Human health damage characterisation factors for particulate matter emissions to air for application in life cycle analysis

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Empa - Swiss Federal Laboratories for Materials Science and Technology,

Dominic Notter and Hans-Jörg Althaus

6 Literature review of human health effects

Existing LCA methods define PM in very general terms (i.e., total mass of PM). However, this evaluation of PM neglects the highly complex nature and variable health impacts of PM. This literature search aims to develop a more refined description of PM in LCAs that better reflects the contribution of PM to adverse effects than does mass alone. The purpose of the literature review described herein is to identify characteristics of PM that are associated with human health effects in epidemiology studies and that can be incorporated into the LCA methodology.

6.1 A short introduction into odds ratio and relative risk

The relation between particle concentration and health effect is described with relative risks (RR) or odds ratios (OR)[29]. In statistics and mathematical epidemiology, RR is the risk of an event (or of developing a disease) relative to exposure. Relative risk is a ratio of the probability of the event occurring in the exposed group versus a non-exposed (less exposed) group. A RR of 1 means there is no difference in risk between the two groups. An RR of > 1 means the event is more likely to occur in the experimental group than in the control group. As long as the OR is around 1, there is more or less no difference between of RR and OR. When OR is more than 2.5 or less than 0.5 or probability of outcome in the unexposed group is more than 0.1 (10%), a correction should be applied[30, 31]. In this study, values of OR higher than 1.1 and smaller 0.97 were discarded. Thus, in order to simplify the reading of this report all estimates of association with RR and OR are presented as RR only but it is referred to both, RR and OR.

Mean values of RR can be analysed with paired t-test in order to get an answer to the risk differences between the two compared substances. Paired sample t-tests analysis over the 95% CI (of each data-point provided in the literature studies) provides insight into the explained variance of the compared substances. The hypothesis is that the CI for each size class is smaller than CI for PM_{10}. This would support that the variance for the health outcomes is smaller when PM is split in different size classes.

Power analysis can be used to calculate the minimum sample size required so that it is reasonably likely to detect an effect of a given size[32, 33]. Required sample size was calculated for a better interpretation of the analysed results from literature search. The sample size calculation was performed with an online power analysis tool[34] using a Power of 0.8 and a significance level α of 0.05.

6.2 Literature review of epidemiology studies on the association between exposure to particulate matter and human health outcomes

Katherine Clark, Michael Riediker of IST, Lausanne

Dominic Notter, Hans-Joerg Althaus of EMPA, Dübendorf

Background

Airborne particles can come from a variety of sources and contain variable chemical constituents. Some particles are formed by natural processes, such as volcanoes, erosion, sea spray, and forest fires, while other are formed by anthropogenic processes, such as

industrial- and motor vehicle-related combustion, road-related wear, and mining. In general, larger particles (those greater than 2.5 μm) are formed by mechanical processes, while those less than 2.5 μm are formed by combustion processes. The chemical composition of particles is highly influenced by the source: for combustion-related particles, factors such as temperature of combustion, fuel type, and presence of oxygen or other gases can also have a large impact on PM composition. These differences can often be observed at a regional level, such as the greater sulphate-composition of PM in regions that burn coal for electricity production (which contains sulphur) versus regions that do not[35].

Most countries maintain air monitoring networks, and studies based on the resulting data are the most common basis for epidemiology studies on the health effects of PM. Data from these monitoring stations can be used to evaluate the relationship between community-level exposure to ambient particles and health outcomes (i.e., morbidity or mortality from various causes). Respiratory and cardiovascular outcomes are the most commonly assessed, although studies have also considered other related specific outcomes such as diabetes and congenital heart disease.

The data on particle characteristics is usually not very detailed and most often includes some combination of $PM_{2.5}$, PM_{10}, sulphate, and NO_2. Other descriptors that are less commonly found include particle number (ultrafine particles), metal components of PM, local traffic intensity, and EC/OC. Measures of association are usually reported per 10 $\mu g/m^3$ or interquartile range increase in pollutant concentration. As the exposure data are taken from regional monitoring stations, the measurements are not representative of an individual's exposure.

