air pollution	NA†	Taxi-motorbike drivers 13	24.6±6.4	<0.001
				Intermediate exposure suburban group 20	2.1±0.6	
		Environmental air pollution	NA†	Street food vendors 16	34.7±9.8	<0.001
				Intermediate exposure suburban group 20	2.1±0.6	
		Environmental air pollution	NA†	Gasoline salesmen 20	37.2±8.1	<0.001
				Intermediate exposure suburban group 20	2.1±0.6	
		Environmental air pollution	NA†	Street side residents 11	23.78±6.9	<0.001
				Intermediate exposure suburban group 20	2.1±0.6	

† N/A not applicable; NA not available; PAH polycyclic aromatic hydrocarbons; c-PAH carcinogenic polycyclic aromatic hydrocarbons; B[a]P benzo [a] pyrene; ETS environmental tobacco smoke
¥ The sample sizes reported in the summary tables refer to subjects with measurments available both before and after change in work conditions

Table 6 - Results on the association between air pollution and oxidatively damaged nucleobases/deoxynucleosides in urine or mononuclear blood cells; comparison of means analysis

First author, Year	Area, country	Exposure definition/source Referents' definition	Biomarker	Groups Sample size (Total: 2827)	Level (Mean ± SD, unless otherwise stated)	Controlled confounders
Suzuki 1995	Japan	Sampling before and after a stay in a street	8-oxoGua in urine (HPLC-ECD)	3	After:9.9±2.5 Before: 4.22±2.0 (pooled data from several timepoints 0-24 after exp.)	Cross-over study
Calderon-Garciduenas 1999	Mexico	Children in urban and low-polluted area	8-oxodG in nasal epithelial cells (immunohistochemistry)	Exposed: 86 Controls: 12	602 ± 195* 210 ±122	NA†
Autrup 1999; Loft 1999	Copenhagen, Denmark	Bus drivers in the city center and rural/suburban controls	8-oxodG in urine (HPLC-ECD)	Exposed: 29 Controls:20	1.74 ± 4,69 1.54 ± 4.29	Age, BMI†, metabolic and DNA repair phenotype
Staessen 2001	Belgium	Adolescents from industrial and rural areas	8-oxodG in urine (HPLC-ECD)	Peer: 100 Wilrijk: 42 Hoboken: 58	0.44 (0.40-0.48) 0.57 (0.49-0.66)* 0.49 (0.42-0.56) Geometric mean and 95% CI	Sex, smoking
Chuang 2003	Taiwan	Taxi-drivers and controls	8-oxodG in urine (ELISA)†	Exposed: 95 Controls: 75	0.33± 0.20* 0.20 ± 0.14	Age, education, exercise
Lai 2005	Taipei city, Taiwan	Highway toll station workers and controls	8-oxodG in urine (ELISA)	Exposed: 47 Controls: 24	13.3±7.1* 8.4±6.2	Age, smoking
Harri 2005	Finland	Garage/waste workers and controls	8-oxodG in urine and MNBC (HPLC-ECD)	**Urine:** Exposed: 29 Controls: 36 **MNBC:** Exposed: 19 Controls: 18	Winter: 1.52 ± 0.44 1.56 ± 0.61 Summer: 1.61±0.33 1.43±0.4 4.84± 0.17 4.11 ±0.16	Age, smoking, BMI
Vinzents 2005	Copenhagen, Denmark	Sampling after cycling in traffic-intense streets or laboratory	FPG sites in MNBC	15	Traffic: 0.08 (0-0.04)* Lab: 0.02 (0-0.04)	Cross-over study
Avogbe 2005	Rep. of Benin	Subjects from urban and rural areas	FPG sites in MNBC	Taximoto: 24 Roadside: 37 Suburban: 42 Rural: 27	1620 ± 310* 1250 ± 198* 1110 ± 188* 650 ± 160	Metabolic genes
Fanou 2006	Rep. of Benin	Taxi-moto drivers and controls	8-oxodG in MNBC (HPLC-ECD)	Exposed: 35 Controls: 6	2.05±1.25* 1.11±0.82	NA†
Cavallo 2006	Italy	Airport personnel and controls	FPG sites in MNBC	Exposed: 41 Controls: 31	55.86 ± 12.85* 43.01 ± 7.97	Age, smoking, dietary habits
Bräuner 2007	Copenhagen, Denmark	Sampling before and after controlled exposure to street PM	FPG sites in MNBC	29	Air: 0.53 (0.37-0.65)* FA†:0.38 (0.31-0.53) Median and quartiles	Age, sex, smoking, CVD†, BMI
Singh 2007	Prague (Czech Rep.) Kosice (Slovakia) Sofia (Bulgaria)	City policemen, bus drivers and controls	8-oxodG (LC-MS/MS) M_1dG (immunoslot blot) In MNBC	Exposed: 98 Controls: 105 Exposed: 198 Controls: 156	33.0±30.1 29.2±21.2 58.3±37.5 49.2±30.3	Smoking, demographic variables, diet
Novotna 2007	Prague, Czech Rep.	Policemen and controls sampled in different seasons	ENDOIII/FPG sites in MNBC	Exposed: 54 Controls: 11	Jan: 2.91± 1.84* Sep: 2.12 ± 1.62 Jan:1.36± 1.53 Sep: 1.22 ± 0.96	Metabolic and DNA repair genotypes
Rossner, Jr. 2007,	Prague, Czech Rep.	Bus drivers and controls sampled in	8-oxodG in urine	Exposed: 50	7.59 ± 2.25*	Medical history, lifestyle

2008		there different seasons	(ELISA)		6.73 ± 2.48* 5.67 ± 2.50*	
				Controls: 50	6.29 ± 2.59 5.51 ± 2.36 3.82 ± 1.73	
Buthbumrung 2008	Thailand	Schoolchildren in Bangkok and rural controls	8-oxodG in leukocytes and urine (HPLC-ECD)	Exposed: 40 Controls: 32 Exposed 43 Controls: 32	0.25 ± 0.13 0.08 ± 0.34 2.16 ± 1.84 1.32 ±1.24	Metabolic genes
Danielsen 2008	Sweden	Sampling before and after controlled exposure to wood smoke	8-oxodG 8-oxoGua in urine: HPLC-GC/MS FPG sites in MNBC	13	16.4% (95% CI: -6.9,45.5) 79.3% (95% CI -12.9,269) -15% (95% CI:-31.1,4.9)	Cross-over study
Palli 2009	Florence, Italy	Metropolitan area	FPG sites in MNBC	Exposed 44 Controls: 27	5.0 ± 3.06 4.11 ± 3.96	Sex, smoking, season
Svecova 2009	Teplice and Prachatice (Czech Rep.)	Children	8-oxodG in urine (ELISA)	Teplice: 495 Prachatice:399	14.6 (3.1-326.5) 15.2 (3.0-180.8)	Ethinicity, mothers smoking, education, sex, age, atopic diseases
Bagryantseva 2010	Praque, Czech Rep.	Bus drivers, garage men and office workers	8-oxodG in urine (ELISA)	Bus drivers: 50 Garage men: 20 Controls: 50	5.67 ± 2.5* 6.54 ± 6.9* 3.82 ± 1.73	Age, vitamins, plasma lipids, metabolic and DNA repair genes
			EndoIII/Fpg sites in lymphocytes	Bus drivers: 50 Garage men: 20 Controls: 50	2.35 ± 2.17 2.56 ± 2.52 2.55 ±2.86	
Han 2010	Taiwan	Bus drivers and office workers	8-oxodG in urine (ELISA)	Exposed: 120 Controls: 58	9.5 ± 5.7* 7.3 ± 5.4	Age, BMI, smoking. Alcohol, areca chewing, tea, coffee energy drink, exercise
Fan 2011	GuangZhou City, China	Children	8-oxodG in urine (ELISA)	Exposed: 39 Controls: 35	20.87 ± 14.42 16.78 ± 13.30	Age, sex, height, weight, passive smoking, diet, transportation tool and time taken to/from school
Rossner, Jr, 2011	Praque and Ostrava (Czech Rep.)	Policemen and office workers	8-oxodG in urine (ELISA)	Ostrava: 75 Praque: 65	4.28 ± 2.27 4.84 ± 1.61	Age, passive smoking, cotinine, plasma lipids, vitamins, DNA repair gens

