Costs of Health Damage from Atmospheric Emissions of Toxic Metals
Part 3: Analysis for Mercury and Lead

Vincent Nedellec
VNC
135 rue de Villiers, 78300 Poissy, France
vincent.nedellec3@gmail.com

and

Ari Rabl
Senior Scientist (retired), ARMINES/Ecole de Mines de Paris
Consultant on Environmental Impacts
6 av. Faidherbe, 91440 Bures sur Yvette, France
ari.rabl@gmail.com

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Abstract

In this part of the series we explain the detailed literature review and the calculations of impacts and damage costs of mercury and lead. Methodology and general assumptions are explained in the companion paper, Part 1 of this series. For mercury the damage cost is 15,761 €$_{2010}$/kg if there is a no-effect threshold, 35,821 €$_{2010}$/kg if there is none; 88% is due to mortality from heart disease, the rest from loss of IQ points. For lead the damage cost is 20553 €$_{2010}$/kg, about 80% due to mortality and 20% due to IQ loss; there does not seem to be a no-effect threshold. These costs are per kg of emitted pollutant. The spreadsheet with the calculations can be found at http://www.arirabl.org/software/ [1].

1. Mercury

1.1. Introduction

The dispersion of Hg in the environment requires an analysis very different from the other metals, for two reasons. First, by far the most toxic form of Hg is methyl mercury (MeHg), created by aquatic organisms, and therefore essentially all of the significant exposure of the public comes from ingestion of fish and shellfish. Second, since much of the emission is in the form of metallic Hg whose atmospheric residence time is long enough to cause nearly uniform mixing in the hemisphere, much of the impact is global and a global assessment is needed. Spadaro and Rabl [2008] have presented a global assessment of the neurotoxic impacts of Hg emissions in the northern hemisphere.

The main assumptions of Spadaro and Rabl are the following:

1) For an assessment of global impacts of Hg emissions to air the dependence on emission site can be neglected because the residence time of metallic Hg in the atmosphere is sufficiently large to imply a fairly uniform hemispherical

[1] Because of rounding, the multiplication of the some of the numbers in this paper differs slightly from the stated results.

distribution of the ingestion exposure. Even though the actual distribution of ambient total Hg is not very uniform (because of the contribution of reactive gaseous Hg and particulate Hg), the ingestion exposure of MeHg becomes far more uniform because of the wide international trading of seafood.

2) A comprehensive transfer factor, defined as incremental average intake due to an incremental emission, can be estimated as ratio of average intake and total (natural + anthropogenic) global emission at steady-state conditions.
3) The worldwide average intake from fish and seafood is about 2.4 μg/day-person of MeHg as reported by UNEP [2002].
4) The worldwide emission rate is about 6000 tonnes/yr, as estimated by the recent UN study [UNEP 2002]; about one third of that is from natural sources.
5) The neurotoxic impact can be estimated by using as proxy the ERF of Axelrad et al [2007]. This ERF is converted to an ingestion dose using conversion factors from the literature and applied to women of child bearing age.
6) The ERF is assumed to be a straight line, with two possibilities for a threshold, either no threshold or a threshold corresponding to the reference dose RfD of EPA [2001a].
7) The average ingestion intake of women of child bearing age is equal to the average intake reported by UNEP [2002]; for the threshold case a distribution of worldwide intake similar to that in the USA [NCHS 2005] is assumed.
8) The social cost of an IQ point lost in each country is calculated by modifying the value in the USA (taken as $\$_{2005}$18,000/IQ point) in proportion to the GDP/capita, adjusted for purchase power parity (PPP).

In the present paper we summarize the analysis of Spadaro and Rabl and add cardiovascular impacts, because in the meantime the evidence for the reality of cardiovascular effects of Hg has become sufficiently strong. To begin, the transfer factor from emission to average intake per person is

$$T_{av} = 4.0\text{E-}07\ (\mu g_{MeHg}/day)/(kg_{Hg}/yr) \quad (1)$$

The product of T_{av} and the world population, 6.4 billion, (times the ratio of molecular weights Hg/MeHg) is the intake fraction. Because of bioconcentration it is relatively high, 0.9E-03, despite the low percentage of emitted Hg that gets converted to MeHg.