Particle size is an important descriptor for understanding where in the human respiratory system the particles will deposit: as a general rule, smaller particles penetrate to deeper regions of the lungs. Initial studies on the health effects of particulate matter focused on mass of the particles, including either all particles (often termed total suspended particulate or TSP) or PM_{10} (all particles with an aerodynamic diameter less than 10 μm). More recently, studies have considered both PM_{10} and $PM_{2.5}$, with the latter corresponding more directly to combustion-related processes. UFPs are a dominant source of particles in terms of PNC, yet are negligible in terms of mass. Very few epidemiology studies have measured the effect of UFPs on health; however, the numbers of studies on this topic are increasing. In addition to size, chemical composition is of importance when understanding the toxicity of particles. Some studies consider the composition of particles in addition to mass; however this is not common, in part due the cost and labour involved in such analyses.

Methods

A literature review was conducted with the aims of identifying particle characteristics in addition to total mass that can be used to distinguish particle health effects. The literature on particle health effects is vast, and therefore a systematic review was not possible. Rather, priority was given to studies that:

- Were papers or reports of consensus opinions.
- Have had a significant impact on the understanding of human health effects or particles.
- Included a detailed analysis of particle composition or properties.
- Addressed specific sources of particles (i.e., source apportionment studies or studies of acute events [volcanoes, forest fires]).

Toxicology studies were not included. Although such studies play an important role in identifying mode of action and pre-clinical effects, limited efforts were focused on the most human-relevant data.

Results

Mass of $PM_{2.5}$ and PM_{10}:

Mass-based measurements of particles are the most commonly-used measures in epidemiology studies on the effect or particulate matter on health. These measures are most easily and commonly collected, providing a large dataset for conducting such studies. For example, a quick search in PubMed using the search terms 'epidemiology', 'particulate', and 'matter' yields over 7000 hits. A review of all of the literature in this field is not feasible, but targeted reviews of existing health assessments of PM are informative.

The United States Environmental Protection Agency (US EPA) has undertaken perhaps the most thorough assessment of the health effects of particulate matter in their Integrated Scientific Assessment for Particulate Matter[36]. The purpose of this assessment is to support US air quality regulations. This document, of which the most recent 2009 version numbers over 2000 pages, evaluates the existing knowledge available to estimate the effect of PM on human and environmental health, and includes studies on toxicology, epidemiology, controlled human exposure, atmospheric science, and other disciplines. This document provides a detailed analysis of the effects of $PM_{2.5}$ and PM_{10} in particular, however is primarily focused on data relevant to the United States. The sections on epidemiology studies include reviews of hundreds of epidemiology studies, and the conclusions based on these reviews are summarized below.

The EPA ISA states the following regarding the effects of long and short term exposure to $PM_{2.5}$ and PM_{10}. For more details on any individual effect, refer to the source page within the document.

1. Short term effects of $PM_{2.5}$

   Regarding cardiovascular effects of short term exposure to $PM_{2.5}$

   "Epidemiologic studies that examined the effect of $PM_{2.5}$ on cardiovascular emergency department (ED) visits and hospital admissions reported consistent positive associations (predominantly for ischemic heart disease [IHD] and congestive heart failure [CHF]), with the majority of studies reporting increases ranging from 0.5 to 3.4% per 10 $\mu g/m^3$ increase in $PM_{2.5}$. These effects were observed in study locations with mean 24-h average $PM_{2.5}$ concentrations ranging from 7-18 $\mu g/m^3$ (Section 6.2.10)". (p. 2-9)

"The multicity studies evaluated reported consistent increases in cardiovascular mortality ranging from 0.47 to 0.85% in study locations with mean 24-h average $PM_{2.5}$ concentrations above 12.8 μg/m^3 (Table 6-15)". (p. 2-9)

Regarding respiratory effects of short term exposure to $PM_{2.5}$

"Most studies reported effects in the range of ~1% to 4% increase in respiratory hospital admissions and ED visits and were observed in study locations with mean 24-h average $PM_{2.5}$ concentrations ranging from 6.1-22 μg/m^3." (p. 2-10)

"The multicity studies evaluated reported consistent, precise increases in respiratory mortality ranging from 1.67 to 2.20% in study locations with mean 24-h average $PM_{2.5}$ concentrations above 12.8 μg/m^3 (Table 6-15)". (p. 2-10)

Regarding all cause mortality effects of short term exposure to $PM_{2.5}$

"The evaluation of multicity studies found that consistent and precise risk estimates for all-cause (nonaccidental) mortality that ranged from 0.29 to 1.21% per 10 μg/m^3 December 2009 2-10 increase in $PM_{2.5}$ at lags of 1 and 0-1 days. In these study locations, mean 24-h average $PM_{2.5}$ concentrations were 12.8 μg/m^3 and above (Table 6-15)" (p. 2-11)

