Appendix 1

Health Impact Assessment of Outdoor Air Pollution

SELECTION OF OUTCOMES AND EXPOSURE RESPONSE FUNCTIONS FOR HEALTH IMPACT ASSESSMENT OF PARTICLES AND OZONE

Review Of The Evidence

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INTRODUCTION

During the last 20 years there has been a growing evidence that current air pollution (AP) levels in Europe are associated with measurable health effects. It has also been reported that the health consequences of air pollution exposure are not equally spread among the population and that there are groups at particular risk, such as children (Schwartz J, 2004).

The special vulnerability and susceptibility of children with respect to AP exposure is related to their characteristics different from adults: lung and immune system not completely developed, incomplete metabolic systems, high rates of respiratory infections and different activity patterns.

Health Impact Assessment (HIA) of Air Pollution can be an interesting input for decision making in environmental policies. Calculating the impact of AP on health outcomes such as the number of deaths, changes in life expectancy, hospital admissions and other morbidity outcomes enables to assess both the actual impact of current pollution and the expected benefice of reducing it to certain levels. APHEIS (Air pollution and Health: an European Information System) carried out a HIA in 26 European cities, and calculated for suspended particles, the number of attributable deaths, hospital admissions and reduction in life expectancy in the general population (Apheis, 2004). Yet, few attempts have been made to evaluate in Europe the specific impact of AP in children.

Workpackage 5 of the ENHIS programme aims at evaluating the health impact (HI) of AP with a special focus in children.

This draft report summarises the review carried out to select health outcomes in children associated with suspended particles and ozone, and health outcomes in adults associated with ozone (for suspended particles-adults/general population see Apheis 3 findings www.apheis.net).

OBJECTIVES

Main objective:

To identify health outcomes for which the current scientific knowledge allows health impact assessment of particles (children) and ozone (children and adults)

Specific objectives:

- To select published studies specifying estimates of concentration response functions by health outcome and age group
- To extract and synthesise the information gathered.
- To choose the concentration response functions suitable for its use in WP5 of ENHIS project

METHODS

Due to the amount of new scientific information on air pollution and health effects published during the last decade, it is beyond the scope of ENHIS-WP5 to review primary scientific literature. Therefore, we have focused on results of systematic reviews and assessments of expert panels. We have greatly benefited from the WHO project *Systematic Review of Health Aspects of Air Quality in Europe,* especially from the report on 'Meta-analysis of time series studies and panel studies of particulate matter (PM) and ozone (O_3)' (Anderson, 2004), and the assessment about causality made by the experts panel of 'the review of health impact of air pollution on children (WHO, 2004).

For gathering the information, we checked the websites and the reports of the World Health Organisation and the European Commission on air pollution and health effects, and carried out a search on Medline for 'meta-analysis + air pollution', ' air pollution + dose response', 'systematic review + air pollution', for the years 2003 and 2004. We extracted the main outcomes and risk estimates of the resulting publications into a first draft table, which was checked by the group of experts of ENHIS-WP5. As a result of their input, we added 5 new references into the table and included the Californian Air Resources Board (CARB) website as an information source.

To select (the most) suitable estimates for HIA we observed the following criterion:

- It was considered preferable to use summary estimates from meta-analysis

?? Only original studies involving great populations were deemed suitable for HIA

?? Only statistically significant estimates were selected for HIA (In meta-analysis this applies to the summary estimates)

RESULTS

Considering the nature of the undergoing health effects and the feasibility of their use in a HIA, it seems convenient to categorize health outcomes in three groups:

?? Mortality outcomes. Mortality data are usually comparable between countries: Mortality rates are available at the local level and, therefore, local HIA is feasible.

?? Hospital admissions. They are recorded on a regular basis in the countries of the EU. Data are not directly comparable between countries, and might not be available for every participating centre. When the information is available, local rates can be computed. Local assessment, hence, is possible, provided that there are suitable RR available.

?? Other morbidity outcomes. There are a number of health outcomes that have been mainly used in panel studies to assess AP effects: Lower respiratory symptoms, cough, medication use, restricted activity. Generally speaking, those data are not recorded on a regular basis, and hardly can be available at local level. HIA of AP due to physiologic changes in lung function is still more difficult.

Following this scheme, tables 1-3 in annex 1 summarise the main results of 23 studies/reviews. The information included is related to the health outcome, city in which the study has been carried out, contaminant indicator used, resulting RR or OR and some comments on the type of study.