† BMI body mass index; NA not available; CVD cardiovascular disease; ELISA enzyme-linked immunosorbent assay**;** FA filtered air

Table 6a. Confounding in studies of DNA adducts

Adjustment	Number of studies	References
Several relevant confounders including smoking but not diet	7	Hemminki 1994, Nielsen 1996, Peluso 2005, Peluso 2008, Ruchirawa 2002, Topinka 2007, Yang 1996,
Several relevant confounders including smoking including diet	7	Binkova 1995, Nielsen 1996 (2), Pavanello 2006, Pedersen 2009, Sorensen 2003, Tuntawiroon 2007, Whyatt 1998,
Smoking	1	Palli 2008
Various Risk Alleles	1	Garcia-Suastegui 2011
Confounding not relevant	1	Marczynski 2005
No information about confounding factors	6	Ayi Fanou 2011, Herbstman 2012, Merlo 1997, Pavanello 2009, Perera 1991, Topinka 1997

Table 7 - Results on the association between air pollution and oxidatively damaged nucleobases/deoxynucleosides in urine or mononuclear blood cells; linear regression and correlation analysis

First author, year	Area, country	Exposure definition/source	Biomarkers and methods	Sample size (Total: 1642)	Effect Measure≠	Controlled confounders
Lagorio 1994	Rome Italy	Filling station attendants	8-oxodG in urine (HPLC-ECD)	65	r = 0.34* (benzene)	Age, length of employment, smoking, exposure to X-ray
Sørensen 2003a	Copenhagen, Denmark	Students living in the metropolitan area	8-oxodG (HPLC-ECD) in urine and MNBC FPG/EndoIII sites in MNBC	50	β = 0.010* (8-oxodG, lymphocytes) β = -0.007 (8-oxodG, urine) β = 0.0025 (EndoIII) β = 0.014 (FPG)	Season, sex, outdoor temperature
Sørensen 2003b	Copenhagen, Denmark	Healthy subjects living in the metropolitan area	FPG/EndoIII sites in MNBC 8-oxodG (HPLC-ECD) in urine and MNBC	40	r_s = 0.39* Non-significant	Smoking, type of work, sex, genotype (metabolism)
Vinzents 2005	Copenhagen, Denmark	Sampling after cycling in traffic-intense streets or laboratory	FPG sites in MNBC	15	β=$1.5x10^{-3}$ per ultrafine particle time weighted exposure unit	Cross-over study
Bräuner 2007	Copenhagen, Denmark	Sampling before and after controlled exposure to street PM	FPG sites in MNBC	29	NC_{12}†: β = -0.033 NC_{23}: β =0.066* NC_{57}: β=0.040*	Age, sex, smoking, CVD†, BMI† included in model
Chuang 2007	Taipei, Taiwan	College students living in the metropolitan area	8-oxodG in plasma (ELISA)	76	PM10: -9.2%, (95% CI: -21.5;3.2) PM2.5: -5.0% (95% CI: -14.3-4.4) O3: 2.2% (95% CI: 0.9;3.5)	Sex, age, BMI, weekday, temperature, relative humidity
De Coster 2008	Flanders, Belgium	Industrial and urban areas	8-oxodG in urine (ELISA)	399	β = 0.179 (95% CI: 0.077-0.282) with 1-OHP as biomarker of internal exposure	Age, Sex, recent smoking
Svecova 2009	Teplice&Prachatice (Czech Rep.)	Children living in the two areas	8-oxodG in urine (ELISA)	Teplice: 495 Prachatice:399	β=0.16* (air pollutants)	Ethinicity, mothers smoking, education, sex, age, atopic diseases
Allen 2009	Washington, USA	Subjects with MetS with controlled exposure to diesel exhaust	8-oxodG in urine (ELISA) †	10	β = 0.087 (95% CI: -0.13; 0.31)	Cross-over study
Kim 2009	Boston, USA	Subjects with hypertension and controls (panel study)	8-oxodG in urine (ELISA)	21	β=-0.60 (hypertensive) β=1.1 (controls)	Age, sex, smoking, time of the day
Bagryantseva 2010	Praque, Czech Rep.	Bus drivers, garage men and office workers	8-oxodG in urine (ELISA)	120	β= 0.105 /BaP β= 0.026 (PAH)	Age, vitamins, plasma lipids, metabolic and DNA repair genes
			EndoIII/FPG sites in lymphocytes	120	β=-0.62 (BaP) β=-0-056 (PAH)	
Lee 2010	Taiwan	Inspection station workers and controls	8-oxodG in urine (ELISA)	Exposed:11 Controls: 32	β=7.47 (SE = 3.3)*	Smoking, cooking at home
Fan 2011	GuangZhou City, China	Children in a kindergarten	8-oxodG in urine (ELISA)	74	r=0.055 (OH-PAH)	Age, sex, height, weight, passive smoking, diet, transportation to/from kindergarten
Mori 2011	Tokyo	Children in a kindergarten	8-oxodG in urine (ELISA)	76	β=0.216 (Ln(1-OHP))	Age, sex, Mn, As, vitamin A, vitamin C, cotinine
Ren 2011	Boston, USA	Eldery subjects	8-oxodG in urine (ELISA)	320	PM2.5: 30.8% (95% CI: 9.3-52.2)	Age, BMI, smoking, vitamins
Rossner, Jr 2011	Praque, Czech Rep.	Policemen	8-oxodG in urine (ELISA)	59	β= 0.04* (PM2.5 stationary monitoring station) β=0.16 (BaP) β=-0.02 (PAH)	Age, cotinine, cholesterol, triglycerides

≠ r = correlation coefficient; β = linear regression coefficient (change in levels of oxidatively damaged nucleobases for every unit change in exposure); % per cent difference
† MetS metabolic syndrome; ELISA enzyme-linked immunosorbent assay; BMI body mass index; CVD cardiovascular disease, $NC_{\text{size cut off}}$ Number concentration.

Table 7a. Confounding in studies of oxidative damaged to nucleobases in blood or urine

Adjustment	Number of studies	References
Several relevant confounders including smoking	23	Autrup 1999, Brauner 2007, Cavallo 2006, Chuang 2003, Chuang 2007, De Coster 2008, Fan 2011, Han 2011, Harri 2005, Kim 2009, Lagorio 1994, Lai 2005, Lee 2010, Loft 1999, Palli 2009, Ren 2011, Rossner 2007, Singh 2007, Sorensen 2003a, Sorensen 2003b, Staessen 2001, Svecova 2008, Svecova 2009
Metabolic and/or DNA repair gene polymorphisms	5	Avogbe 2005, Bagryantseva2010, Buthbumrung 2008, Novotna 2007, Rossner 2011
Confounding not relevant	4	Allen 2009, Danielsen 2008, Suzuki 1995, Vinzents 2005,
No information about confounding factors	2	Ayi Fanou 2006, Calderón-Garcidueñas 1999,

Table 8 – Results on the association between air pollution and CAs in the cells of exposed individuals; logistic regression and comparison of means analyses.

