


META-ANALYSIS: CARDIOVASCULAR EFFECTS IN WORKERS OCCUPATIONALLY EXPOSED TO URBAN POLLUTION

META-ANALISI: EFFETTI SULL'APPARATO CARDIOVASCOLARE IN LAVORATORI ESPOSTI A INQUINAMENTO URBANO

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Key words: cardiovascular system, cardiovascular diseases, urban pollution

 **Parole chiave:** sistema cardiovascolare, malattie cardiache, inquinamento urbano

Abstract

Background: Many studies showed a connection between exposition to high levels of urban pollution (especially to particulate and traffic noise) and the onset of even deadly cardiovascular diseases.

DESIGN: Meta-analysis of case-control design.

Objectives: The aim of this study is to estimate the association between cardiovascular effects and occupational exposition to atmospheric pollution in urban environment.

Methods: DATA SOURCES: Biomedcentral, MEDLINE/ PubMed, MEDLINE/ National Library of Medicine (NLM), MEDLINE Plus, Nioshtic-2, Scopus, TOXNET/Toxline, unpublished studies known by the authors and acts of national and international conferences between 1988 and May 2010 included. There has not been any kind of language or typological restriction.

CRITERIA OF ELEGIBILITY: The research on cardiovascular effects includes control cases of workers exposed to urban pollution, compared with non-exposed subjects.

PARTICIPANTS AND INTERVENTIONS: The selected studies present outdoor workers exposed to urban pollution (drivers and petrol pump attendants) and a control group of indoor workers (managers, university students and other selected subjects).

STUDY APPRAISAL AND SYNTHESIS METHODS: The evidences (independently taken from two different authors) have been grouped in two classes, the first one formed by continuous variables (systolic blood pressure, diastolic blood pressure, heart rate, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides) and the second one by discontinuous variables (electrocardiographic abnormalities prevalence, hypertension prevalence, hypercholesterolemia prevalence).

The studies related to both classes and presenting more than one variable for each class have been included and used, in order to elaborate the results. We calculated heterogeneity in each variable (ES calculation for continuous variables and OR calculation for discontinuous variables).

Results: On 378 publications, we have selected and included 16 articles. The variables show statistically irrelevant differences between exposed group and control group, except regarding the triglycerides. Limitations. The controlled studies are limited and characterized by a non-homogeneous evaluation of both expositional times of workers to urban pollution and of professional expositional values.

Conclusions: Considering the heterogeneity and the lack of studies, it is impossible at the moment to document effects on the cardiovascular system in workers exposed to urban pollution. The results of this meta-analysis only suggest the association of urban pollution with alteration of triglycerides blood levels (referring to just three studies). As reported in scientific literature on this subject, it is necessary to conduct a future professional investigation on this subject with more qualified and homogeneous studies.

Abstract

Introduzione: Numerosi studi hanno dimostrato un'associazione tra esposizione ad elevati livelli di inquinamento urbano (nella fattispecie l'esposizione al particolato sia a breve che a lungo termine e il rumore da traffico veicolare) e insorgenza nonché mortalità per patologie cardiovascolari.

DESIGN: meta-analysis of case-control design.

Obiettivi: Valutare l'associazione esistente tra effetti cardiovascolari ed esposizione occupazionale ad inquinamento atmosferico in ambiente urbano.

Metodi: DATA SOURCES: Biomedcentral, MEDLINE/ PubMed, MEDLINE/ National Library of Medicine (NLM), MEDLINE Plus, Nioshtic-2, Scopus, TOXNET/Toxline, inclusi gli studi non ancora pubblicati di cui gli autori erano a conoscenza e gli atti dei Convegni nazionali ed internazionali, dal 1988 al Maggio 2010. Non è stata effettuata nessuna restrizione, di lingua o tipo di pubblicazione, alla ricerca.

STUDY ELIGIBILITY CRITERIA: sono stati inclusi gli studi caso-controllo in cui i lavoratori esposti ad inquinamento urbano sono stati comparati con quelli non esposti in relazione agli effetti sull'apparato cardiovascolare.

PARTICIPANTS, AND INTERVENTIONS: sono stati selezionati gli studi in cui la popolazione degli esposti all'inquinamento urbano era costituita da addetti ad attività in ambiente outdoor, viabilisti, benzinai ed autisti professionisti mentre il gruppo dei controlli era rappresentato da addetti ad attività indoor, amministrativi, studenti universitari e soggetti selezionati tra la popolazione generale.

STUDY APPRAISAL AND SYNTHESIS METHODS: i dati, estratti da due autori diversi in modo indipendente, sono stati raggruppati in due classi di variabili, la prima costituita da variabili continue (pressione arteriosa sistolica, pressione

arteriosa diastolica, frequenza cardiaca, colesterolo totale, colesterolo HDL, colesterolo LDL, trigliceridi) e la seconda da variabili discontinue (alterazioni elettrocardiografiche, ipertensione, ipercolesterolemia, ipertrigliceridemia). Gli studi che riportavano i dati relativi ad entrambe le classi e per ciascuna classe più variabili sono stati inseriti e quindi utilizzati più volte per l'elaborazione dei risultati. Per ciascuna variabile è stata calcolata l'eterogeneità, per le variabili continue è stato effettuato il calcolo dell'ES mentre per le variabili discontinue è stato effettuato il calcolo dell'OR e della sua significatività.