According to the assessment about causality made by the experts panel of 'The Review Of Health Impact of Air Pollution on Children' (WHO, 2004), the children-outcomes for which there is sufficient evidence to infer causal relationship with air pollutants are the followings:

?? Particulate pollution and respiratory deaths in the post-neonatal period.

?? Air pollution and adverse effects on lung function development: both reversible and chronically decreased lung growth, with dearer relationships for particulates and traffic related air pollution.

?? Air pollution and aggravation of asthma, mainly to exposure to particulates and ozone

?? Bronchitis and cough due to particulate exposure

DISCUSION

The number of health outcomes for which there is sufficient evidence of causality and suitable estimates of dose response functions varies greatly depending on the contaminant and the age group involved. In general, there are more studies assessing health effects in the whole population than in specific age groups.

Children and particles

Mortality

Woodruff and Lipfert gave effect estimates of postneonatal mortality from all- and respiratory causes (Lipfert also of infant and neonatal mortality), and Sudden Infant Death syndrome (SIDS). We have considered post-neonatal mortality a suitable outcome for HIA, as causality has been reported to be sufficient for post-neonatal respiratory mortality. Besides post-neonatal mortality can be a better outcome to mirror the impact of AP, rather than neonatal mortality in which death causes not directly related to newborn's exposure to environmental pollution are bound to be more important.

A recently published meta-analysis (Lacasaña, 2005) has provided combine estimates for both acute and chronic exposure effects of PM_{10} on postneonatal mortality for all- and respiratory causes. Highly consistent results were found regardless of the different study designs used. The summary estimate of the postneonatal mortality increase due to chronic exposures to 10 $\mu g/m^3$ of PM_{10} is 5%, whereas for acute exposure is 3%. In other words, short and long term effects are quite the same in the case of the deaths below 1 yr.

For the purpose of the HIA the most reliable estimates may be the results from Lacasaña's meta-analysis for all and respiratory causes, and Woodruff's estimate for SIDS for being an original research based on a very large population results (table 1). We propose HIA to be based on annual mean levels of PM_{10}, because this indicator fits best those used in these studies

Hospital admissions:

Anderson's meta-analysis did not produce any statistically significant summary results. They provide a summary RR estimate based on three studies for respiratory hospital admissions in 0-14 yr children [1.010 (0.998-1.021) for 10 $\mu g/m^3$ increase in PM_{10} daily Mean]

Other morbidity outcomes

Summary RR estimates per 1 $\mu g/m^3$ increase in PM_{10} were calculated for 5-17 yr old children by Ward and Ayres for lower respiratory symptoms [1.004 (1.002-1.005)], cough [1.004 (1.002-1.006)] and changes in peak expiratory flow. On the other hand Anderson's meta-analysis yielded a positive but statistically no significant estimate for medication use by children 5-15 yr old with asthma [RR 1.005 (0.981-1.029) for 10 $\mu g/m^3$ increase in PM_{10}] and a summary estimate smaller than 1 [0.999 (0.987-1.011) for 10 $\mu g/m^3$ increase in PM_{10}] for cough in symptomatic children between 5-15 yrs

The lack of agreement between results prevents their use in HIA.

Children and ozone

The relationships between ozone and most of the outcomes have not been clearly shown.

Mortality

The time-series study of Loomis, conducted in Mexico DF, reported statistically significant and positive RR estimates [1.0278 (1.0029-1.0526) for 10 ppb increase in O_3 daily levels]. Ha, also in a time series study, found a negative association between ozone levels and total postneonatal mortality, and, based on a limited number of deaths, a positive association with postneonatal respiratory mortality [Respectively, 1.226 (0.588-2.558) and 0.892 (0.843-0.994) for 16.1 ppb increase in 8-hr mean of O_3).

The lack of agreement between results prevents their use in HIA.

Hospital admissions

Anderson's combined estimate for respiratory admissions in children 0-14 yr, though based only on 3 studies, was <1 and statistically no significant [RR=0.999 (0.987-1.012) for 10 $\mu g/m^3$ increase in 8-hr mean of O_3]. In Canada, Burnett found positive and statistically significant results in 0-2 yr children [RR=1.35 (1.19-1.52) for 45 ppb increase in ozone max hourly mean]

The lack of agreement between these results prevents their use for HIA.