1.2. Neurotoxic Effects

Spadaro and Rabl take the ERF of Axelrad et al [2007] because it is derived by an integrative analysis of the New Zealand, the Seychelles, and the Faroe Islands studies, with a method that uses the maximum of information from all three studies. Thus it holds promise to be much more reliable than a single study. Axelrad et al assume a linear ERF and their central estimate of the slope is 0.18 IQpoints per ppm increase of maternal hair mercury.

To relate the Hg concentration in maternal hair to the MeHg intake D by ingestion, Axelrad et al indicate a concentration ratio hair/cord blood of 0.2 $ppm_{hair}/(\mu g/L_{cord})$. The concentration in cord blood is higher than in maternal blood, but there is considerable uncertainty about the ratio cord blood concentration/maternal blood concentration. Spadaro and Rabl assume a ratio of 1.65 $\mu g/L_{cord}/(\mu g/L_{mat})$, the mean of the meta-analysis by Stern and Smith [2003]. To relate

blood concentration to dietary intake, they take the model of Stern [2005] for the ratio of blood concentration and intake dose

$$\text{blood concentration/intake dose} = 0.61\ \mu g/L_{mat}/(\mu g/day). \quad (2)$$

The coefficient 0.61 accounts for blood volume, absorption and elimination rate.

Multiplying these factors one obtains a dose conversion factor

$$0.2\ ppm_{hair}/(\mu g/L_{cord})*1.65\ \mu g/L_{cord}/(\mu g/L_{mat})*0.61\ \mu g/L_{mat}/(\mu g/day) = 0.2013\ ppm_{hair}/(\mu g/day) \quad (3)$$

and an ERF slope of

$$s_{ERF} = 0.18\ IQpoints/ppm_{hair} * 0.2013\ ppm_{hair}/(\mu g/day) = 0.036\ IQpoints/(\mu g/day) \quad . \quad (4)$$

The ERF expresses the IQ loss of the child as function of the MeHg intake of the mother. For the cost per IQ point lost Spadaro and Rabl take $c_{IQpoint,USA}$ = \$18,000/IQpoint in the USA, as average of several studies. It is the loss of lifetime earnings per IQ point, calculated as discounted total value at the time of birth. For IQloss due to Hg we find it convenient to consider the lifetime loss of each birth cohort, multiplied by the birth rate.

The cost of IQ loss in each country k is the product of the transfer factor T_{av} of Eq.1, the ERF slope of Eq.4, the birth rate b_k, the population p_k and the cost of an IQ point P_k; the worldwide cost is the sum over all countries

$$C_{IQ} = T_{av}\, s_{ERF} \quad \sum_k b_k\, p_k\, P_k \quad . \quad (5)$$

For the unit cost P_k in each country we assume proportionality to GDP_{PPP}/capita, the per capita GDP adjusted for purchase power parity [2]. Instead of applying the GDP_{PPP}/capita factor to P_k, one can apply it to the birth rates b_k and define a modified worldwide birth rate b^*_{world}

$$b^*_{world} = \sum_k b_k \frac{p_k}{p_{world}} \frac{(GDP_{PPP}/capita)_k}{(GDP_{PPP}/capita)_{USA}} \quad . \quad (6)$$

Thus Eq.5 can be replaced by

$$C_{IQ} = T_{av}\, b^*_{world}\, p_{world}\, s_{ERF,IQ}\, c_{IQpoint,USA} \quad (7)$$

where b^*_{world} is the fraction of the world population p_{world} that is affected per year by Hg, weighted by GDP/capita (in other words, the worldwide GDP-weighted birthrate). The numerical value is b^*_{world} = 0.00315/yr. Inserting Eqs.1, 4 and 6, together with p_{world} = 6,430,000,000 persons and $c_{IQpoint,USA}$ = \$18,000/IQpoint into Eq.7 we obtain a worldwide damage cost of 5,284 \$/kg due to IQ loss [3]. We convert to € with an exchange rate of 1.3 \$/€

[2] http://www.cia.gov/cia/publications/factbook

[3] The result \$3,400/kg of Spadaro and Rabl for loss of IQpoints includes a discount factor of 0.64, which we now believe not to be appropriate because $c_{IQpoint,USA}$ = \$18,000/IQpoint is already discounted to the time of birth.

and multiply by 1.047 for inflation to obtain a worldwide damage cost of 4,257 €$_{2010}$/kg for IQ loss, without threshold.