Risultati: Su un totale di 378 pubblicazioni, sono stati selezionati ed inclusi nella meta-analisi 16 articoli. Le variabili studiate non mostrano differenze statisticamente significative nel gruppo degli esposti rispetto ai controlli tranne che per i trigliceridi.

LIMITATIONS: gli studi controllati risultano essere limitati e sono caratterizzati da una non omogenea valutazione sia dei tempi di esposizione dei lavoratori all'inquinamento urbano sia dei valori di esposizione professionale.

Conclusioni: Considerata l'eterogeneità e la scarsità degli studi, soprattutto per alcuni parametri, al momento non è possibile documentare, nei lavoratori professionalmente esposti all'inquinamento urbano, la presenza di effetti avversi sull'apparato cardiovascolare. Infatti l'analisi dei risultati ottenuti con la nostra meta-analisi suggerisce la sola associazione tra inquinamento urbano e alterazioni dei livelli ematici di trigliceridi, il risultato è inoltre relativo perché riferito a tre studi. A fronte di quanto riportato in materia dalla letteratura scientifica relativamente alla popolazione generale, è necessario che la ricerca futura approfondisca tale tematica in ambito professionale con studi condotti in maniera più idonea ed omogenea.

Introduction

Urban pollution is a considerable health problem all-over the world (1).

Many observational and experimental studies in general population found an association between urban pollution and mortality due to cardiovascular diseases, considering urban pollution a possible joint cause of their onset(2-7).

Even if the process implying this connection is not yet fully explained, it is possible to recognize some risk factors, such as the exposition to chemical agents short-term (2,8-11) and long-term (2, 5, 12-15) exposition to particulate matter, lead, (16-21)cadmium (4), carbon monoxide(22) and to traffic noise (12-13,23-24).

The aim of this meta-analysis is to conduct a systematic revision of the scientific evidence on cardiovascular effects in workers exposed to urban pollution (25).

The intention is to determine possible cardiovascular effects and especially modifications of risk factors (as blood pressure, heart rate, lipid blood levels) of urban pollution on workers.

Methods

The study has been conducted and reported as in the MOOSE Consensus Statement (26).

We did a systematic research of observational studies (control-cases from January 1988 to May 2010) reporting cardiovascular effects in exposed (cases) and non-exposed (control) subjects to urban pollution. We also considered known but not yet published data and acts of national and international conferences. A further examination of the bibliography in previously published articles, reviews and meta-analysis on this subject has been conducted, in order to find other useful publications. There has not been any kind of language or typological restriction to the research. The utilizable works have been identified with a systematic research on the following on-line search engines: Biomedcentral, MEDLINE/ PubMed, MEDLINE/ National Library of Medicine (NLM), MEDLINE Plus, Nioshtic-2, Scopus, TOXNET/Toxline.

The research has been conducted introducing the following keywords, combined with "Boolean Operators":

- police workers (or police officers or traffic police or traffic wardens) AND cardiac function, cardiovascular function, heart disease, cardiac diseases, cardiovascular diseases, cardiac system, cardiovascular system, blood pressure, heart rate, electrocardiogram, electrocardiography, hypertension;
- mail carriers (or postal workers) AND cardiac function, cardiovascular function, heart disease, cardiac diseases, cardiovascular diseases, cardiac system, cardiovascular system, blood pressure, heart rate, electrocardiogram, electrocardiography, hypertension;
- street vendors (or shop vendors) AND cardiac function, cardiovascular function, heart disease, cardiac diseases, cardiovascular diseases, cardiac system, cardiovascular system, blood pressure, heart rate, electrocardiogram, electrocardiography, hypertension;
- bus drivers AND cardiac function, cardiovascular function, heart disease, cardiac diseases, cardiovascular diseases, cardiac system, cardiovascular system, blood pressure, heart rate, electrocardiogram, electrocardiography, hypertension;
- taxi drivers AND cardiac function, cardiovascular function, heart disease, cardiac diseases, cardiovascular diseases, cardiac system, cardiovascular system, blood pressure, heart rate, electrocardiogram, electrocardiography, hypertension;
- filling station attendants (or petrol station attendants or gas station attendants or gasoline station attendants) AND cardiac function, cardiovascular function, heart disease, cardiac diseases, cardiovascular diseases, cardiac system, cardiovascular system, blood pressure, heart rate, electrocardiogram, electrocardiography, hypertension;
- road sweepers (or street sweepers or road cleaners or street cleaners) AND cardiac function, cardiovascular function, heart disease, cardiac diseases, cardiovascular diseases, cardiac system, cardiovascular system, blood pressure, heart rate, electrocardiogram, electrocardiography, hypertension.

Selection process and Data abstraction

Two reviewers independently evaluated title, abstract and keywords in each resulting study and applied criteria of exclusion and inclusion. The same procedure was applied to full texts and used for the choice of the relevant data, in order to increase the reliability of the study. We included control-case studies dealing with both outdoor workers (cases – as local policemen and professional drivers) and indoor workers (controls – as administrative local agents, employees, university students and other selected subjects). Firemen and street maintenance staff were excluded, considering that their exposition to urban pollution is occasional and added to other harmful specific pollutions that can have effects on the cardiovascular system. We only considered the research in which the connection between urban pollution and cardiovascular effects had been studied according to at least one of the following variables: systolic blood pressure (SBP) and diastolic blood pressure (DBP) or hypertension prevalence, heart rate (HR), electrocardiographic abnormalities (ECGA).