2. Long term effects of $PM_{2.5}$

Regarding cardiovascular effects of long term exposure to $PM_{2.5}$

"Evidence from toxicological studies provides biological plausibility and coherence with studies of short-term exposure and cardiovascular morbidity and mortality, as well as with studies that examined long-term exposure to $PM_{2.5}$ and cardiovascular mortality. Taken together, the evidence from epidemiologic and toxicological studies is sufficient to conclude that a causal relationship exists between long-term exposures to $PM_{2.5}$ and cardiovascular effects." (p. 2-12)

Regarding respiratory effects of long term exposure to $PM_{2.5}$

"Recent epidemiologic studies conducted in the U.S. and abroad provide evidence of associations between long-term exposure to $PM_{2.5}$ and decrements in lung function growth, increased respiratory symptoms, and asthma development in study locations with mean $PM_{2.5}$ concentrations ranging from 13.8 to 30 μg/m^3 during the study periods (Section 7.3.1.1 and Section 7.3.2.1)…. Collectively, the evidence from epidemiologic and toxicological studies is sufficient to conclude that a causal relationship is likely to exist between long-term exposures to PM and respiratory effects." (p. 2-12)

Regarding mortality effects of long term exposure to $PM_{2.5}$

"The evidence for cardiovascular and respiratory morbidity due to short- and long-term exposure to $PM_{2.5}$ provides biological plausibility for cardiovascular- and respiratory-related mortality. Collectively, the evidence is sufficient to conclude that a causal relationship exists between long-term exposures to $PM_{2.5}$ and mortality." (p. 2-12).

Regarding reproductive and developmental effects of long term exposure to $PM_{2.5}$

"The epidemiologic literature does not consistently report associations between long-term exposure to PM and preterm birth, growth restriction, birth defects or decreased sperm quality. Toxicological evidence supports an association between $PM_{2.5}$ and PM_{10} exposure and adverse reproductive and developmental outcomes, but provide little mechanistic information or biological plausibility for an association between long-term PM exposure and adverse birth outcomes (e.g., low birth weight or infant mortality). New evidence from animal toxicological studies on heritable mutations is of great interest, and warrants further investigation. Overall, the epidemiologic and toxicological evidence is suggestive of a causal relationship between long-term exposures to $PM_{2.5}$ and reproductive and developmental outcomes." (p. 2-13)

Regarding cancer, mutagenicity, and genotoxicity effects of long term exposure to $PM_{2.5}$

"Collectively, the evidence from epidemiologic studies, primarily those of lung cancer mortality, along with the toxicological studies that show some evidence of the mutagenic and genotoxic effects of PM is suggestive of a causal relationship between long-term exposures to $PM_{2.5}$ and cancer." (p. 2-13)

3. Short term effects of $PM_{10-2.5}$

Regarding cardiovascular effects of short term exposure to $PM_{10-2.5}$

"Generally positive associations were reported between short-term exposure to $PM_{10-2.5}$ and hospital admissions or ED visits for cardiovascular causes…. The $PM_{10-2.5}$ associations with cardiovascular hospital admissions and ED visits were observed in study locations with mean 24-h average $PM_{10-2.5}$ concentrations ranging from 7.4 to 13 $\mu g/m^3$. These results are supported by the associations observed between $PM_{10-2.5}$ and cardiovascular mortality in areas with 24-h average $PM_{10-2.5}$ concentrations ranging from 6.1-16.4 $\mu g/m^3$ (Section 6.2.11)." (p. 2-17)

Regarding respiratory effects of short term exposure to $PM_{10-2.5}$

"A number of recent epidemiologic studies conducted in Canada and France found consistent, positive associations between respiratory ED visits and hospital admissions and short-term exposure to $PM_{10-2.5}$ in studies with mean 24-h average concentrations ranging from 5.6-16.2 $\mu g/m^3$ (Section 6.3.8). In these studies, the strongest relationships were observed among children, with less consistent evidence for adults and older adults (i.e., ≥ 65 years). In a large multicity study of older adults, $PM_{10-2.5}$ was positively associated with respiratory hospital admissions in both single and copollutant models with $PM_{2.5}$. In addition, a U.S.-based multicity study found evidence for an increase in respiratory mortality upon short-term exposure to $PM_{10-2.5}$, but these associations have not been consistently December 2009 2-18 observed in single-city studies (Section 6.3.9)." (p. 2-18)