First author, Year	Area/ Country	Exposure	Controlled Confounders	Groups Sample Size (Total: 1265)	Mean (% frequencies∆) ± SD	P
Knudsen, 1999	Copenhagen, Denmark	Air pollution (urban)	Metabolic genotypes, DNA repair, age, sex	office workers 41	2.46 ± 1.98	
				postal workers 60	2.12 ± 1.38	Not significant
				Bus drivers – high exposure 55	2.84 ± 1.87	
				Bus drivers – low + medium exposure 45	2.24 ± 1.57	Not significant
Sram 1999	Czech Republic	Urban air pollution	Maternal height and pre-pregnancy weight, parity, marital status, education and maternal smoking, season and the year of the study	Pregnant Mothers: Industrial + residential heating (Teplice) 131	1.54 ± NA†	
				Pregnant Mothers: Residents in agricultural districts (Prachatice) 48	1.04 ± NA†	<0.05
Kyrtopoulos, 2001	Athens and Halkida, Greece	Air pollution (in city of studying)	Smoking	Students in Athens (higher PAH† exposure & lower PM2.5† exposure) 222	0.88±0.97	
				Students in Halkida (lower PAH exposure & higher PM2.5 exposure) 149	1.06±1.12	Not significant
Burgaz, 2002	Ankara, Turkey	Air pollution (traffic related)	Age, sex, smoking habits	Traffic policemen 18	1.29±0.30	
				Control group 5	0.26±0.14	<0.05
				Taxi drivers 29	1.82±0.34	
				Control group 5	0.26±0.14	<0.01
Sram, 2007	Prague, Czech Republic	c-PAHs† on respirable air particles (<2.5 m)	Smoking, medical histories	Sampling in January: higher PM† and PAH exposures 61	0.27±0.18	
				Sampling in March: lower PM and PAH exposures 61	0.16±0.17	<0.001
Zidzik, 2007	Kosice (Slovakia), Prague(Cz.Republic) & Sofia (Bulgaria)	cPAH	Sex	Exposed policemen in Kosice 51	2.6±2.64	
				Controls in Kosice 55	2.14± 1.61	Not significant
				Exposed policemen in Prague 52	2.33±1.53	
				Controls in Prague 50	1.94±1.28	Not significant
				Exposed policemen in Sofia 50	3.04±1.64	
				Controls in Sofia 45	1.79±0.77	<0.05
				Exposed bus drivers in Sofia 50	3.6±1.63	
				Controls in Sofia 45	1.79±0.77	<0.05
Balachandar, 2008	Tamilnadu, India	ETS†	Age	Group I : <6hrs exposure/day and <30yrs old		
				Passive smokers 18	5.00 ± 1.68,	
				Controls 18	1.16 ± 0.92,	Significant
				Group II : >6hrs exposure/day and >30yrs old		
				Passive smokers 25	9.04 ± 3.73	
				Controls 25	2.76 ± 2.12.	Significant
Rossnerova, 2011	Prague and Ceske Budejovice, Czech Republic	Air pollution (urban vs. rural)	Sex	Mothers in Prague (urban) 86	0.80 ± 0.27	<0.001
				Mothers in Ceske Budejovice (rural) 92	0.61 ± 0.21	
					Linear Regression Coefficient (95% CI)	
Garcia-Suastegui, 2011	Mexico City, Mexico	Air pollution – PM10	Unadjusted	91 individuals sampled during dry season	NA	0.669
		Air pollution – PM2.5				0.399
		Air pollution – PM10	Unadjusted	80 individuals sampled during rainy season	NA	0.709
		Air pollution – PM2.5				0.843
					Logistic regression OR∞ (95% CI)	
Rossner, 2011	Prague and Ostrawa, Czech Republic	Air pollution at residence	Age, benzene exposure, cotinine plasma levels, total, HDL, and LDL cholesterol levels, triglycerides, Vitamins a, C and E in plasma and various gene expressions	Subjects in Prague (less polluted) 64		
				Subjects in Ostrawa (more polluted) 75	0.18 (0.05-0.67)∞	0.010

† NA not available; PAH polycyclic aromatic hydrocarbons; PM2.5 particulate matter with dimater less than 2.5 microns; N/A not applicable; c-PAH carcinogenic polycyclic aromatic hydrocarbons; ETS environmental tobacco smoke.

Δ Percentage of cells with chromosomal aberrations

∞ Odds ratio of having chromosomal aberrations above median, for subjects in Prague compared to subjects in Ostrawa

Table 9 – Results on the association between air pollution and MN in peripheral blood cells of exposed individuals: linear regression analyses

First Author, Year	Area/ Country	Exposure	Controlled Confounders	Effect Measure≠	Sample Size (Total: 1478)	Subject desription	p
Neri, 2006	Review	Environmental Pollutants	Not applicable		1071	Children: 1-16 yrs old 4 studies in total – 4 with statistically significant results	
Ishikawa, 2006	Shenyang city, China	Air pollution (ambient)	Smoking habits, sex, age, metabolic enzyme and DNA repair gene polymorphisms		66	Female industrial	
				β: 1.57	63	Female rural residents	<0.05
Pedersen, 2009	Copenhagen, Denmark	Residential traffic density (validated by indoor levels of nitrogen dioxide and PAH)	ETS exposure, use of open fireplace, prepregnancy weight, folate levels, vitamin B12 levels, maternal education and season of delivery	β: -0.1	75	Women	
				β: 0.4	69	Umbilical cords	0.02
				Mean (% frequencies) ± SD			
Merlo, 1997	Genova, Italy	Ambient PAH concentrations	Sex	3.73 ± 1.6	82	Traffic police workers	
				4.03 ± 1.61	52	Urban residents	0.38
Rossnerova, 2011	Prague and Ceske Budejovice, Czech Republic	Air pollution (urban vs. rural)	Sex	8.35 ± 3.06	86	Mothers in Prague (urban)	
				6.47 ± 2.35	92	Mothers in Ceske Budejovice (rural)	<0.001

≠ β = linear regression coefficient (change in micronuclei frequencies (frequency per 1000 cells) per unit change in exposure)
† PBLs peripheral blood lymphocytes; N/A not applicable; PM10 particulate matter with dimater less than 10 microns; polycyclic aromatic hydrocarbons.

Table 10 - Results on the association between air pollution and methylation changes in the cells of exposed individuals.

First author, Year	Area/ Country	Exposure	Outcome	Controlled Confounders	Effect Measure≠	CI†	Sample Size (Total: 1499)	Subject desription	P
Baccarelli, 2007	Boston, USA	Ambient Black Carbon (hourly concentrations measured at a monitoring site approximately 1 km from the site of examination (7 day mean))	LINE-1 methylation	Multiple clinical and environmental covariates	r: -0.11	(-0.18) (-0.04)	718	subjects from the Normative Aging Study	0.002
		Ambient Black Carbon (hourly concentrations measured at a monitoring site approximately 1 km from the site of examination (7 day mean))	Alu methylation	Multiple clinical and environmental covariates					Not significant
Baccarelli, 2009	Boston, USA	PM2.5† concentrations (7day mean)	LINE-1 methylation	Age, BMI, cigarette smoking, pack-years, statin use, fasting blood glucose, diabetes mellitus, percent lymphocytes, and neutrophils in differential blood count, day of the week, season, and outdoor temperature	r: -0.13	(-0.19) (-0.06)	718	subjects from the Normative Aging Study	<0.001
		PM2.5 concentrations (7day mean)	Alu methylation	Age, BMI, cigarette smoking, pack-years, statin use, fasting blood glucose, diabetes mellitus, percent lymphocytes, and neutrophils in differential blood count, day of the week, season, and outdoor temperature	r: -0.01	(-0.07) (0.05)			0.71
Tarantini, 2009	Brescia, Northern Italy	PM10 (first day of the week and after 3 days of work)	LINE-1 methylation	Unadjusted	0.02%	SE: 0.11	63	workers	0.89
		PM10 (first day of the week and after 3 days of work)	Alu methylation	Unadjusted	0%	SE: 0.08			0.99
		PM10 (first day of the week and after 3 days of work)	iNOS promoter methylation	Unadjusted	-0.61%	SE: 0.26			0.02
		PM10 (average level of individual exposure)	LINE-1 methylation	Age, BMI, smoking, number of cigarettes/day	β: -0.34	SE: 0.09			0.04
		PM10 (average level of individual exposure)	Alu methylation	Age, BMI, smoking, number of cigarettes/day	β: -0.19	SE: 0.17			0.04
		PM10 (average level of individual exposure)	iNOS promoter methylation	Age, BMI, smoking, number of cigarettes/day	β: -0.55	SE: 0.58			0.34
Madrigano, 2011	New York, USA	PM2.5 (IQR increase over a 90 day period)	LINE1	Season, time, smoking, BMI, alcohol intake, medication, batch, % WBC type	0.03%	(-0.12) (0.18)	706	subjects from the Normative Aging Study	Not Significant
			Alu		0.03%	(-0.07) (0.13)			Not Significant
		Black Carbon (IQR increase over a 90 day period)	LINE1	Season, time, smoking, BMI, alcohol intake, medication, batch, % WBC type	-0.21%	(-0.50) (0.09)			Not Significant
			Alu		-0.31%	(-0.12) (-0.50)			P<0.05
		SO_4 (IQR increase over a 90 day period)	LINE1	Season, time, smoking, BMI, alcohol intake, medication, batch, % WBC type	-0.27%	(-0.02) (-0.52)			P<0.05
			Alu		-0.03%	(-0.20) (0.13)			Not Significant
Herbstman, 2012	New York, USA	PAH exposure – prenatal	Global Methylation	Ethnicity	β: -0.11	(-0.21) (0.00)	164	cord blood samples	0.05