We also considered blood lipids levels as total cholesterol (TCHO), LDL cholesterol (LDL) and HDL cholesterol (HDL), triglycerides (TRY) or prevalence hypertriglyceridemia or hypercholesterolemia, considering their importance in cardiovascular pathologies. All the articles not concerning our aim were excluded (articles not specifically dealing with the above-mentioned tasks, not based on the control-case system and with incomplete or lacking data).

Data analysis

The Effects Size (ES), reflecting the strength of the relationship between two variables, was performed by Standardized Mean Difference (SMD) or Weighted Mean Difference (WMD), at the presence of heterogeneity, when the data were expressed in the media and Standard Deviation, for continuous variables (Class I). While it was expressed by Odds Ratio (OR) when the data were expressed as frequency, for the discontinuous variables (Class II). For measures of ES based on the Odd Ratio (OR), a ratio of 1.0 indicates the lack of differences among the studied groups. The heterogeneity among the used data, referring to the variability or differences among studies in estimating the effect, was assessed with the Index of Inconsistency (I²). Using I² we calculated the percentage of variance due to heterogeneity rather than the real case. If the value of I² was close to zero the observed variance was due to chance, if it was higher the variance was due to several factors that need to be investigated. The calculation of ES was made using the Random Effects Model (REM) for high values of I² and the Fixed Effects Model (FEM) for I² values close to zero (40).

Results

With the application of this criteria, we chose 378 publications. All the articles not inherent with our research were excluded. We examined the full texts of 80 potentially acceptable articles and 16 of them (reported on table 1) respected the criteria for inclusion. All the subjects (7714 workers) were divided into two groups, the exposed (EX – 3699 outdoor workers) and the control group (C – 4015 indoor workers).

Table 1 - Characteristics of included studies

Study	Country	Partecipan s	Study design	Outcomes	Method	Main results	Evaluated Variables
Biava 1992 [27]	Italy	292 traffic policemen / 60 hospital employees used as control group	Cross-sectional study	The effects caused by exposition to urban pollutants (chemical matters, IPA, benzene, asbestos, lead, monoxide).	Objective examination Spirometry Electrocardiogram Neurological visit Determination of motor conduction's velocity of median nerve Psychological questionnaire Blood lead levels Blood carboxyhemoglobin levels Chemistry exam (blood test)	There is a statistically significant difference between exposed group and control group about musculo-skeletal disorders and about blood lead level.	Cardiac disorders EX Male 2/179 (1.2), EX Female 0/113 (-) C Male: 1/36 (2.7), C Female 1/24 (4.1)
Bigert 2003 [28]	Swedish	106 professional drivers / 1482 control group selected from general population	Observational study	Heart attack risk in professional drivers (bus, taxi and truck drivers)	Valuation of heart attack risk factors: • smoke cigarette's habit • alcohol's consumption • physical exercise during spare time • overweight • diabetes	Results of this study show that Odds Ratio for heart attack in bus drivers is 2.14 (IC 95% 1.34-3.41), in taxi drivers heart attack is 1.88 (IC 95% 1.19-2.98) and in truck drivers heart attack is 1.66 (IC	Prevalence hypertension EX 30/106 C 23/1482

					<ul style="list-style-type: none"> • mellitus hypertension • social-economical status • work commitments 	95% 1.22-2.26)	
Cervone 1993 [29]	Italy	28 men traffic policemen / 14 control group selected from general population	Observational study	Effects of exposure to urban pollution on health and the activation of immune system in traffic policemen	Anamnestic questionnaire Blood pressure Chemistry exams (blood test) Urinary lead levels Lymphocyte subpopulations' study	Urinary lead values are significantly increased in exposed group compared to control group (p<0.01).	EX: SBP 123.8 (13.6), DBP 82.4 (8.6), CHOL TOT 238 (46), TRY 185 (124), GLY 97 (15) C: SBP 127.2 (16.1), DBP 78.6 (9.3), CHOL TOT 229 (55), TRY 137 (85), GLY 97 (27)
Hedberg 1993 [30]	Sweden	440 men professional drivers / 1000 men subjects control group	Observational study	Risk factors of cardiovascular disease in professional drivers.	Anamnestic questionnaire Objective examination Blood pressure Chemistry exams (blood test)	Results of this study show that Odds Ratio (OR) for cardiovascular risk in professional drivers is 3.18 (IC 95% 2.41-4.20) compared to control group.	EX: CHOL TOT 6.32 (6.19-6.45), HDL 1.26 (1.23-1.30), TRY 1.85 (1.51-2.19), Prevalence hypertension 33/440. C: CHOL TOT 6.30 (6.22-6.39), HDL 1.28 (1.25-1.30), TRY 1.63 (1.55-1.71), Prevalence hypertension 35/1000.
Mormontoy 2006 [31]	Peru	52 traffic policemen / 50 police officers employed in indoor activity	Cross-sectional study	Blood lead levels and the effects of exposure to vehicular traffic on cardiovascular system	Anamnestic questionnaire Blood pressure Chemistry exams (blood test) Blood lead levels	Blood lead levels are statistically increased in exposed group compared to control group.	EX: SBP 113.02 (9.29), DBP 73.94 (7.75) C: SBP 114.18 (8.20) DBP 75.20 (8.35)
Pala 2002 [32]	Turkey	78 traffic policemen / 21 police officers employed in indoor activity	Observational study	Blood lead levels and the effects of exposure to vehicular traffic on cardiovascular system	Anamnestic questionnaire Blood pressure Chemistry exams (blood test) Blood lead levels	Results of this study show that there is not a statistically significant difference between exposed group and control group about blood pressure and blood lead levels.	EX: SBP 119.5 (16.3), DBP 75.9 (10.2) C: SBP 116.4 (13.2) DBP 76.20 (10.50)
Sakata 2007 [33]	Nepal	27 men taxi drivers / 9 men university students and farmhands	Observational study	The dose-response relationship between blood lead levels and erythropoietin serum concentration in taxi drivers exposed to lead of vehicular emission.	Blood pressure Chemistry exams (blood test) Heart rate Erythropoietin serum levels Urine analysis	Erythropoietin serum levels are significantly reduced in exposed group compared to control group. Blood lead levels are increased in exposed group compared to control group.	EX: SBP 135 (12), DBP 79.0 (10), HR 78 (10), CHOL TOT 149 (28), CHOL HDL 37.9(7.8) C: SBP 122 (8), DBP 78 (9), HR 71(4), CHOL TOT 157(26), CHOL HDL 37.6(9.3)
Sancini 2010 [34]	Italy	115 traffic police smokers / 115 police officers employed in indoor activity smokers 280 traffic	Observational study	Blood pressure changes and electrocardiographic abnormalities in traffic policemen exposed to urban pollution	Anamnestic questionnaire Objective examination Blood pressure Electrocardiogram	Blood systolic pressure average value at rest and electrocardiographic abnormalities' frequency is statistically increased in non smoker male subjects of	SMOKERS: EX. Male: SBP 126 (13.2), DBP 78.5 (9.1), ECG abnormalities 8 (19.0) C Male: SBP 129 (14.2), DBP 81.4 (10.5), ECG abnormalities 13