Regarding mortality effects of short term exposure to $PM_{10-2.5}$

"The majority of studies evaluated in this review provide some evidence for mortality associations with $PM_{10-2.5}$ in areas with mean 24-h average concentrations ranging

from 6.1-16.4 μg/m^3. However, uncertainty surrounds the $PM_{10-2.5}$ associations reported in the studies evaluated due to the different methods used to estimate $PM_{10-2.5}$ concentrations across studies (e.g., direct measurement of $PM_{10-2.5}$ using dichotomous samplers, calculating the difference between PM_{10} and $PM_{2.5}$ concentrations). In addition, only a limited number of $PM_{10-2.5}$ studies have investigated potential confounding by gaseous copollutants or the influence of model specification on $PM_{10-2.5}$ risk estimates." (p. 2-19)

With regards to the shape of the concentration-response curve, most of the studies evaluated in the PM ISA supported the use of no threshold log-linear models.

The World Health Organization (WHO) has developed Air Quality Guidelines (AQG) for ambient PM_{10} and $PM_{2.5}$ [37]. These guidelines are primarily based on published analyses of the data from selected epidemiological studies of $PM_{2.5}$ exposure, such as the Harvard Six-Cities study and the American Cancer Society study[38-40]. There are few large epidemiology studies of the effects of $PM_{10-2.5}$, yet it may also be hazardous and is the more widely-used measure of ambient air pollution: therefore, the WHO PM_{10} issued guidelines for PM_{10} that are based on those for $PM_{2.5}$, using a multiplier of 2. (In other words, the ratio of $PM_{2.5}$ to PM_{10} is assumed to be 0.5).

The WHO annual air quality guideline for $PM_{2.5}$ is 10 μg/m^3, a concentration which deciphers the lower range at which significant effects were observed in epidemiologic studies. Interim targets were also issued for countries that could not immediately meet the AQG, however these estimates are associated with higher long term mortality. Based on their mortality estimates associated with different $PM_{2.5}$ levels, the WHO estimate a 6% increase in mortality per long term 10 μg/m^3 increase in $PM_{2.5}$ above 10 μg/m^3 (and likewise 20 μg/m^3 increase in PM_{10}).

The WHO also issued short term (24 hours) air quality guidelines for $PM_{2.5}$ of 25 μg/m^3, which were based on meta-analyses of data from the US and Europe, and found consistent with data from Asia. These were based on the assumption of a 0.5% increase in mortality per 10ug/m^3 increase in daily PM_{10} concentration (and thus 5 μg/m^3 increase in daily $PM_{2.5}$ concentration)[37].

Brook, et al.[41] (2010) published a second scientific statement of the American Heart Association regarding the association between particulate matter and cardiovascular disease. This statement was assembled by a multi-disciplinary group of particulate matter experts that reviewed the previous AHA statement and the evidence that had been published since that statement. The group reviewed and commented on evidence regarding mortality, morbidity, association with specific diseases, biological mechanisms, and susceptible groups. A summary of the statements regarding mortality and morbidity due to PM are presented here in Brook et al.[41].

With regards to time series analysis of short term exposure to PM, "The overall evidence from time-series analyses conducted worldwide since publication of the first AHA statement confirms the existence of a small, yet consistent association between increased mortality and short-term elevations in PM_{10} and $PM_{2.5}$ approximately equal to a 0.4% to 1.0% increase in daily mortality (and cardiovascular death specifically) due to a 10 μg/m^3

elevation in $PM_{2.5}$ during the preceding 1 to 5 days (Table 2)." (p. 2338)
With regards to cohort studies on long term exposure to PM, "The overall evidence from the cohort studies demonstrates on average an approximate 10% increase in all-cause mortality per 10 μg/m^3 elevation in long-term average $PM_{2.5}$ exposure. The mortality risk specifically related to CVD appears to be elevated to a similar (or perhaps even greater) extent, ranging from 3% to 76% (Table 3). This broader estimated range in risk compared with the short-term effects observed in time series is due to several recent cohort studies that demonstrated larger cardiovascular mortality risks (e.g., >30%) than in earlier cohort observations. This may reflect superior aspects of these studies that allowed for a better characterization of the cardiovascular risk of long-term exposure, the fact that these cohorts consisted of only women, or other unclear reasons." (p. 2341)