Other morbidity outcomes

CARB provided a meta-estimate for emergency room visits for asthma in people under 18 yrs based on 4 studies (RR=1.0231 (1.0134-1.0329) for 10 ppb increase in maximum hourly O_3 levels]. For the rest of morbidity outcomes in annex 1- table 2 the scientific knowledge is insufficient for HIA.

Adults/General Population and ozone

Mortality

Anderson's meta-analysis, Aphea2 and Bell's study give meaningful results. Concordance between them is quite high, though estimates tend to be bigger in Europe than in the USA. Estimates for all cause mortality from Anderson's meta-analysis are not statistically significant, while Aphea2 (Gryparis, 2004) gives statistically significant estimates for total, cardiovascular and respiratory mortality for the summer period.

Aphea results (not included in Anderson's metaanalysis) are deemed to be the most adequate for HIA within ENHIS project.

Hospital admissions

Anderson's combined estimates for respiratory admissions in 15-64 yr and > 64 yr groups are statistically no significant [RR = 1.001 (0.991-1.012), and 1.005 (0.998-1.012) for 10 $\mu g/m^3$ increase in max 8 hr O_3 levels, respectively]

Other morbidity outcomes

Studies reporting other morbidity outcomes are scarce. The results have not been considered suitable for HIA.

EXPOSURE RESPONSE FUNCTIONS SELECTED FOR HEALTH IMPACT ASSESSMENT

Following the methodology explained above, the studies, outcomes and RRs selected as most suitable for HIA are those of table 1:

Table 1: Selected risk estimates for HIA, by study and outcome, for children (ozone and particles) and adults/general population (ozone)

	OUTCOME	POLLUTANT	RR	SOURCE (From ORIGINAL SOURCE)
CHILDREN - PARTICLES				
	Total postneonatal mortality (1 month-1 year)	PM_{10} Annual Mean	RR=1.048 (1.022-1.075) ?10µg/m^3	Lacasaña et al 2005
	Postneonatal respiratory mortality ICD9 460-519 ICD10 J00-J99	PM_{10} Annual Mean	RR=1.216 (1.102-1.342) ?10µg/m^3	Lacasaña et al 2005
	Postneonatal Sudden Infant Death Syndrome (SIDS) mortality (normal birth weight =2500g) ICD9 798.0 –ICD10 R95	PM_{10} Annual Mean	Adjusted Odds Ratio AOR=1.12 (1.07-1.17) ?10µg/m^3	Woodruff et al. 1997
	Cough	PM_{10} Daily Mean	OR=1.041 (1.020-1.062) ?10µg/m^3	Ward & Ayres 2004
	Lower respiratory symptoms LRS	PM_{10} Daily Mean	OR=1.041 (1.020-1.051) ?10µg/m^3	Ward & Ayres 2004
CHILDREN – OZONE				
	Emergency room visits for asthma <18 Y ICD9 493, ICD10 J45 J46	Ozone Maximum 1 h	RR=1.0116 (1.0067-1.0165) ?10µg/m^3	CARB 2004
ADULTS/GENERAL POPULATION				
	Total mortality all causes ICD9 <800 ICD10 A00-R99	Ozone Maximum 8 h Summer	RR= 1.0031 (1.0017-1.0052) ?10µg/m^3	Gryparis et al 2004 (APHEA 2)
	Respiratory mortality ICD9 460-519 ICD10 J00-J99	Ozone Maximum 8 h Summer	RR= 1.0113 (1.0074-1.0151) ?10µg/m^3	Gryparis et al 2004 (APHEA 2)
	Cardiovascular mortality ICD9 390-459 ICD10 I00-I99	Ozone Maximum 8 h Summer	RR= 1.0046 (1.0022-1.0073) ?10µg/m^3	Gryparis et al 2004 (APHEA 2)

For a question of coherence with mortality findings, it was decided, with the experts' advice, to include RRs for hospital admissions in the health impact assessment calculations, even if they were not statistically significant. More concretely, it was decided that if there was not any new RR published by the time of making the calculations, the RRs for respiratory hospital admissions from Anderson's meta-analysis (Anderson R, 2004) could be used although they were not statistically significant (see Table 2). The rationale for that is that if there is sufficient evidence to accept a causal relationship between air pollution and respiratory mortality - both in children-PM and adults-O_3- we should easily accept that there will also be

an impact on hospital admissions. One explanation for the not statistically significant findings for respiratory hospital admissions could be an insufficient statistical power of the studies.