		police non smokers / 280 police officers employed in indoor activity non smokers				exposed group compared to men non smoker control group Blood systolic pressure average value at rest is statistically increased in non smoker male subjects of exposed group compared to men smokers of exposed group. Electocardiographic abnormalities'frequency is statistically increased in non smoker male subjects of control group compared to men smoker control group	(30.9) EX. Female SBP 114.4 (13.6), DBP 72.6 (9.8), ECG abnormalities 4(5.4) C Female SBP 114.6 (14.2), DBP 73.2 (9.8), ECG abnormalities 7(9.5) NON SMOKERS: EX Male: SBP 134.7 (19.2), DBP 82.2 (8.9), ECG Abnormalities 30 (20.8) C Male: SBP 128.6 13.6(), DBP 81.3 (8.4), ECG Abnormalities 15(10.4) EX Female: SBP 116.2 13.8), DBP 72.9 (9.5), ECG Abnormalities 16(11.7) C Female: SBP 116.6 (12.5) DBP 75.9 (14.7), ECG Abnormalities 15 (11)
Sardelli 1995 [35]	Italy	120 traffic policemen / 30 administrative workers	Observational study	Health effects of exposure to urban pollution and noise in traffic policemen	Anamnestic questionnaire Objective examination Blood pressure Cardiology visit Electrocardiogram Othorinolaryngology visit Chest radiography Audiometry Chemistry exams (blood test) Pneumotacograph	Blood cholesterol levels are significantly increased in exposed group compared to control group. Spirometry shows that respiratory obstructive diseases are increased in exposed group compared to control group and that mild hypertension is increased in exposed group more than control in group.	EX: prevalence hypercholesterolemia 80/120 Prevalence Hypertension moderate: N. 14 ECG Abnormalities prevalence: N. 28 C: prevalence hypercholesterolemia 8/30 Prevalence Hypertension moderate: N. 2 ECG Abnormalities prevalence: N. 8
Tomao 2002[14]	Italy	118 men traffic policemen 118 police officers employed in indoor activity	Observational study	Lipid metabolism in traffic policemen exposed to urban pollution.	Anamnestic questionnaire Objective examination Chemistry exams (blood test)	HDL average values are significantly reduced in exposed group compared to control group, instead triglycerides average values are significantly increased in exposed group compared to control group.	EX: CHOL TOT 208.2 (46.4), HDL 29.9 (7.2), TRY 173.8 (168.9). C: CHOL TOT 202.6 (36.8), HDL 55.3 (9.9), TRY 138.1 (88.7).
Tomei 2004[12]	Italy	77 non smokers traffic policemen / 87 non smokers police	Observational study	Blood pressure changes in traffic policemen exposed to urban pollution	Anamnestic questionnaire Objective examination Chemistry exams (blood test) Blood pressure	Blood systolic pressure average value monitored during 24 hours is statistically increased in non smoker male	EX: SBP 135 (12), DBP 79.0 (10), CHOL TOT m 225.8 (55.2), CHOL TOT f 188.6 (40.7), CHOL HDL m 43.4