With regards to exposure to PM and hospitalization: "Excess cardiovascular mortality and increased rates of hospitalizations are similarly associated with day-to-day changes in PM air pollution (Tables 2 and 4). However, significant differences between geographic regions in the risk relationships have been observed, and more investigation is required to explain this heterogeneity." (p. 2343)

Cooke et al.[42] (2007) performed an expert elicitation with 6 European experts in epidemiology and exposure assessment to determine their views on the impact of $PM_{2.5}$ on mortality. The experts were provided with background material, reports, and publications, and asked to estimate the effect of certain changes in $PM_{2.5}$ concentration on mortality rates in various regions of the world. Overall, the results suggested that regulatory risk assessments underestimate the effect of $PM_{2.5}$ on mortality. However, the effect estimates among the experts were quite variable.

Roman et al.[43] (2008) performed a similar expert elicitation on the impact of $PM_{2.5}$ on mortality, however with 12 leading experts from the US. The experts generally estimated effects that were above those of the American Cancer Society study median of 0.6% per μg/m^3 and below the original Six Cities median of 1.2% per μg/m^3. As with the European experts, the experts generally estimated effects of $PM_{2.5}$ and uncertainty in these estimates were generally higher than those in the EPA risk assessment for PM.

Particle number concentration

As particle size decreases, the mass of the particles becomes increasing negligible. Ultrafine particles are a dominant source of particles in terms of PNC, yet are negligible in terms of mass. Although thought to be potent in terms of human health effects, the presence of these particles is not well-accounted for in the mass-based assessments of $PM_{2.5}$ or PM_{10}. Recently, more studies have started assessing PNC in addition to mass in air pollution epidemiology studies.

Hoek, et al.[44] (2010) conducted an expert elicitation among toxicologists, epidemiologists, and clinicians that have well-established expertise in ultrafine particles. The purpose was to estimate the particle-response relationship and corresponding uncertainty for urban air pollution. The limited amount of information, particularly the lack of long-term studies and few studies on hospital admissions, contributed to uncertainty among the experts. Overall, the experts estimated a median (95% confidence interval (CI)) of 0.30% (0.10, 0.90%)

reduction in deaths associated with a 1,000 /cm^3 decrease in UFP. For hospital admissions, the median estimates were 0.20% and 0.16% for cardiovascular and respiratory diseases, respectively (95% CI not reported).

We identified and reviewed 11 studies that specifically considered the human health effects of PNC on health. About half of these studies considered UFP specifically, whereas others considered PNC, which was typically not further defined. Based on the instrumentation used to make PNC measurements, the size ranges included in this metric were likely on the order of 20 to 1,000 nm. Overall, these studies support the findings of the expert group gathered by Hoek, et al. and suggest an increased risk of adverse cardiovascular and respiratory outcomes for increasing PNC (UFP and PNC). A summary of the results for CVD and respiratory outcomes are shown in Figures 9 and 10, respectively. Based upon the studies reviewed here, the expert elicitation estimate of 0.3% reduction in deaths per 1,000 particles/cm^3 seems plausible.