Table 2: Complementary risk estimates for HIA on respiratory hospital admissions, by study, for children (particles) and adults (ozone)

	OUTCOME	POLLUTANT	RR	SOURCE
CHILDREN - PARTICLES				
	Respiratory hospital admissions 0-14 Y ICD9 460-519 ICD10 J00-J99	*PM_{10}* Daily Mean	*RR= 1.010 (0.998-1.021) ?10µg/m³*	*Anderson 2004*
ADULTS/GENERAL POPULATION				
	Hospital respiratory admissions 15-64 Y ICD9 460-519 ICD10 J00-J99	*Ozone Maximum 8 h*	*RR=1.001 (0.991-1.012) ?10µg/m³*	*Anderson et al 2004*
	Hospital respiratory admissions >64 Y ICD9 460-519 ICD10 J00-J99	*Ozone Maximum 8 h*	*RR=1.005 (0.998-1.012) ?10µg/m³*	*Anderson et al 2004*

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ANNEX 1

Table 1. CHILDREN AND PARTICLES: Main characteristics of reviewed studies identified.

MORTALITY

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (From ORIGINAL SOURCE)	COMMENTS
Total infant mortality	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.12 (1.09-1.15) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)
Total infant mortality	Federal District of Mexico	$PM_{2.5}$ 27,4µg/m^3 (SD=10,5) 0–6 days before death	Adjusted Rate Ratio ARR=1.069 (1.025-1.113) ?10µg/m^3 lag 3-5 days	Glinianaia et al 2004 (From Loomis et al 1999)	Time series. 2798 infant deaths. (40 %< 28d) and (60%=28d and <1Y). Estimation by Poisson regression controlling for the Mean Temperature of the 3 days before death and nonparametrically smoothed periodic cycles. Other: relative humidity, GAM, adjust for extra-Poisson variation. Also adjusted for other pollutants examined (O_3, NO_2), but the results are not given
Total infant mortality ICD-9 (excluded external causes >E800)	Federal District of Mexico	$PM_{2.5}$ 27,4µg/m^3 (SD=10,5) (w=3days)+ (3-day-lag)	Adjusted Odds Ratio AOR=1.0687 (1.0248-1.1126) ?10µg/m^3	Loomis et al 1999	Time series. 2798 infant deaths. (40 %< 28d) and (60%=28d and <1Y). Estimation by Poisson regression controlling for the Mean Temperature of the 3 days before death and nonparametrically smoothed periodic cycles. Other: relative humidity, GAM, adjust for extra-Poisson variation. Also adjusted for other pollutants examined (O_3, NO_2), but the results are not given
Child and infant mortality <5 Y	World	PM_{10}	RR=1.0166 (1.0034-1.0300) ?10µg/m^3	Valent et al 2004	Arithmetic mean of RR Conceicao (Brazil) Loomis (Mexico) Saldiva (Brazil) Gouveia (Brazil) Ostro (Bangkok)
Infant respiratory mortality ICD-9 460-519 AND 769-770	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.18 (1.11-1.26) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)
Infant respiratory mortality ICD-9 460-519	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.14 (0.96-1.35) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)
Total neonatal mortality	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.13 (1.09-1.18) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)
Neonatal respiratory mortality ICD-9 460-519 AND 769-770	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.17 (1.09-1.26) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (From ORIGINAL SOURCE)	COMMENTS