		officers employed in indoor activity 43 smokers traffic policemen / 29 smokers police officers employed in indoor activity		through ambulatory monitoring of blood pressure during 24 hours.	Monitoring of blood pressure during 24 hours	subjects of exposed group compared to men non smoker control group. Blood diastolic pressure average values monitored during 24 hours, between 6 am and 11 am and between 10 pm and 6 am, are statistically increased in non smoker male subjects of exposed group compared to non smoker male subjects in control group.	(5.8), CHOL HDL f 58.7 (13.2), TRY m 181 (198.2), TRY f 107 (48), LDL m 146 (34.4), LDL f 108.3 (31.4). C: SBP 122 (8), DBP 78 (9), CHOL TOT m 230.4 (26.9), CHOL TOT f 191.1 (26.8), CHOL HDL m 43.1 (3.65), CHOL HDL f 48.7 (8.9), TRY m 167.8 (56), TRY f 95.9 (31.5), LDL m 153.7 (26.85), LDL f 125.3 (30.9).
Volpino 2004[13]	Italy	68 men traffic policemen / 62 police officers employed in indoor activity	Observational study	The effects of exposure to urban pollution on cardiovascular and respiratory systems in traffic policemen	Anamnestic questionnaire Objective examination Chemistry exams (blood test) Blood pressure Heart rate Respiratory frequency Electrocardiogram Stress electrocardiogram Hemogasanalysis Spirometry	Diastolic pressure average values during rest period are statistically increased in exposed group compared to control group. Diastolic pressure average values during stress are statistically increased in exposed group compared to control group.	EX: Prevalence Hypertension 16/68 SBP 130 (12.6), DBP 85.7 (8.5), C: Prevalence Hypertension 16/62 SBP 127 (8.4), DBP 81.9 (6.8),
Wang 2001 [36]	Taiwan	1761 male bus drivers / 536 male administrative workers	Observational study	Cardiovascular risk factors in bus drivers exposed to vehicular emissions and urban pollution	Anamnestic questionnaire Objective examination Chemistry exams (blood test) Electrocardiogram	Hypertension, hypercholesterolemia, hypertriglyceridemia and electrocardiograph abnormalities are statistically increased in exposed group compared to control group.	EX: Prevalence Hypertension 986/1761, Prevalence hypercholesterolemia 598/1761 Prevalence hypertriglyceridemia 376/1761. C: Prev. Hyper 164/536 Prevalence hypercholesterolemia 162/536 Prevalence hypertriglyceridemia 166/536.
Zefferino 2003[37]	Italy	30 traffic policemen, studied during a working day / 30 traffic policemen studied during a day off.	Observational study	The effects of exposure to urban pollution on heart rate in policemen employed in emergency care	Anamnestic questionnaire Objective examination PSS test (Professional Stress Scale Test) Cortisol salivary levels Salivary IL-1B levels Electrocardiogram Study of heart rate variability	Cortisol levels are significantly higher at the beginning of work shift than at the end. In the morning during holiday, average cortisol concentration is statistically decreased compared to cortisol concentration in the afternoon. T test shows statistically significant difference between average cortisol	EX HR during work 78.53 (10.47) C: HR during holiday 74.46 (8.84)

						levels at the same time during holidays and working days. IL1-B average concentration at the beginning of work shift is higher than at the end of work shift ($p < 0.05$) Statistical analysis shows statistically significant association between LF/HF (low frequency/high frequency) of heart rate measured at 8 am of day off and the difference of salivary cortisol levels at work.	
Zefferino 2006[38]	Italy	30 traffic policemen studied during a working day / 30 traffic policemen studied during a day off.	Observational study	Some salivary stress markers in policemen employed in emergency care.	Anamnestic questionnaire Objective examination PSS test (Professional Stress Scale Test) Cortisol salivary levels Salivary IL-1B levels Electrocardiogram Blood pressure	Cortisol levels are significantly higher at the beginning of work shift than at the end ($p < 0.05$). During holiday in the morning, average cortisol concentration is statistically decreased compared to cortisol concentration in the afternoon ($p < 0.05$). T test shows statistically significant difference between cortisol average levels at the same hour during holiday and working days ($p < 0.05$). IL1-B average concentration at the beginning of work shift is higher than at the end ($p < 0.05$).	EX: SBP/ DBP during work 135.3/89 (14.6/9.9) C: SBP/ DBP during holiday 131.8/ 84 (14.6/8.7)
Zhang 1994[39]	China	36 traffic policemen and 277 gasoline workers / 342 administrative workers	Observational study	The aim of this study is to evaluate the effects of lead exposure on workers' health.	Anamnestic questionnaire Objective examination Electrocardiogram Urinary lead levels Urinary diethyl lead levels Triethyl lead levels	Results show no statistically differences between exposed group and control group about electrocardiographic abnormalities.	EX (Traffic policemen and 277 gasoline workers): ECG Abnormalities prevalence 18.5/277, 8.33/36 C: ECG Abnormalities prevalence 6.43/342

We grouped the studies according to the nature of each investigated variable and identified two classes of variables: continuous variables (systolic blood pressure, diastolic blood pressure, heart rate, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides) and discontinuous variables (electrocardiographic abnormalities prevalence, hypertension prevalence, hypercholesterolemia prevalence).

Even if at first we identified a prevalence of hypertriglyceridemia, we did not conduct statistical analysis on it, because it was treated in one work only. The studies that reported data for both classes and several variables for each class were entered and processed more than once for the elaboration of results. Evaluating the parameters for Class I, we included a total of 3774 workers divided into two groups: 2037 subjects in the exposed group (EX) and 1737 subjects in the control group (C). In the assessment of parameters related to discontinuous variables we included a total of 11737 workers: 6978 EX and 4759 C. Table 2-3 summarise the results of studies.