As for a possible threshold, EPA [2001a] noted "*no evidence of a threshold arose for methylmercury-related neurotoxicity within the range of exposures…*". Axelrad et al [2007] also argue for linear ERF without threshold. We find the possibility of a straight line without threshold not only plausible but probable. Hg is a neurotoxicant that damages the developing brain and reduces the IQ, similar to Pb. Also, like Pb it is a substance that has only harmful effects, by contrast to other metals (for instance Se) that are toxic at high doses but of which the organism needs a certain minimum to survive. Furthermore, whereas in the past the ERF for IQ decrement due to Pb was believed to have a threshold, more recent studies have found that at the lowest doses the ERF for Pb is at least as high as the extrapolation of the high dose points, and quite possibly even higher [Lanphear et al 2005]. Nonetheless we also evaluate the impacts if there is a no-effect threshold dose D_{th}, assuming the same slope s_{ER}. As threshold we take the oral reference dose RfD 6.7 μg/day of EPA [2001a], noting, however, that it is not a no-effect level but intended as guideline for protecting the population with a sufficient margin of safety. Spadaro and Rabl calculate the fraction of the incremental intake above this threshold as $f_{thr} = 0.44$.

1.3. Cardiovascular Effects

The great difficulty of identifying cardiovascular effects in epidemiological studies lies in the masking by the simultaneous protective effects of polyunsaturated fatty acids in fish. Thus it is not surprising that different studies have reached opposite conclusions about the cardiovascular effects attributable to MeHg. For example Virtanen et al [2005] see significant increase of the risks of acute coronary events and cardiovascular and all-cause mortality due to MeHg. Salonen et al [2000] find that that mercury accumulation in the human body is associated with accelerated progression of carotid atherosclerosis. Choi et al [2009] find that increased MeHg exposure promotes the development of cardiovascular disease. Valera et al [2009] find that mercury is associated with increasing BP and pulse pressure among Nunavik Inuit adults after considering the effect of fish nutrients (n-3 fatty acids and selenium) and other confounders. As an indication of possible mechanisms Yaginuma-Sakurai et al [2010] found that heart rate variability was significantly affected by Hg exposure.

On the other hand, Mozaffarian et al [2011] found no evidence of any clinically relevant adverse effects of mercury exposure on coronary heart disease, stroke, or total cardiovascular disease in U.S. adults (a total of 51,529 men and 121,700 women). The study by Yoshizawa et al [2002] of myocardial infarction among health care professionsals did not find an association with MeHg when analyzing the entire study population, although there was an elevated association when dentists were excluded.

Mozaffarian and Rimm [2006] carried out a meta-analysis of studies of mercury exposure and risk of coronary heart disease and found an RR of 1.12 (CI 0.71 to 1.75). The conflicting evidence has been reviewed by Mozaffarian [2009] and by Roman et al [2011]. Roman et al conclude that at least some of the cardiovascular effects are real, and they recommend the development of an ERF relating MeHg exposures with myocardial infarction for use in regulatory benefits analyses of future rules targeting Hg air emissions. But since they do not provide an explicit ERF, we rely instead on Rice, Hammitt and Evans [2010] who characterize the hair mercury to fatal heart attack risk coefficient ΔRR (fractional increase in

risk/μg Hg per g hair) by using a triangular distribution with a mode of 0.066, a minimum of 0, and a maximum value of 0.17, values drawn from the work of Salonen et al [1995]. Hence we take

$\Delta RR = 0.066$ increase in risk of fatal heart attack per $(\mu g_{Hg}/g_{hair})$. (8)