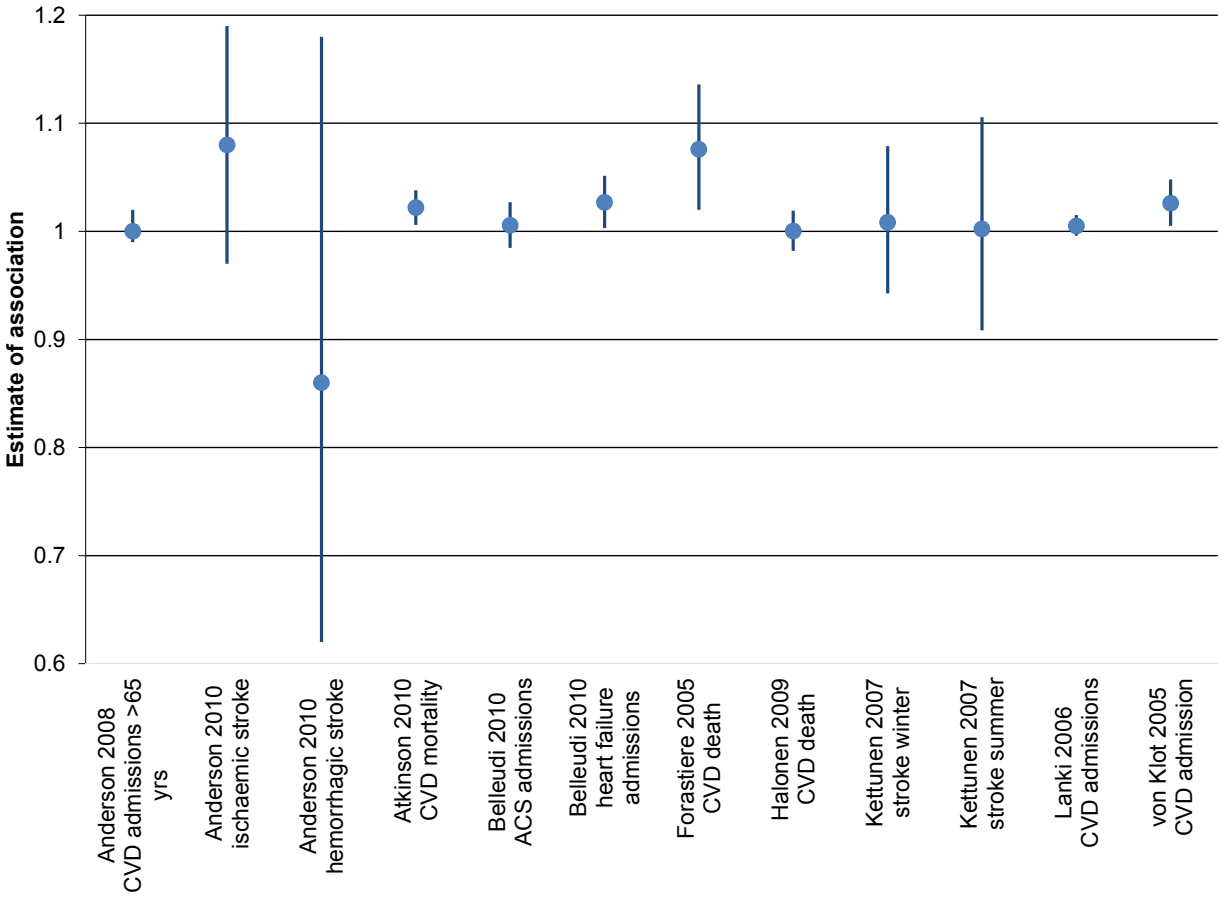

Figure 9. Estimates of association with 95% confidence interval for PNC on cardiovascular outcomes.