≠ r = correlation coefficient; β = linear regression coefficient (change in DNA methylation levels (**%5mC)** per unit change in exposure); % per cent difference
† CI confidence interval; LINE-1long interspersed nuclear element-1; PM10 particulate matter with diameter of less than 10 microns; tHcy total homocysteine; BMI body mass index; PM2.5 particulate matter with diameter of less than 2.5 microns; PAH polycyclic aromatic hydrocarbons.

Figure 1 - Flow Chart of Literature Review

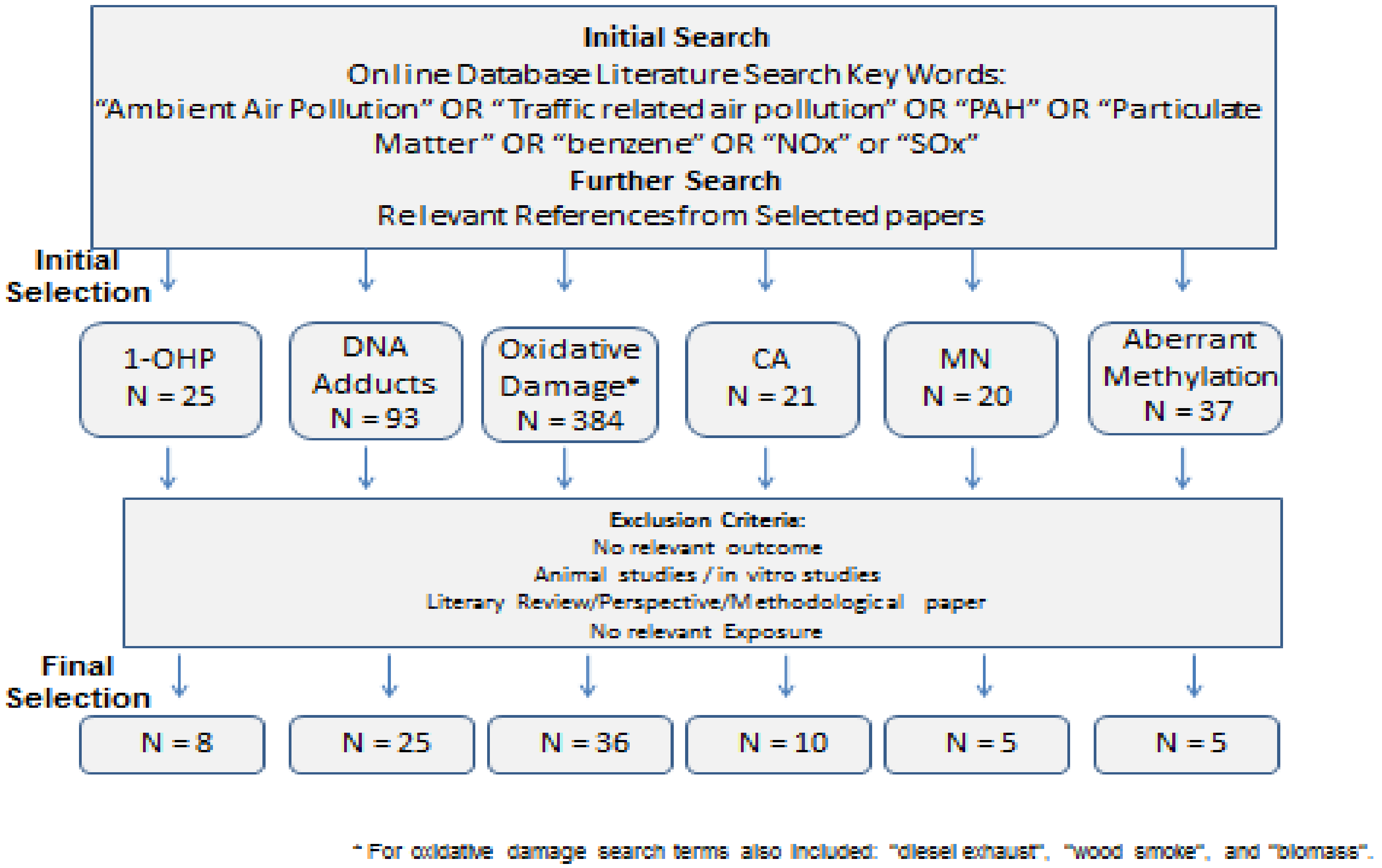
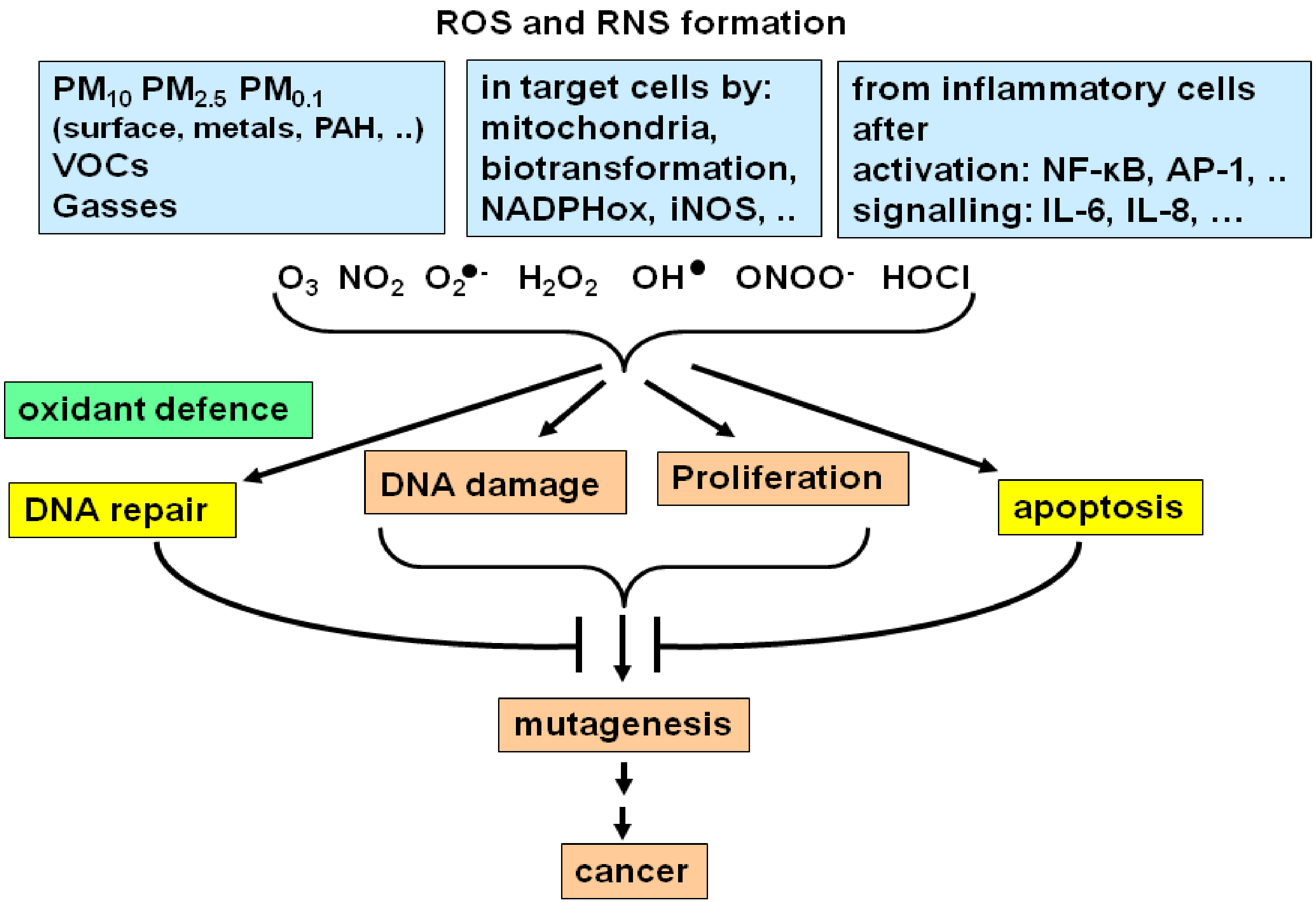
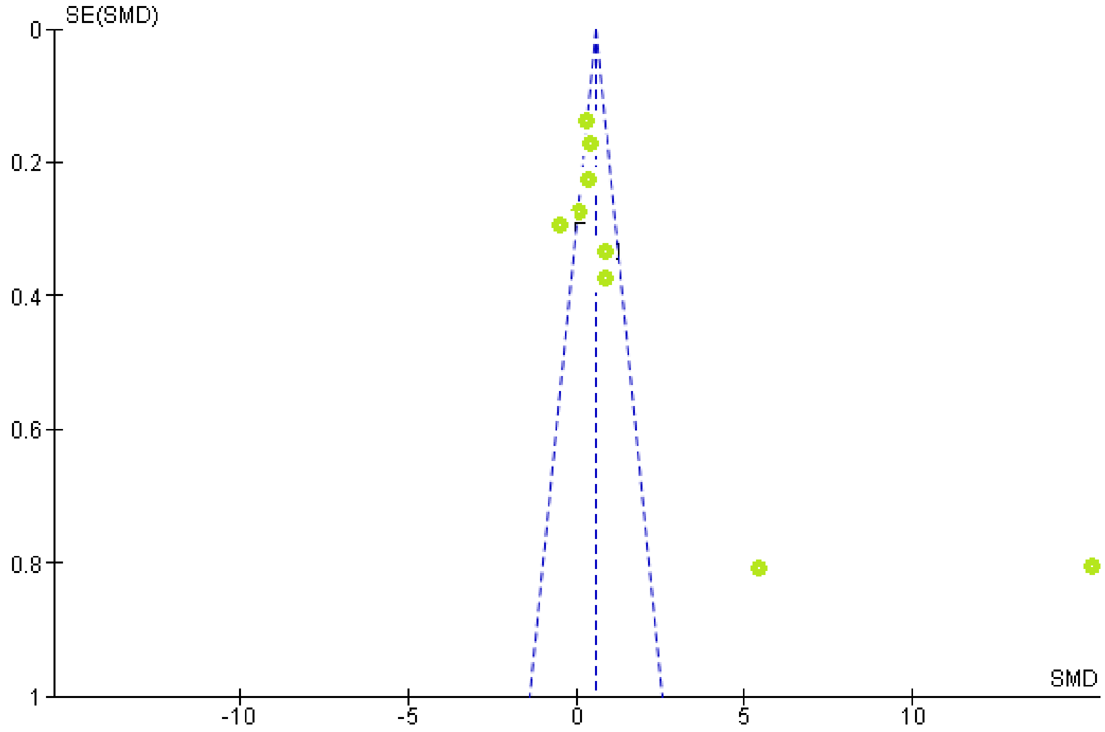