Total postneonatal mortality	Czech Republic/USA	PM_{10}	RR=1.048 (1.022-1.075) ?10µg/m^3	Lacasaña et al 2005	Chronic exposure. Meta-analysys of 3 studies : Woodruff et al 1997 (Cohorts), Bobak & Leon 1992, 1999 (Geographical)
Total postneonatal mortality	USA	PM_{10} 28,4µg/m^3 (range: 18,0-44,8) PM_{10} levels for the first two months of life	Adjusted Odds Ratio AOR=1.04 (1.02-1.07) ?10µg/m^3	Woodruff et al 1997	Cohorts. 86 US metropolitan statistical areas. 4M infants (1989-1991). Adjust for potential confounding variables: maternal education, maternal race, parental maritus status, maternal smoking during pregnancy. Infants with missing information were excluded. Logistic model included: Temperature, Date of birth.
Total postneonatal mortality	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.10 (1.04-1.15) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)
Total postneonatal mortality	Seoul	PM_{10} Daily mean (69,2µg/m^3)	RR= 1.03 (1.02-1.04) ?10µg/m^3	Glinianaia et al 2004 (From Ha et al 2003)	Time series 1.045 postneonatal deaths. Adjustment from seasonality, temperature, relative humidity, day of week
Total postneonatal mortality	Mexico City/Seoul	PM_{10}	RR=1.033 (1.024-1.043) ?10µg/m^3	Lacasaña et al 2005	Acute exposure. Meta-analysis of 2 time series studies: Loomis 1999 and Ha 2003
Postneonatal respiratory mortality	Czech Republic/USA	PM_{10}	RR=1.216 (1.102-1.342) ?10µg/m^3	Lacasaña et al 2005	Chronic exposure. Meta-analysys of 3 studies : Woodruff et al 1997 (Cohorts), Bobak & Leon 1992, 1999 (Geographical)
Postneonatal respiratory mortality ICD-9 460-519 AND 769-770	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.21 (1.05-1.39) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)
Postneonatal respiratory mortality (low birth weight =2500g) ICD-9 460-519	USA	PM_{10} 28,4µg/m^3 (range: 18,0-44,8) PM_{10} levels for the first two months of life	Adjusted Odds Ratio AOR=1.05 (0.91-1.22) ?10µg/m^3	Woodruff et al 1997	Cohorts. 86 US metropolitan statistical areas. 4M infants (1989-1991). Adjust for potential confounding variables: maternal education, maternal race, parental maritus status, maternal smoking during pregnancy. Infants with missing information were excluded. Logistic model included: Temperature, Date of birth.
Postneonatal respiratory mortality (normal birth weight=2500g) ICD-9 460-519	USA	PM_{10} 28,4µg/m^3 (range: 18,0-44,8) PM_{10} levels for the first two months of life	Adjusted Odds Ratio AOR=1.20 (1.06-1.36) ?10µg/m^3	Woodruff et al 1997	Cohorts. 86 US metropolitan statistical areas. 4M infants (1989-1991). Adjust for potential confounding variables: maternal education, maternal race, parental maritus status, maternal smoking during pregnancy. Infants with missing information were excluded. Logistic model included: Temperature, Date of birth.
Postneonatal respiratory mortality	Seoul	PM_{10} Daily mean	RR= 1.18 (1.14-1.21) ?10µg/m^3	Glinianaia et al 2004 (From Ha et al 2003)	Time series 1.045 postneonatal deaths. Adjustment from seasonality, temperature, relative humidity, day of week