Results of Continuous variables: Class I

Systolic and diastolic blood pressure, evaluated in eight studies (12,13,29,31,32,33,34,38), and heart rate, in two studies (33,37), show no statistically significant differences in the exposed compared to controls. The studies were heterogeneous between them.

For the lipid parameters, total cholesterol (measured in four studies (12,14,29,33), and LDL cholesterol, measured in one study (12) show no statistically significant differences and are characterized by a low index of heterogeneity. HDL cholesterol (measured in three studies, (12,14,33) shows no statistically significant differences, but is characterized by a high level of heterogeneity. Regarding triglycerides, measured in three studies (12,14,29), there is a statistically significant difference in the exposed compared to controls, with a low index of heterogeneity.

Table 2 - The results of Class I (continuous variables)

VARIABLE	NUMBER OF SUBJECTS	P	I ² %	Meta-analysis index
Systolic blood pressure	EX: 518 C: 417	P 0.239	37.4	SMD 0.093 [-0.062; 0.247]
Diastolic blood pressure	EX: 518 C: 417	P 0.126	47.8	SMD 0.121 [-0.34; 0.275]
Heart rate	EX: 57 C: 39	P 0.126	47.8	WMD 0.121 [-0.34; 0.275]
Total cholesterol	EX: 293 C: 257	P 0.358	0.00	WMD 0.094 [-0.106;- 0.295]
HDL cholesterol	EX: 265 C: 243	P 0.43	98.4	SMD 0.897 [-3.171; 1.37]
LDL cholesterol	EX: 120 C:116	P 0.87	0.00	WMD 0.054 [-0. 485; 0.378]
Tryliceridaes	EX: 266 C: 248	P 0.009	0.00	WMD 0.280 [0.070; 0.489]

EX = Experimental Group

C = Control Group

P: = Probability

I² = Heterogeneity Index

SMD = Standardized Mean Difference

WMD =Weighted Mean Difference

Results of Not-continuous variables: Class II

Prevalence of electrocardiographic abnormalities, evaluated in five studies (12,27,35,36,39) took twice and the prevalence of hypertension (assessed in two studies (35,36), do not give statistically significant differences in the exposed compared to controls, with a high degree of heterogeneity.

Regarding the data on the prevalence of hypercholesterolemia (evaluated in two studies (35,36), there are not statistically significant differences in the exposed compared to controls, with a high degree of heterogeneity.

Table 3 - The results of Class II (not-continuous variables)

VARIABLE	NUMBER OF SUBJECTS	P	I²%	Meta-analysis index
Electrocardiographic alterations	EX: 2602 C: 1083	P 0.702	73.0	OR = 1.165 [0.53; 2.55]
Hypertension	EX: 2495 C: 3110	P 0.169	86.3	OR = 1.39 [0.86; 2.33]
Hypercholesterolemia	EX: 1881 C: 566	P 0.37	87.6	OR = 1.73 [0.51; 5.86]

EX = Experimental Group

C = Control Group

n.s. = not significant

P = Probability

I² = Heterogeneity Index

ES = Effect Size

OR = Odd ratio

Conclusions

Many studies in the general population show the association between exposure to urban pollution and cardiovascular effects, such as hypertension (41), ischemic heart disease, arrhythmias, heart failure, stroke and sudden death (3), probably for alterations of the cardiac autonomic and myocardial perfusion and electrical instability (3, 5, 42, 43). In addition, airborne particulates, according to the theory of Twickler et al (44), conveyed by the lipids, would be able to infiltrate the vessel intima by promoting the formation of atherosclerotic plaques. Hence the importance of early assessment in subjects exposed to any load changes in heart rate, blood pressure, lipid blood levels and electrocardiogram.

The meta-analysis shows that the association between occupational exposure to urban air pollution and cardiovascular effects gives statistically significant values in outdoor workers only for the blood levels of triglycerides. This value is however relative, as reported in only three studies (12,14,29).

The result is confirmed by the work of Wang, that was not included in the meta-analysis because it is a single work. The study, conducted on a large number of subjects, reports a statistically significant difference in the prevalence of hypertriglyceridemia between bus drivers and skilled workers.

We found the same limitation of controlled studies also in the evaluation of other examined variables. Reviewed studies are heterogeneous, as to the outcomes. Among 16 studies of our meta-analysis, only five focused on the association between urban pollution and effects on the cardiovascular system (12,13,30,31,34). One of the remaining studies (36), (analyzing the incidence of coronary heart disease in professional drivers) identified among

the potential risk factors both urban pollution and specific work factors. Four studies assessed the effects of urban pollution on health, including the cardiovascular system (27,29,35,39).

One study (14) investigated the effects of urban pollution on the lipidic asset; this alteration is a known cardiovascular risk factor. In their work, Pala and Sakata (32,33), evaluated blood lead levels respectively in policemen and taxi drivers; the first incorporated blood pressure within the parameters of the assessment. The second incorporated heart rate and the lipidic asset.

In conclusion, three more studies (28,37), dealing with subjects professionally exposed to urban pollution, attributed the cardiovascular effects in outdoor workers to stress.

Even in literature it comes out stress is higher in workers exposed to urban pollution (45-48).