Figure 2 – Putative Mechanisms of cancer through oxidative damage from air pollution



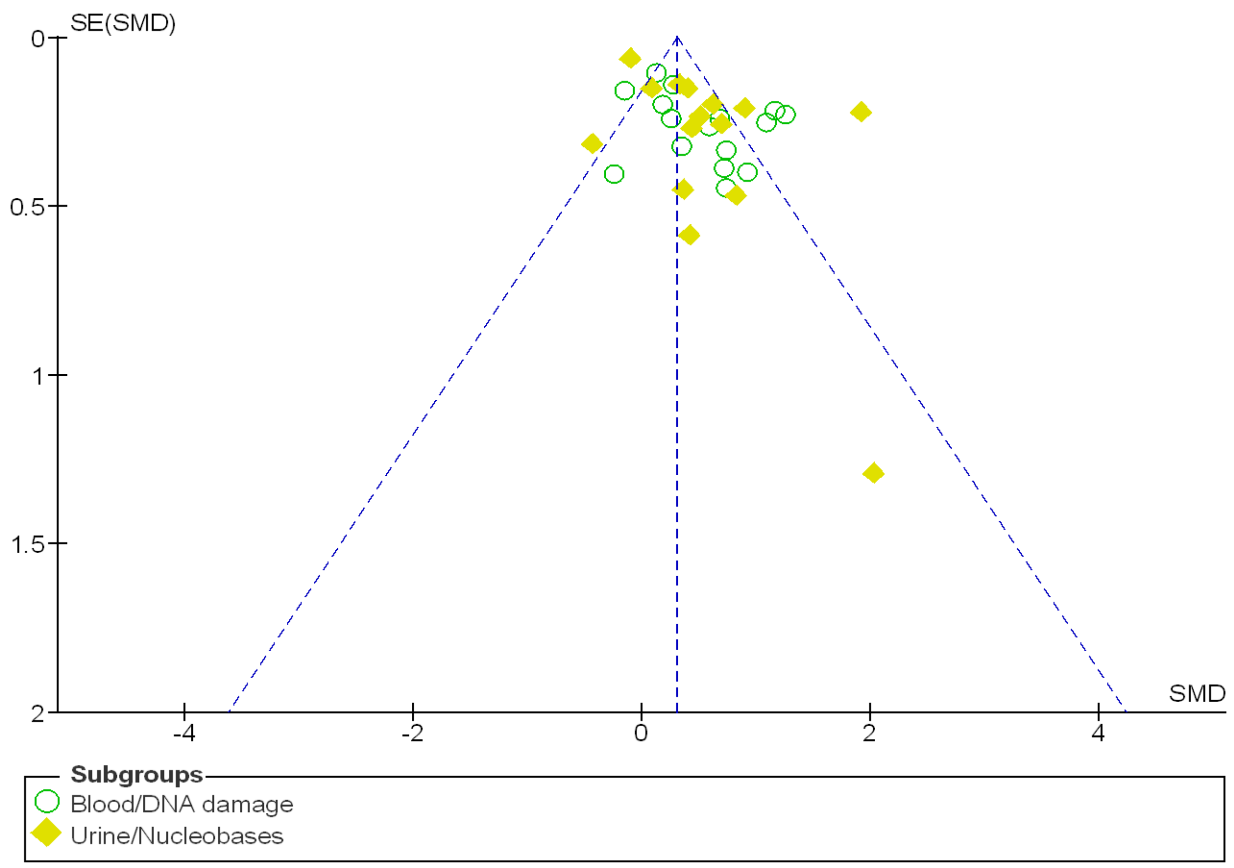
Adapted from: Risom, L, P. Møller, and S. Loft (2005) Oxidative stress-induced DNA damage by air pollution, Mutat. Res. 592:119-137

Figure 3 - Funnel plot of the standard error of the standardized mean difference (SMD) vs the SMD of studies on DNA adducts (in a fixed effects model to get the pseudo CI lines).