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (From ORIGINAL SOURCE)	COMMENTS
Postneonatal Sudden Infant Death Syndrome (SIDS) mortality (normal birth weight =2500g) ICD9 798.0	USA	PM_{10} 28,4µg/m^3 (range: 18,0-44,8) PM_{10} levels for the first two months of life	Adjusted Odds Ratio AOR=1.12 (1.07-1.17) ?10µg/m^3	Woodruff et al 1997	Cohorts. 86 US metropolitan statistical areas. 4M infants (1989-1991). Adjust for potential confounding variables: maternal education, maternal race, parental maritus status, maternal smoking during pregnancy. Infants with missing information were excluded. Logistic model included: Temperature, Date of birth.
Sudden Infant Death Syndrome (SIDS) mortality	USA	PM_{10} Annual mean	Adjusted Odds Ratio AOR=1.15 (1.07-1.24) ?10µg/m^3	Glinianaia et al 2004 (From Lipfert et al 2000)	Cross-sectional 1443768 births and 13041 infant deaths (8362 neonatal deaths; 4679 postneonatal deaths). 2354 infant deaths due to respiratory causes, 1918 SIDS deaths. Socio-economic factors, mother's smoking, month of birth. Not adjusted for other pollutants examined (SO_2, CO, SO_4)

MORBIDITY

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (From ORIGINAL SOURCE)	COMMENTS
Respiratory hospital admissions 0-14 Y	Europe	PM_{10}	RR= 1.010 (0.998-1.021) ?10µg/m^3	Anderson 2004	WHO Meta-analysis. Time series 3 cities, population of 10 million people
Cough in symptomatic children 5-15 Y	Europe	PM_{10}	OR= 0.999 (0.987-1.011) ?10µg/m^3	Anderson 2004	WHO Meta-analysis. Panel studies
Consultation for asthma 0-14 Y	London	PM_{10}	RR=1.025 (1.000-1.052) ?10µg/m^3	Hajat et al 1999	
Consultation for Upper respiratory diseases (URD) excluding allergic rhinitis 0-14 Y	London	PM_{10}	RR=1.007 (0.999-1.014) ?10µg/m^3	Hajat et al 2002	
Medication use by children with asthma 5-14 Y	Europe	PM_{10}	OR=1.005 (0.981-1.029) ?10µg/m^3	Anderson 2004	WHO Meta-analysis. 31 studies
Change in PEF (Peak Expiratory Flow) (L/min) 5-17 Y	World	PM_{10} Daily Mean	-0.033 (-0.047-0.019) (L/min) ?1µg/m^3	Ward & Ayres 2004	Meta-analysis. Pooled effect estimate. Random effects model. 13 studies with different age range (5-17 Y). Symptomatic and non-symptomatic children
Cough 5-17 Y	World	PM_{10} Daily Mean	OR=1.004 (1.002-1.006) ?1µg/m^3	Ward & Ayres 2004	Meta-analysis. Pooled effect estimate. Random effects model. 13 studies with different age range (5-17 Y). Symptomatic and non-symptomatic children
Lower respiratory symptoms LRS 5-17 Y	World	PM_{10} Daily Mean	OR=1.004 (1.002-1.005) ?1µg/m^3	Ward & Ayres 2004	Meta-analysis. Pooled effect estimate. Random effects model. 13 studies with different age range (5-17 Y). Symptomatic and non-symptomatic children

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (From ORIGINAL SOURCE)	COMMENTS
Change in PEF (Peak Expiratory Flow) (L/min) 5-17 Y	World	$PM_{2.5}$	-0.144 (-0.243-0.044) (L/min) ?1µg/m^3	Ward & Ayres 2004	Meta-analysis. Pooled effect estimate. Random effects model. 13 studies with different age range (5-17 Y). Symptomatic and non-symptomatic children
Cough 5-17 Y	World	$PM_{2.5}$	OR=1.010 (1.005-1.016) ?1µg/m^3	Ward & Ayres 2004	Meta-analysis. Pooled effect estimate. Random effects model. 13 studies with different age range (5-17 Y). Symptomatic and non-symptomatic children
Lower respiratory symptoms LRS 5-17 Y	World	$PM_{2.5}$	OR=1.009 (1.002-1.016) ?1µg/m^3	Ward & Ayres 2004	Meta-analysis. Pooled effect estimate. Random effects model. 13 studies with different age range (5-17 Y). Symptomatic and non-symptomatic children

Table 2. CHILDREN AND OZONE: Main characteristics of reviewed studies identified.

MORTALITY

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (FROM ORIGINAL SOURCE)	COMMENTS
Total infant mortality ICD-9 (excluded external causes >E800)	Federal District of Mexico	Ozone Daily mean 44,1ppb (SD=15,7) Windows of 1 to 4 days duration, beginning from 0 to 5 days before death	1.0278 (1.0029-1.0526) ?10ppb 3 day lag	Loomis et al 1999	Time series. 2798 infant deaths. (40 %< 28d) and (60%=28d and <1Y). Estimation by Poisson regression controlling for the Mean Temperature of the 3 days before death and nonparametrically smoothed periodic cycles. Other: relative humidity, GAM, adjust for extra-Poisson variation. Also adjusted for other pollutants examined (O_3, NO_2), but the results are not given
Postneonatal respiratory mortality	Seoul	Ozone Mean 8 h (21,2ppb)	RR= 1.226 (0.588-2.558) ?16.1ppb	Ha et al 2003	Time series 71 deaths. Adjustment from seasonality, temperature, relative humidity, day of week
Total postneonatal mortality	Seoul	Ozone Mean 8 h (21,2ppb)	RR= 0.892 (0.843-0.944) ?16.1ppb	Ha et al 2003	Time series 1045 deaths. Adjustment from seasonality, temperature, relative humidity, day of week