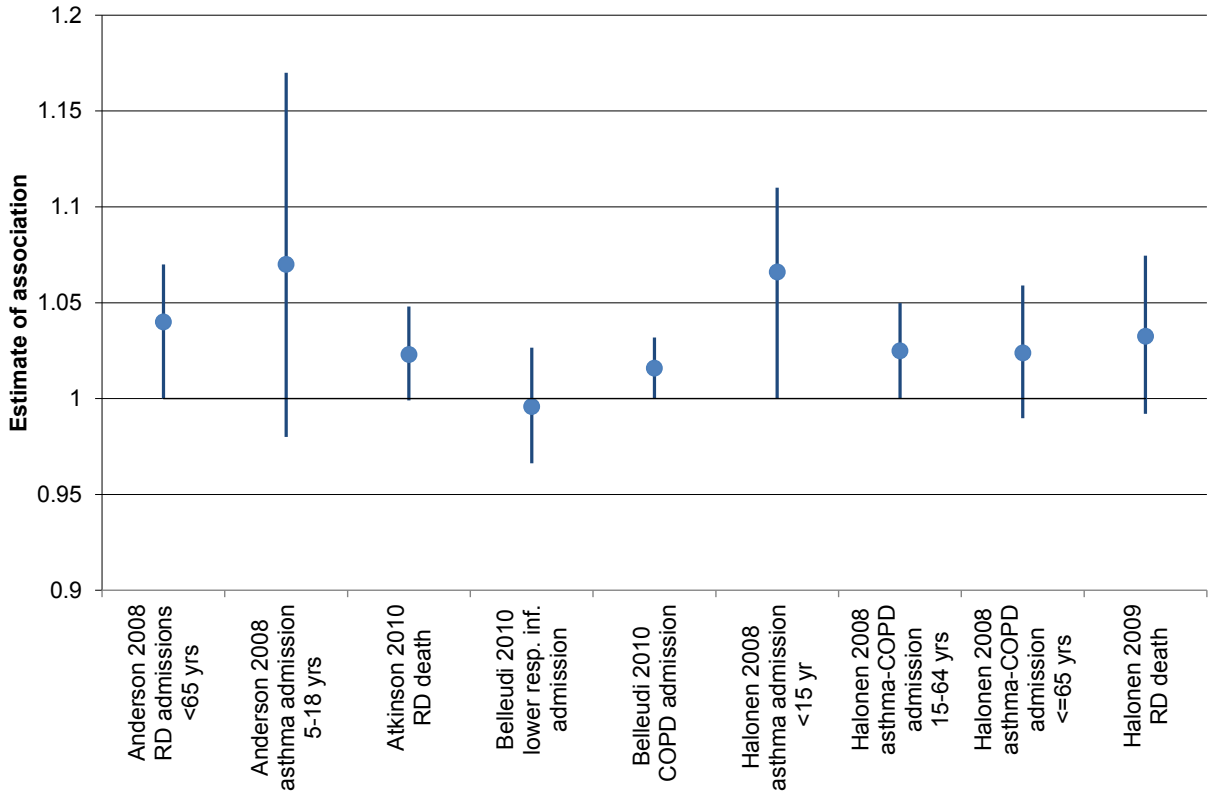

Figure 10. Estimates of association with 95% confidence interval for PNC on respiratory outcomes.

Andersen et al.[45] (2008) measured health effect in terms of respiratory or CVD hospital admissions by size and number concentration. The total number concentration (NC) was not statistically significant. Authors used interquartile ranges (IQR) for modelling (3907/cm^3).

Andersen et al.[46] (2010) considered effects of UFP and PM_{10} on incidence of stroke. Several types of stroke were considered, and the association was strongest (and most significant) for mild ischaemic stroke without atrial fibrillation (odds ratio, OR =1.21). OR do not show high associations when considering all ischaemic or haemorrhagic strokes in general. Effects measured per IQR change in UFP (3918 /cm3).

Atkinson et al.[47] (2010) associated PNC with daily mortality and admissions, particularly for cardiovascular diseases lagged 1-day; increases in PNC (10,166 n/cm^3) were associated with 2.2% (95% CI 0.6% to 3.8%) and 0.6% (0.4% to 1.7%) increases in cardiovascular deaths and admissions, respectively. Secondary pollutants, especially non-primary $PM_{2.5}$, nitrate and sulphate, were more important for respiratory outcomes.

Belleudi et al.[48] (2010) considered the relationship between different PM fractions (PM_{10}, $PM_{2.5}$ and PNC) and admission to the hospital for various reasons. PNC showed an association only with admissions for heart failure (lag 0–5; 2.4% 0.2% to 4.7%) and COPD (lag 0; 1.6% 0.0% to 3.2%) for a 9,392 /cm^3 increase in PNC. The effects were generally stronger in the elderly and during winter.

Forastiere et al.[49] (2005) showed that air pollution on the day of death had the strongest effect on cardiovascular death (e.g., 7.6% increase [95% CI, 2.0–13.6%]) for an interquartile range of PNC, 27,790 particles/cm^3.

Halonen et al.[50] (2008) assessed relationship between respiratory outcomes and particulate matter by size range, including nucleation (<0.03 µm), Aitken (0.03–0.1 µm) and accumulation (0.1–0.29 µm) mode particles. For the purpose of this study, the Aitken mode was considered as UFP (results showed higher significance than for nucleation mode). Observations were per IQR increase in particles (5760 /cm^3).

Halonen et al.[51] (2009) considered association between hospital admissions for CVD and RD and particle number. They found that there was a suggestion of an association of hospital admissions for arrhythmia with Aitken mode particles and $PM_{2.5}$ from traffic. Otherwise few associations were observed between various sizes and types of particles for either cardiovascular admissions or mortality. In contrast, most particle fractions had positive associations with admissions for pneumonia and asthma-chronic obstructive pulmonary disease (COPD). For the purpose of this review, the Aitken mode was considered as UFP (results showed higher significance than for nucleation mode). Observations were per IQR increase in Aitken mode particles (2467 /cm^3).