NOTE: Three studies not reporting means and standard deviations were excluded (Nielsen 1996a, Nielsen 1996b, Marczynski 2005).

Figure 4 - Funnel plot of the standard error of the standardized mean difference (SMD) vs the SMD of all the studies on oxidative DNA damage shown in Table 5-Supplemental Material (in a fixed effects model to get the pseudo CI lines).



In the papers without report of SD this was estimated from the data as explained in the review and meta-analysis paper of Møller and Loft P 2010 (70).

Supplemental Material References

- Abbey DE NN. Long- term inhalable particles and other air pollutants related to mortality in nonsmokers. *Am J Resp Crit Care Med* 1999;:373–82.
- Allen J, Trenga CA, Peretz A, *et al.* Effect of diesel exhaust inhalation on antioxidant and oxidative stress responses in adults with metabolic syndrome. *Inhal Toxicol* 2009;**21**:1061–7.
- Autrup H, Daneshvar B, Dragsted LO, *et al.* Biomarkers for exposure to ambient air pollution-comparison of carcinogen-DNA adduct levels with other exposure markers and markers for oxidative stress. *Environ Health Perspect* 1999;**107**:233–8.
- Avogbe PH, Ayi-Fanou L, Autrup H, *et al.* Ultrafine particulate matter and high-level benzene urban air pollution in relation to oxidative DNA damage. *Carcinogenesis* 2005;**26**:613–20.
- Ayi-Fanou L, Avogbe PH, Fayomi B, *et al.* DNA-adducts in subjects exposed to urban air pollution by benzene and polycyclic aromatic hydrocarbons (PAHs) in Cotonou, Benin. *Environ Toxicol* 2011;**26**:93–102.
- Baccarelli A, Wright RO, Bollati V, *et al.* Rapid DNA Methylation Changes after Exposure to Traffic Particles. *AmJRespirCritCare Med* 2009;**179**:572–8.
- Baccarelli A, Zanobetti A, Martinelli I, *et al.* Air pollution, smoking, and plasma homocysteine. *EnvironHealth Perspect* 2007;**115**:176–81.
- Bagryantseva Y, Novotna B, Rossner P Jr, *et al.* Oxidative damage to biological macromolecules in Prague bus drivers and garagemen: impact of air pollution and genetic polymorphisms. *Toxicol Lett* 2010;**199**:60–8.
- Balachandar V, Kumar BL, Suresh K, *et al.* Evaluation of chromosome aberrations in subjects exposed to environmental tobacco smoke in Tamilnadu, India. *BullEnvironContamToxicol* 2008;**81**:270–6.
- Beelen R, Hoek G, van den Brandt PA, *et al.* Long-term exposure to traffic-related air pollution and lung cancer risk. *Epidemiology* 2008;**19**:702–10.
- Beeson WL, Abbey DE, Knutsen SF. Long-term concentrations of ambient air pollutants and incident lung cancer in California adults: results from the AHSMOG study.Adventist Health Study on Smog. *EnvironHealth Perspect* 1998;**106**:813–22.
- Binkova B, Lewtas J, Miskova I, *et al.* DNA adducts and personal air monitoring of carcinogenic polycyclic aromatic hydrocarbons in an environmentally exposed population. *Carcinogenesis* 1995;**16**:1037–46.
- Bräuner EV, Forchhammer L, Møller P, *et al.* Exposure to ultrafine particles from ambient air and oxidative stress-induced DNA damage. *Environ Health Perspect* 2007;**115**:1177–82.
- Brunekreef B, Beelen R, Hoek G, *et al.* Effects of long-term exposure to traffic-related air pollution on respiratory and cardiovascular mortality in the Netherlands: the NLCS-AIR study. *ResRepHealth EffInst* 2009;**(139)**:5–71; discussion 73–89.
- Buell P, Dunn JE, Breslow L. Cancer of the lung and Los-Angeles-type air pollution. Prospective study. *Cancer* 1967;**20**:2139–47.
- Burgaz S, Cakmak Demircigil G, Karahalil B, *et al.* Chromosomal damage in peripheral blood lymphocytes of traffic policemen and taxi drivers exposed to urban air pollution. *Chemosphere* 2002;**47**:57–64.
- Buthbumrung N, Mahidol C, Navasumrit P, *et al.* Oxidative DNA damage and influence of genetic polymorphisms among urban and rural schoolchildren exposed to benzene. *Chem Biol Interact* 2008;**172**:185–94.
- Calderón-Garcidueñas L, Wen-Wang L, Zhang YJ, *et al.* 8-hydroxy-2'-deoxyguanosine, a major mutagenic oxidative DNA lesion, and DNA strand breaks in nasal respiratory epithelium of children exposed to urban pollution. *Environ Health Perspect* 1999;**107**:469–74.
- Castaño-Vinyals G, D'Errico A, Malats N, *et al.* Biomarkers of exposure to polycyclic aromatic hydrocarbons from environmental air pollution. *Occupational and Environmental Medicine* 2004;**61**:e12.
- Cavallo D, Ursini CL, Carelli G, *et al.* Occupational exposure in airport personnel: characterization and evaluation of genotoxic and oxidative effects. *Toxicology* 2006;**223**:26–35.
- Chuang C. Oxidative DNA damage estimated by urinary 8-hydroxydeoxyguanosine: influence of taxi driving, smoking and areca chewing. *Chemosphere* 2003;**52**:1163–71.
- Chuang K-J, Chan C-C, Su T-C, *et al.* The Effect of Urban Air Pollution on Inflammation, Oxidative Stress, Coagulation, and Autonomic Dysfunction in Young Adults. *Am J Respir Crit Care Med* 2007;**176**:370–6.
- Danielsen PH, Bräuner EV, Barregard L, *et al.* Oxidatively damaged DNA and its repair after experimental exposure to wood smoke in healthy humans. *Mutat Res* 2008;**642**:37–42.
- De Coster S, Koppen G, Bracke M, *et al.* Pollutant effects on genotoxic parameters and tumor-associated protein levels in adults: a cross sectional study. *Environ Health* 2008;**7**:26–26.
- Dockery DW, Pope CA, Xu X, *et al.* An Association between Air Pollution and Mortality in Six U.S. Cities. *NEnglJMed* 1993;**329**:1753–9.
- Fan R, Wang D, Mao C, *et al.* Preliminary study of children's exposure to PAHs and its association with 8-hydroxy-2'-deoxyguanosine in Guangzhou, China. *Environ Int* Published Online First: 19 April 2011. doi:10.1016/j.envint.2011.03.021
- Ayi Fanou L, Mobio TA, Creppy EE, *et al.* Survey of air pollution in Cotonou, Benin--air monitoring and biomarkers. *Sci Total Environ* 2006;**358**:85–96.
- Filleul L, Rondeau V, Vandentorren S, *et al.* Twenty five year mortality and air pollution: results from the French PAARC survey. *OccupEnvironMed* 2005;**62**:453–60.