A non-uniform assessment of both time of exposure to pollution of urban workers, sometimes not even mentioned, and of values of occupational exposure (environmental monitoring and / or organic) is a further problem. With the exception of Sardelli and Zhang who quoted environmental measures [Sardelli P et al., 1995; Zhang W et al., 1994] and Volpino, Tomei and Sancini who evaluated biological indicators (Sancini A et al., 2010; Tomei F et al., 2004, Volpino P et al., 2004), other authors recruited subjects only considering their work task, simply monitoring the exposure on the base of questionnaires or assuming Mormontoy (Mormontoy W et al., 2006) that traffic police officers are exposed to pollution from vehicular traffic.

Therefore, considering data from the scientific literature, related to the general population, which impute adverse cardiovascular effects to urban pollution and given the data emerging from our meta-analysis on population occupationally exposed, we believe it very important to carry on research occupationally exposed groups. To increase the reliability of the parameters relating to the effects of urban pollution on the cardiovascular system, studies should pay particular attention to procedures ascertaining level and type of pollutants, duration and terms of exposure, age of the subjects evaluated, type of job and presence of other environmental stressors, as well as personal ones, that can affect cardiovascular function, such as smoking, incorrect eating habits and excess fat mass (49).

References

Articles marked with an asterisk are those used for the meta-analysis

1. Brunekreef B, Holgate ST. Air pollution and health. *Lancet* 2002; 360: 1233-1242.
2. Hassing HC, Twickler TB, Kastelein JJ, et al. Air pollution as noxious environmental factor in the development of cardiovascular disease. *Neth J Med* 2009; 67: 116-121.
3. Brook RD. Cardiovascular effects of air pollution. *Clinical Science* 2008; 115: 175-187.
4. Bhatnagar A. Environmental cardiology: studying mechanistic links between pollution and heart disease. *Circ Res* 2006; 99 (7): 692-705.
5. Hoffmann B, Moebus S, Stang A, et al. Heinz Nixdorf RECALL Study Investigative Group. Residence close to high traffic and prevalence of coronary heart disease. *Eur Heart J* 2006; 27 (22): 2696-702.
6. Pope CA 3rd, Burnett RT, Thurston GD, et al. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. *Circulation* 2004; 109 (1): 71-7.
7. Dockery DW. Epidemiologic evidence of cardiovascular effects of particulate air pollution. *Environ Health Perspect* 2001; 109 (Suppl 4): 483-486.
8. Peters A, Dockery DW, Muller JE, et al. Increased particulate air pollution and the triggering of myocardial infarction. *Circulation* 2001a; 103: 2810-2815.
9. Peters A, von Klot S, Heier M, et al. Exposure to traffic and the onset of myocardial infarction. *N Engl J Med* 2004; 1: 1721-1730.
10. Katsouyanni K, Touloumi G, Samoli E, et al. Confounding and effect modification in the short-term effects of ambient particles on total mortality: results from 29 European cities within the APHEA2 project. *Epidemiology* 2001; 12: 521-531.