MORBIDITY

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (FROM ORIGINAL SOURCE)	COMMENTS
Hospital respiratory admissions 0-14 Y	Europe	Ozone Maximum 8-h	RR= 0.999 (0.987-1.012) ?10µg/m^3	Anderson et al 2004	WHO Meta-analysis. Time series Meta-analysis of 3 estimates. Protective effect. Non significant
Hospital respiratory admission 0-2 Y (ICD-9 493, 466, 464.4, 480-486)	Canada	Ozone Maximum 1 h May-August	RR=1,35 (1,19-1,52) ?45 ppb	Burnett et al 2001	15-year period time-series study. Adjusted for other ambient air pollutants and weather.
Emergency room visits for asthma <18 Y	North America	Ozone Maximum 1 h	RR=1,0231 (1,0134-1,0329) ?10 ppb	CARB 2004	Meta-analytic result from 4 studies: Tolbert et al 2000, Friedman et al 2001, Jaffe et la 2003, and Romieu et al 1995
Cough in symptomatic children 7-15 Y	Paris	Ozone	OR= 1.040 (0.920-1.176) ?10µg/m^3	Anderson et al 2004 (From Just et al 2002)	1 Panel study
Consultation for allergic rhinitis ICD 9-477 0-14 Y	London	Ozone	RR=1.082 (1.051-1.116) ?10µg/m^3 Lag 0-3	Hajat et al 2002	
Medication use by children with asthma 5-14 Y	Paris	Ozone	OR=1.41 (1.05-1.89) ?10µg/m^3	Anderson et al 2004 (From Just et al 2002)	1 Panel study
School absences 5-17 Y	California	Ozone Maximum 8 h	62,9% (18,4-124,1) ?20 ppb	Gilliland et al 2001	2081 4th grade school 9-10 Y children. 12 communities included in "Children's health study". Active surveillance system. January-June 1996. Time-Series regression model.

Table 3. ADULTS/GENERAL POPULATION AND OZONE: Main characteristics of reviewed studies identified.

MORTALITY

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (FROM ORIGINAL SOURCE)	COMMENTS
Total mortality all causes	Europe	Ozone Maximum 8 h	RR=1.003 (1.001-1.004) ?10µg/m^3	Anderson et al 2004	WHO Meta-analysis. Non-adjusted for publication bias.
Total mortality all causes ICD 9 <800	Europe	Ozone Maximum 8 h Summer	RR= 1.0031 (1.0017-1.0052) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Total mortality all causes ICD 9 <800	Europe	Ozone Maximum 8 h Winter	RR= 1.0012 (0.988-1.0037) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Total mortality all causes ICD 9 <800	USA	Ozone Maximum 8 h	RR=1.0064 (1.0041-1.0086) ?15ppb	Bell et al 2004	Time series Mean RR of 95 urban communities
Total mortality all causes 2-64 Y	Seoul	Ozone Maximum 8 h	RR= 0.997 (0.999-1.995) ?16.1µg/m^3	Ha et al 2003	Time series 67597 deaths. Adjustment from seasonality, temperature, relative humidity, day of week
Total mortality all causes >65 Y	Seoul	Ozone Maximum 8 h	RR= 1.021 (1.019-1.022) ?16.1µg/m^3	Ha et al 2003	Time series 100316 deaths. Adjustment from seasonality, temperature, relative humidity, day of week
Total mortality all causes ICD 9 <800	Europe	Ozone Maximum 1 h Summer	RR= 1.0033 (1.0017-1.0052) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Total mortality all causes ICD 9 <800	Europe	Ozone Maximum 1 h Winter	RR= 1.0009 (0.975-1.0028) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Total mortality all causes ICD 9 <800	USA	Ozone Maximum 1 h	RR=1.0067 (1.0042-1.0092) ?20ppb	Bell et al 2004	Time series Mean RR of 95 urban communities
Total mortality all causes ICD 9 <800	USA	Ozone Daily mean	RR=1.0052 (1.0027-1.0077) ?10ppb Previous week	Bell et al 2004	Time series Mean RR of 95 urban communities
Total mortality all causes ICD 9 <800	USA	Ozone Daily mean	RR=1.0025 (1.0012-1.0039) ?10 ppb Same day	Bell et al 2004	Time series Mean RR of 95 urban communities
Total mortality all causes ICD 9 <800	USA	Ozone Daily mean	RR=1.0018 (1.0006-1.0030) ?10 ppb Previous day	Bell et al 2004	Time series Mean RR of 95 urban communities