- Freire C, Abril A, Fernández MF, *et al.* Urinary 1-hydroxypyrene and PAH exposure in 4-year-old Spanish children. *SciTotal Environ* 2009;**407**:1562–9.
- García-Suástegui WA, Huerta-Chagoya A, Carrasco-Colín KL, *et al.* Seasonal variations in the levels of PAH-DNA adducts in young adults living in Mexico City. *Mutagenesis* 2011;**26**:385–91.
- Hales S, Blakely T, Woodward A. Air pollution and mortality in New Zealand: cohort study. *Journal of Epidemiology and Community Health* Published Online First: 21 October 2010. doi:10.1136/jech.2010.112490
- Han Y-Y, Donovan M, Sung F-C. Increased urinary 8-hydroxy-2'-deoxyguanosine excretion in long-distance bus drivers in Taiwan. *Chemosphere* 2010;**79**:942–8.
- Hansen ÅM, Wallin H, Binderup ML, *et al.* Urinary 1-hydroxypyrene and mutagenicity in bus drivers and mail carriers exposed to urban air pollution in Denmark. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 2004;**557**:7–17.
- Hansen ÅM, Raaschou-Nielsen O, Knudsen LE. Urinary 1-hydroxypyrene in children living in city and rural residences in Denmark. *SciTotal Environ* 2005;**347**:98–105.
- Harri M, Svoboda P, Mori T, *et al.* Analysis of 8-hydroxydeoxyguanosine among workers exposed to diesel particulate exhaust: comparison with urinary metabolites and PAH air monitoring. *Free Radic Res* 2005;**39**:963–72.
- Hemminki K, Zhang LF, Krüger J, *et al.* Exposure of bus and taxi drivers to urban air pollutants as measured by DNA and protein adducts. *Toxicol Lett* 1994;**72**:171–4.
- Herbstman JB, Tang D, Zhu D, *et al.* Prenatal Exposure to Polycyclic Aromatic Hydrocarbons, Benzo[a]Pyrene-DNA Adducts and Genomic DNA Methylation in Cord Blood. *Environmental Health Perspectives* Published Online First: 17 January 2012. doi:10.1289/ehp.1104056
- Hu S-W, Chan Y-J, Hsu H-T, *et al.* Urinary levels of 1-hydroxypyrene in children residing near a coal-fired power plant. *Environ Res* 2011;**111**:1185–91.
- Ishikawa H, Tian Y, Piao F, *et al.* Genotoxic damage in female residents exposed to environmental air pollution in Shenyang city, China. *Cancer Lett* 2006;**240**:29–35.
- Jerrett M, Burnett RT, Ma R, *et al.* Spatial analysis of air pollution and mortality in Los Angeles. *Epidemiology* 2005;**16**:727–36.
- Katanoda K, Sobue T, Satoh H, *et al.* An Association Between Long-Term Exposure to Ambient Air Pollution and Mortality From Lung Cancer and Respiratory Diseases in Japan. *Journal of Epidemiology* 2011;**21**:132–43.
- Kim JY, Prouty LA, Fang SC, *et al.* Association between fine particulate matter and oxidative DNA damage may be modified in individuals with hypertension. *J Occup Environ Med* 2009;**51**:1158–66.
- Knudsen LE, Norppa H, Gamborg MO, *et al.* Chromosomal Aberrations in Humans Induced by Urban Air Pollution: Influence of DNA Repair and Polymorphisms of GlutathioneS-Transferase M1 and N-Acetyltransferase 2. *Cancer Epidemiology Biomarkers & Prevention* 1999;**8**:303–10.
- Krewski D, Burnett RT, Goldberg M, *et al.* Reanalysis of the Harvard Six Cities Study, Part I: Validation and Replication. *InhalToxicol* 2005;**17**:335–42.
- Kyrtopoulos SA, Georgiadis P, Autrup H, *et al.* Biomarkers of genotoxicity of urban air pollution: Overview and descriptive data from a molecular epidemiology study on populations exposed to moderate-to-low levels of polycyclic aromatic hydrocarbons: the AULIS project. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 2001;**496**:207–28.
- Laden F, Schwartz J, Speizer FE, *et al.* Reduction in Fine Particulate Air Pollution and Mortality: Extended Follow-up of the Harvard Six Cities Study. *AmJRespirCritCare Med* 2006;**173**:667–72.
- Lagorio S, Tagesson C, Forastiere F, *et al.* Exposure to benzene and urinary concentrations of 8-hydroxydeoxyguanosine, a biological marker of oxidative damage to DNA. *Occup Environ Med* 1994;**51**:739–43.
- Lai C, Liou S, Lin H, *et al.* Exposure to traffic exhausts and oxidative DNA damage. *Occup Environ Med* 2005;**62**:216–22.
- Lee M-W, Chen M-L, Lung S-CC, *et al.* Exposure assessment of PM2.5 and urinary 8-OHdG for diesel exhaust emission inspector. *Sci Total Environ* 2010;**408**:505–10.
- Loft S, Poulsen HE, Vistisen K, *et al.* Increased urinary excretion of 8-oxo-2'-deoxyguanosine, a biomarker of oxidative DNA damage, in urban bus drivers. *Mutat Res* 1999;**441**:11–9.
- Madrigano J, Baccarelli A, Mittleman MA, *et al.* Prolonged exposure to particulate pollution, genes associated with glutathione pathways, and DNA methylation in a cohort of older men. *Environ Health Perspect* 2011;**119**:977–82.
- Marczynski B, Preuss R, Mensing T, *et al.* Genotoxic risk assessment in white blood cells of occupationally exposed workers before and after alteration of the polycyclic aromatic hydrocarbon (PAH) profile in the production material: comparison with PAH air and urinary metabolite levels. *Int Arch Occup Environ Health* 2005;**78**:97–108.
- Martínez-Salinas RI, Elena Leal M, Batres-Esquivel LE, *et al.* Exposure of children to polycyclic aromatic hydrocarbons in Mexico: assessment of multiple sources. *Int Arch Occup Environ Health* 2010;**83**:617–23.
- McDonnell WF, Nishino-Ishikawa N, Petersen FF, *et al.* Relationships of mortality with the fine and coarse fractions of long-term ambient PM10 concentrations in nonsmokers. *JExpoAnalEnvironEpidemiol* 2000;**10**:427–36.
- Merlo F, Andreassen A, Weston A, *et al.* Urinary excretion of 1-hydroxypyrene as a marker for exposure to urban air levels of polycyclic aromatic hydrocarbons. *Cancer Epidemiology Biomarkers & Prevention* 1998;**7**:147–55.
- Mills PK, Abbey D, Beeson WL, *et al.* Ambient air pollution and cancer in California Seventh-day Adventists. *ArchEnvironHealth* 1991;**46**:271–80.
- Møller P, Loft S. Oxidative Damage to DNA and Lipids as Biomarkers of Exposure to Air Pollution. *Environ Health Perspect* 2010;**118**:1126–36.