Ketunnen et al.[52] (2007) evaluated the association between stroke and UFP. They found significant associations in the warm season, but not in the cold season. Percent changes in stroke were assessed per 7330 /cm^3 increase in particle concentration.

Lanki et al.[53] (2006) found an association of the same day PNC levels with acute myocardial infarction (AMI). However, associations were only observed in the three cities with hospital discharge registers (v. general AMI registries) where power for city-specific analyses was higher. Effects of air pollution were more pronounced during the warm than the cold season.

Stolzel et al.[54] (2007) found statistically significant associations between elevated ultrafine particle (UFP; diameter: 0.01–0.1 µm) number concentration and total as well as cardio-respiratory mortality, each with a 4 days lag. The relative mortality risk (RR) for a 9748 cm^3 increase in UFP NC was RR: 1.029 and its 95% CI 1.003–1.055 for total mortality. For cardio-respiratory mortality they found RR: 1.031, 95% CI: 1.003–1.060. This study is not included in Figures 9 and 10 because it did not consider CVD and RD separately.

Von Klot et al.[55] (2005) evaluated cardiac readmissions in association with PNC. They found that cardiac readmissions increased in association with same-day estimated PNC per 10000 particles/cm^3. Pooled effect estimates for angina pectoris and myocardial infarction readmissions were comparable

Chemical composition

The analysis of the chemical composition in air monitoring data is relatively recent and there is not a large body of data accumulated yet for detailed analysis.

Volcanic ash

Volcanic ash can have high crystalline silica content, which is associated with silicosis, a scarring of lung tissue. Additionally, the particles can have high surface Fe^{2+} content,

which is associated with the formation of free radicals. Periods of high exposure to volcanic ash are typically not chronic.

Acute respiratory symptoms (e.g., irritation) but no long term effects have been observed in the few (and rather small) studies conducted to date[56].

Wildfire smoke

As with volcanic ash, most exposures to high levels of wildfire particulate are of an acute nature. Studies have shown significant increases in acute respiratory symptoms (e.g., asthma, rhinitis) and smaller but significant increases for more chronic respiratory diseases in vulnerable populations (i.e., bronchitis and COPD in certain age groups)[57-59].

Source apportionment studies

Source apportionment studies use defined emissions profiles from various sources to identify the portion of ambient PM that can be attributed to these sources. The emission profiles can be defined a priori or using statistical analysis of the emission profiles. These studies link health effects to a source, not to a particular component of PM. Studies reviewed so far have considered outcomes such as cause-specific emergency room visits, non-accidental mortality, and changes in cardiac blood factors and sources such mobile source $PM_{2.5}$, biomass combustion $PM_{2.5}$, secondary sulphate $PM_{2.5}$, and traffic speed changes[60-62].

6.3 Chemical composition of PM

In chapter 5.1 it was reported that the analysis of the chemical composition in air monitoring data is relatively recent and there is not a large body of data accumulated yet for detailed analysis. On account of this, the literature search on chemical composition was intensified and a number of studies was found that allows even to perform statistical analysis in some cases. However, for most substances statistical analysis is inappropriate due to a lack of data. The search resulted in a total of 16[60, 62-76] studies which provide RRs to almost 40 different substances.

6.4 Evaluation of the Literature for PNC of UFP and precursor gases of secondary particles (SO_x, NO_x and CO)

The literature review resulted in 28 studies[45-55, 63, 65, 66, 77-89] providing information for PM_{10}, $PM_{2.5}$, PNC and (precursor gases of) secondary particles SO_x, NO_x and CO. Table A1 in the Annex provides single data points of the RR and the CI for PM_{10}, $PM_{2.5}$, PNC, SO_x, NO_x and CO. Table 4 summarizes the total number of data points read out from the 28 studies for all different health endpoints. The blue fields indicate the total number of data points for a single substance (e.g. PNC vs. PNC=40 implies that 40 data points were found for PNC). Numbers in the right upper part of the blue fields indicate the number of data pairs for two substances (e.g. $PM_{2.5}$ vs. PNC=29 implies that there are 29 paired data points for PNC and PM_{10} and paired means that both elements of the pair stem from the same study). In the left lower part the results for sample size from the power analysis are provided. Analysis of the mean values from PNC and $PM_{2.5}$ with paired sample t-test contains 29 data points. Based on the mean values and the standard deviation for PNC