OUTCOME	LOCATION	POLLUTANT	RR	SOURCE (FROM ORIGINAL SOURCE)	COMMENTS
Respiratory mortality All age	Europe	Ozone Maximum 8 h	RR=1.000 (0.996-1.005) ?10µg/m^3	Anderson et al 2004	WHO Meta-analysis. Time series. 12 studies
Respiratory mortality ICD 9 460-519	Europe	Ozone Maximum 8 h Summer	RR= 1.0113 (1.0074-1.0151) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Respiratory mortality ICD 9 460-519	Europe	Ozone Maximum 8 h-winter	RR= 1.0026 (0.950-1.0084) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Respiratory mortality 2-64 Y	Seoul	Ozone Maximum 8 h	RR= 1.098 (1.068-1.130) ?16.1µg/m^3	Ha et al 2003	Time series 2194 deaths. Adjustment from seasonality, temperature, relative humidity, day of week
Respiratory mortality >65 Y	Seoul	Ozone Maximum 8 h	RR= 1.037 (1.026-1.048) ?16.1µg/m^3	Ha et al 2003	Time series 7573 deaths. Adjustment from seasonality, temperature, relative humidity, day of week
Respiratory mortality ICD 9 460-519	Europe	Ozone Maximum 1 h Summer	RR= 1.0113 (1.0062-1.0148) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Respiratory mortality ICD 9 460-519	Europe	Ozone Maximum 1 h-winter	RR= 0.984 (0.933-1.0052) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Cardiovascular mortality All age	Europe	Ozone Maximum 8 h	RR=1.004 (1.003-1.005) ?10µg/m^3	Anderson et al 2004	WHO Meta-analysis. Time series. 13 studies
Cardiovascular mortality ICD 9 390-459	Europe	Ozone Maximum 8 h Summer	RR= 1.0046 (1.0022-1.0073) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Cardiovascular mortality ICD 9 390-459	Europe	Ozone Maximum 8 h-winter	RR= 1.0007 (0.972-1.0041) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Cardiovascular mortality ICD 9 390-459	Europe	Ozone Maximum 1 h Summer	RR= 1.0045 (1.0022-1.0069) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model
Cardiovascular mortality ICD 9 390-459	Europe	Ozone Maximum 1 h-winter	RR= 1.0002 (0.972-1.0030) ?10µg/m^3	Gryparis et al 2004	APHEA 2. Time series Quantitative summary 21 cities Random effects model

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OUTCOME	**LOCATION**	**POLLUTANT**	**RR**	**SOURCE (FROM ORIGINAL SOURCE)**	**COMMENTS**
Hospital respiratory admissions 15-64 Y	Europe	Ozone Maximum 8 h	RR=1.001 (0.991-1.012) ?10µg/m^3	Anderson et al 2004	WHO Meta-analysis
Hospital respiratory admissions >64 Y	Europe	Ozone Maximum 8 h	RR=1.005 (0.998-1.012) ?10µg/m^3	Anderson et al 2004	WHO Meta-analysis
Hospital respiratory admissions all ages Asthma and bronchitis. All ages	USA	Ozone Maximum 1 h	RR=1,0165 (1,0095-1,0231) ?10 ppb	Thurston and Ito 1999	Meta-analysis of 3 studies (Burnett et al 1994, Thurston et al 1994, Burnett et al 1997)
Hospital cardiovascular admissions >64 Y	London	Ozone Maximum 8 h	RR=1.007 (1.002-1.011) ?10µg/m^3	Anderson et al 2004 (From Atkinson et al 1999)	1 estimate
Consultation for allergic rhinitis. 15-64 Y ICD 9-477	London	Ozone Maximum 8 h	RR=1.055 (1.042-1.07) ?10µg/m^3 Lag 0-3	Hajat et al 2002	
Cough in adults with respiratory diseases	Runcom & Widnes UK	Ozone	OR=1.050 (0.910-1.212**)** ?10µg/m^3	Anderson et al 2004 (From Higgins et al 1995)	1 study
Medication use in symptomatic adults	Runcom & Widnes UK	Ozone	OR = 1.440 (1.140-1.810) ?10µg/m^3	Anderson et al 2004 (From Higgins et al 1995)	1 study
Minor restricted activity days (MRADs) 18-64 Y	USA	Ozone Maximum 1 h	0.111% (0.043-0.179) ?1µg/m^3	Ostro ? Rothschil 1989	
Minor restricted activity days (MRADs) 18-64 Y	USA	Ozone Maximum 8 h	1.48% (0.57-2.38) ?10µg/m^3	Ostro ? Rothschil 1989	
Symptom days in general population	USA	Ozone Maximum 8 h	Log OR = 0.00055 (SE 0.00027) ?1ppb	Krupnick et al 1990	