- Mori T, Yoshinaga J, Suzuki K, *et al.* Exposure to polycyclic aromatic hydrocarbons, arsenic and environmental tobacco smoke, nutrient intake, and oxidative stress in Japanese preschool children. *Sci Total Environ* 2011;**409**:2881–7.
- Nafstad P, Haheim LL, Oftedal B, *et al.* Lung cancer and air pollution: a 27 year follow up of 16 209 Norwegian men. *Thorax* 2003;**58**:1071–6.
- Neri M, Ugolini D, Bonassi S, *et al.* Children's exposure to environmental pollutants and biomarkers of genetic damage. II. Results of a comprehensive literature search and meta-analysis. *MutatRes* 2006;**612**:14–39.
- Nielsen PS, Okkels H, Sigsgaard T, *et al.* Exposure to urban and rural air pollution: DNA and protein adducts and effect of glutathione-S-transferase genotype on adduct levels. *IntArchOccupEnvironHealth* 1996;**68**:170–6.
- Nielsen PS, de Pater N, Okkels H, *et al.* Environmental air pollution and DNA adducts in Copenhagen bus drivers--Effect of GSTM1 and NAT2 genotypes on adduct levels. *Carcinogenesis* 1996;**17**:1021–7.
- Novotna B, Topinka J, Solansky I, *et al.* Impact of air pollution and genotype variability on DNA damage in Prague policemen. *Toxicol Lett* 2007;**172**:37–47.
- Palli D, Saieva C, Munnia A, *et al.* DNA adducts and PM10 exposure in traffic-exposed workers and urban residents from the EPIC-Florence City study. *SciTotal Environ* 2008;**403**:105–12.
- Palli D, Sera F, Giovannelli L, *et al.* Environmental ozone exposure and oxidative DNA damage in adult residents of Florence, Italy. *Environ Pollut* 2009;**157**:1521–5.
- Pavanello S, Bollati V, Pesatori AC, *et al.* Global and gene-specific promoter methylation changes are related to anti-B[a]PDE-DNA adduct levels and influence micronuclei levels in polycyclic aromatic hydrocarbon-exposed individuals. *IntJCancer* 2009;**125**:1692–7.
- Pavanello S, Pulliero A, Saia BO, *et al.* Determinants of anti-benzo[a]pyrene diol epoxide–DNA adduct formation in lymphomonocytes of the general population. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis* 2006;**611**:54–63.
- Pedersen M, Wichmann J, Autrup H, *et al.* Increased micronuclei and bulky DNA adducts in cord blood after maternal exposures to traffic-related air pollution. *EnvironRes* 2009;**109**:1012–20.
- Peluso M, Munnia A, Palli D, *et al.* Bulky DNA adducts and lung cancer risk: a prospective study in EPIC investigation. *AACR Meeting Abstracts* 2005;**2005**:512–a.
- Peluso M, Srivatanakul P, Munnia A, *et al.* DNA adduct formation among workers in a Thai industrial estate and nearby residents. *SciTotal Environ* 2008;**389**:283–8.
- Perera F, Brenner D, Jeffrey A, *et al.* DNA adducts and Related Biomarkers in Populations Exposed to Environmental Carcinogens. 1991.
- Pope C, Thun M, Namboodiri M, *et al.* Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. *AmJRespirCritCare Med* 1995;**151**:669–74.
- Pope III CA, Burnett RT, Thun MJ, *et al.* Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution. *JAMA* 2002;**287**:1132–41.
- Pope CA, Burnett RT, Turner MC, *et al.* Lung Cancer and Cardiovascular Disease Mortality Associated with Ambient Air Pollution and Cigarette Smoke: Shape of the Exposure–Response Relationships. *Environmental Health Perspectives* 2011;**119**:1616–21.
- Raaschou-Nielsen O, Bak H, Sørensen M, *et al.* Air Pollution from Traffic and Risk for Lung Cancer in Three Danish Cohorts. *Cancer Epidemiology Biomarkers & Prevention* 2010;**19**:1284–91.
- Raaschou-Nielsen O, Andersen ZJ, Hvidberg M, *et al.* Lung Cancer Incidence and Long-Term Exposure to Air Pollution from Traffic. *Environmental Health Perspectives* 2011;**119**:860–5.
- Ren C, Fang S, Wright RO, *et al.* Urinary 8-hydroxy-2'-deoxyguanosine as a biomarker of oxidative DNA damage induced by ambient pollution in the Normative Aging Study. *Occup Environ Med* 2011;**68**:562–9.
- Rossner Jr. P, Uhlirova K, Beskid O, *et al.* Expression of XRCC5 in peripheral blood lymphocytes is upregulated in subjects from a heavily polluted region in the Czech Republic. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis* 2011;**713**:76–82.
- Rossner P Jr, Svecova V, Milcova A, *et al.* Oxidative and nitrosative stress markers in bus drivers. *Mutat Res* 2007;**617**:23–32.
- Rossner P Jr, Rossnerova A, Sram RJ. Oxidative stress and chromosomal aberrations in an environmentally exposed population. *Mutat Res* 2011;**707**:34–41.
- Rossnerova A, Spatova M, Pastorkova A, *et al.* Micronuclei levels in mothers and their newborns from regions with different types of air pollution. *Mutat Res* 2011;**715**:72–8.
- Ruchirawa M, Mahidol C, Tangjarukij C, *et al.* Exposure to genotoxins present in ambient air in Bangkok, Thailand--particle associated polycyclic aromatic hydrocarbons and biomarkers. *SciTotal Environ* 2002;**287**:121–32.
- Singh R, Kaur B, Kalina I, *et al.* Effects of environmental air pollution on endogenous oxidative DNA damage in humans. *Mutat Res* 2007;**620**:71–82.
- Sørensen M, Autrup H, Hertel O, *et al.* Personal exposure to PM2.5 and biomarkers of DNA damage. *Cancer Epidemiol Biomarkers Prev* 2003;**12**:191–6.
- Sørensen M, Skov H, Autrup H, *et al.* Urban benzene exposure and oxidative DNA damage: influence of genetic polymorphisms in metabolism genes. *The Science of The Total Environment* 2003;**309**:69–80.
- Sram RJ., Beskid O, Rössnerova A, *et al.* Environmental exposure to carcinogenic polycyclic aromatic hydrocarbons : The interpretation of cytogenetic analysis by FISH. *Toxicology letters* 2007;**172**:12–20.
- Srám RJ, Binková B, Rössner P, *et al.* Adverse reproductive outcomes from exposure to environmental mutagens. *Mutat Res* 1999;**428**:203–15.
- Staessen JA, Nawrot T, Hond ED, *et al.* Renal function, cytogenetic measurements, and sexual development in adolescents in relation to environmental pollutants: a feasibility study of biomarkers. *The Lancet* 2001;**357**:1660–9.

- Suzuki J, Inoue Y, Suzuki S. Changes in the urinary excretion level of 8-hydroxyguanine by exposure to reactive oxygen-generating substances. *Free Radic Biol Med* 1995;**18**:431–6.
- Svecova V, Rossner Jr. P, Dostal M, *et al.* Urinary 8-oxodeoxyguanosine levels in children exposed to air pollutants. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis* 2009;**662**:37–43.
- Svecova V, Milcova A, Lnenickova Z, *et al.* Seasonal variability of oxidative stress markers in city bus drivers. Part I. Oxidative damage to DNA. *Mutation Research* 2008;**642**:14–20.
- Tarantini L, Bonzini M, Apostoli P, *et al.* Effects of particulate matter on genomic DNA methylation content and iNOS promoter methylation. *EnvironHealth Perspect* 2009;**117**:217–22.
- Topinka J, Sevastyanova O, Binkova B, *et al.* Biomarkers of air pollution exposure—A study of policemen in Prague. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis* 2007;**624**:9–17.
- Topinka J., Binkova B., Mrackova G., *et al.* DNA adducts in human placenta as related to air pollution and to GSTM1 genotype. *Mutation research Genetic toxicology and environmental mutagenesis* 1997;**390**:59–68.
- Tuntawiroon J, Mahidol C, Navasumrit P, *et al.* Increased health risk in Bangkok children exposed to polycyclic aromatic hydrocarbons from traffic-related sources. *Carcinogenesis* 2007;**28**:816–22.
- Turner MC, Krewski D, Pope CA, *et al.* Long-term Ambient Fine Particulate Matter Air Pollution and Lung Cancer in a Large Cohort of Never-Smokers. *American Journal of Respiratory and Critical Care Medicine* 2011;**184**:1374 –1381.
- Vineis P, Hoek G, Krzyzanowski M, *et al.* Air pollution and risk of lung cancer in a prospective study in Europe. *IntJCancer* 2006;**119**:169–74.
- Vinzents PS, Møller P, Sørensen M, *et al.* Personal exposure to ultrafine particles and oxidative DNA damage. *Environ Health Perspect* 2005;**113**:1485–90.
- Whyatt RM, Santella RM, Jedrychowski W, *et al.* Relationship between ambient air pollution and DNA damage in Polish mothers and newborns. *EnvironHealth Perspect* 1998;**106 Suppl 3**:821–6.
- Yang K, Airoldi L, Pastorelli R, *et al.* Aromatic DNA adducts in lymphocytes of humans working at high and low traffic density areas. *Chemico-Biological Interactions* 1996;**101**:127–36.
- Yorifuji T, Kashima S, Tsuda T, *et al.* Long-term exposure to traffic-related air pollution and mortality in Shizuoka, Japan. *OccupEnvironMed* 2010;**67**:111–7.
- Zidzik J, Kalina I, Salagovic J, *et al.* Influence of PAHs in ambient air on chromosomal aberrations in exposed subjects : International study - EXPAH. *Mutation Research* 2007;**620**:41–8.