11. Mills NL, Donaldson K, Hadoke PW, et al. Adverse cardiovascular effects of air pollution. *Nat Clin Pract Cardiovasc Med* 2009; 6: 36-44.
12. *Tomei F, Rosati MV, Baccolo TP, et al. Ambulatory (24 Hour) Blood Pressure Monitoring in Police Officers. *J Occup Health* 2004; 46: 235-243.
13. *Volpino P, Tomei F, La Valle C, et al. Respiratory and cardiovascular function at rest and during exercise testing in a healthy working population: effects of outdoor traffic air pollution. *Occup Med* 2004; 54: 457-482.
14. *Tomao E, Tiziana PB, Rosati V, et al. The effects of air pollution on the lipid balance of traffic police personnel. *Ann Saudi Med* 2002; 22 (5-6): 287-290.
15. Hoek G, Brunekreef B, Goldbohm S, et al. Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. *Lancet* 2002; 360: 1203-1209.
16. Papanikolaou NC, Hatzidaki EG, Belivanis S, et al. Lead toxicity update. A brief review. *Med Sci Monit* 2005; 11: 329-336
17. Ademuyiwa O, Ugbaja RN, Idumebor F, et al. Plasma lipid profiles and risk of cardiovascular disease in occupational lead exposure in Abeokuta, Nigeria. *Lipids Health Dis* 2005; 4: 19.
18. Al-Saleh I, Shinwari N, Mashhour A, et al. Is lead considered as a risk factor for high blood pressure during menopause period among Saudi women? *Int J Hyg Environ Health* 2005; 208: 341-56.
19. Karita K, Yano E, Dakeishi M, et al. Benchmark dose of lead inducing anemia at the workplace. *Risk Anal* 2005; 25: 957-962.
20. Eibensteiner L, Del Carpio Sanz A, Frumkin H, et al. Lead exposure and semen quality among traffic police in Arequipa, Peru. *Int J Occup Environ Health* 2005; 11: 161-166.
21. Khalil N, Wilson JW, Talbott EO, et al. Association of blood lead concentrations with mortality in older women: a prospective cohort study. *Environ Health* 2009; 8: 15.
22. Maitre A, Bonnetterre V, Huillard L, et al. Impact of urban atmospheric pollution on coronary disease. *Eur Heart J* 2006; 27 (19): 2275-84.
23. Leon Bluhm G, Berglind N, Nordling E, et al. Road traffic noise and hypertension. *Occup Environ Med* 2007; 64: 122-6.
24. Tomei G, Anzani MF, Casale T, et al. Extra-auditory effects of noise. *G Ital Med Lav Ergon* 2009; 31 (1): 37-48.
25. Everitt BS, Howell DC. *Encyclopaedia of statistics in behavioural science*. Chichester, West Sussex (UK): John Wiley and Sons, Ltd 2005.
26. Meta-analysis of Observational Studies in Epidemiology. A proposal for reporting. Consensus Statement. *JAMA*, April 19, 2000 – Vol 283, No. 15.
27. *Biava PM. Indagine epidemiologica sulle condizioni di salute dei vigili urbani di Milano in rapporto all'inquinamento da traffico veicolare. *Med Lav* 1992; 83 (3): 249-258.
28. *Bigert C, Gustavsson P, Hallqvist J, et al. Myocardial Infarction Among Professional Drivers. *Epidemiology* 2003; 14: 333-339.
29. *Cervone M, Pavone D, Tracanna A, et al. Sottopopolazioni linfocitarie nei vigili urbani di Pescara (studio preliminare). In Atti 56° Congresso Nazionale della Società Italiana di Medicina del Lavoro e Igiene Industriale. Venezia 21- 23 October 1993, Vol II: 731-734.
30. *Hedberg GE, Jacobsson KA, Janlert U, et al. Risk indicators of ischemic heart disease among male professional drivers in Sweden. *Scand J Work Environ Health* 1993; 19: 326-33.
31. *Mormontoy W, Gastañaga C, Gonzales GF, et al. Blood lead levels among police officers in Lima and Callao, 2004. *Int J Hyg Environ Health* 2006; 209: 497-502.
32. *Pala K, Akis N, Izgi B, et al. Blood lead levels of traffic policemen in Bursa, Turkey. *Int J Hyg Environ Health* 2002; 205: 361-365.
33. *Sakata S, Shimizu S, Ogoshi K, et al. Inverse relationship between serum erythropoietin and blood lead concentrations in Kathmandu tricycle taxi drivers. *Int Arch Occup Environ Health* 2007; 80: 342-345.
34. *Sancini A, Palermo P, Di Giorgio V, et al. Cardiovascular parameters in workers exposed to urban pollutions. *G Ital Med Lav Ergon* 2010 Jan-Mar; 32 (1): 32-9.

35. *Sardelli P, D'Aniello MA, Padula M, et al. Sorveglianza sanitaria e rilevazione del rischio ambientale in un campione di vigili urbani di Napoli. In Atti 58° Congresso SIMLII. Bologna 11-14 October 1995, 1087-1091.
36. *Wang PD. Coronary heart disease risk factors in urban bus drivers. Public health. 2001; 115: 261-264.
37. *Zefferino R, Facciorusso A, Lasalvia M, et al. Salivary markers of work stress in an emergency team of urban police (1 degree step). G Ital Med Lav Erg 2006; 28: 472-477.
38. *Zefferino R, L'Abbate N, Facciorusso A, et al. Assessment of heart rate variability (HRV) as a stress index in an emergency team of urban police. G Ital Med Lav Ergon 2003; 25: 167-169.
39. *Zhang W, Zhang GG, He HZ, Bolt HM. Early health effects and biological monitoring in persons occupationally exposed to tetraethyllead. Int Arch Occup Environ Health 1994; 65: 395-399.
40. Borenstein M, Hedges LV, Higgins J, et al. Introduction to metaanalysis. Chichester, West Sussex (UK): John Wiley and Sons, Ltd 2009.
41. Urch B, Silverman F, Corey P, et al. Acute blood pressure responses in healthy adults during controlled air pollution exposures. Environ Health Perspect. 2005; 113: 1052-1055.
42. Folino AF, Scapellato ML, Canova C, et al. Individual exposure to particulate matter and the short term arrhythmic and autonomic profiles in patients with myocardial infarction. European Heart Journal 2009; 30: 1614-1620.
43. Sun Q, Hong X, Wold LE. Cardiovascular effects of ambient particulate air pollution exposure. Circulation 2010; 121 (25): 2755-65.
44. Twickler M, Iinga-Thie G, Cramer MJ. Trojan Horse Hypothesis: Inhaled Airborne Particles, Lipid Bullets, and Atherogenesis. JAMA, May 24/31, 2006 - Vol 295, No. 20
45. Winkleby MA, Ragland DR, Syme SL. Self-reported stressors and hypertension: evidence of an inverse association. Am J Epidemiol 1988; 127: 124-134.
46. Schnall PL, Pieper C, Schwartz JE, et al. The relationship between job strain, workplace diastolic blood pressure, and left ventricular mass index. Results of a case-control study. JAMA 1990; 263: 1929-1935.
47. Albright CL, Winkleby MA, Ragland DR, et al. Job strain and prevalence of hypertension in a biracial population of urban bus drivers. Am J Public Health 1992; 82 (7): 984-989.
48. Nyklíček I, Vingerhoets JJ, Van Heck GL. Hypertension and objective and self-reported stressor exposure: a review. J Psychosom Res 1996; 40: 585-601.
49. Andreozzi P, Viscogliosi G, Servello A, et al. Predictive medicine in Cardiovascular Diseases. What next? Prevent Res 2011; 1 (1): 53-59.

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