We assume that this is also the risk increase for all cardiovascular mortality and that the latter represents one half of the total mortality. Like the calculation of IQ loss in Section 1.2 we consider the lifetime LE loss for each birth cohort rather than the annual loss of the entire population, so instead of Eq.2 of Part 1 we use

$$\Delta LE/\Delta RR = 10.34 \text{ YOLL/lifetime.} \quad (9)$$

Applying the dose conversion factor of Eq.3 we thus obtain and ERF slope of

$s_{ERF} = 0.342$ YOLL/ppm_{hair} * 0.2013 $ppm_{hair}/(\mu g/day) = 0.069$ YOLL/(μg/day) for LE loss. (10)

It expresses the lifetime LE loss due a specified daily intake of MeHg. The calculations are the same as for IQ loss, and the result is a damage cost contribution of 46,723 €/kg_{Hg}, without threshold and without discounting. Like for other non-cancer mortality impacts we assume a lag of 10 yr and a discount factor of 0.676 to reduce this cost to 31,564 €$_{2010}$/kg_{Hg}. In the case of a threshold we multiply by $f_{thr} = 0.44$ to find 13,888 €$_{2010}$/kg_{Hg}.

1.4. Summary

The results for the marginal damage costs are summarized in Table 1. With the assumption of uniform mixing in the atmosphere of the hemisphere, it does not matter where the pollutant is emitted and the result is relevant for global policy decisions. As explained at the end of Section 1.2 we find the no threshold result more plausible. Mortality contributes 88% of the total discounted damage cost.

Table 1. Summary of damage costs contributions for Hg, in €$_{2010}$ per kg emitted into air. The units for cases are YOLL for mortality and IQ points for IQ loss. Threshold = 6,7E-03 mg_{Hg}/kg_{body}/day [EPA 2001a] and $f_{thr} = 0.44$.

Endpoint	Cases/kg_{Hg}	Undiscounted, no threshold	Lag [yr]	Discount factor	Discounted, no threshold	Discounted, with threshold
Mortality	0.56	46,723	10	0.68	31,564	13,888
IQ loss	1.36	4,257	0	1	4,257	1,873
Total €$_{2010}$/kg_{Hg}		**50,980**			**35,821**	**15,761**

2. Lead

2.1. Introduction

An extensive literature links lead exposure to adverse effects in humans. The neurotoxic effects of Pb are well known. Increased mortality, even at low doses, has been found in several recent studies. Other end points include anemia, hypertension, renal dysfunction, spontaneous abortion, and possible effects on male fertility. The International Agency for Research on Cancer [IARC 2006] has determined that inorganic lead is probably carcinogenic to humans (Group 2A) and that organic lead compounds are not classifiable as to their carcinogenicity to humans (Group 3). EPA does not provide any ERFs for cancer, but the information on carcinogenicity of Pb has not been revised since 1993.

In the past most studies looked at groups with high exposures, especially workers exposed to lead in the workplace. In recent years studies of the general population have found harmful effects even at low levels of exposure that used to be considered safe. Most studies have used concentrations of Pb in blood as a biomarker of exposure. Pb in bones, as measured by a non-invasive XRF device, is also used by some studies. The relation between such biomarkers and the true exposure is not simple because of the complexity of the distribution and storage behavior of Pb in the body. Very roughly speaking, the half life of Pb in blood is about 30 days, in bones about 30 years. In bones there are the relatively fast and small trabecular bone compartment and the relatively slow and large cortical bone compartment. Up to adult age the concentration in bones builds up as a result of chronic exposure. In later years it can decrease again and release Pb to blood.

Pb in blood is therefore mostly an indicator of recent exposure, whereas Pb in bones is an indicator of past exposure, but the relationships are variable, depending on age, time distribution of the exposure and other factors. For specific situations the relationships can be analyzed by means of biokinetic models [EPA 2001b]. For the relation between Pb in blood and exposure there are some fairly general indicators. Children appear to absorb more Pb via the gastrointestinal tract than adults for a given level of exposure and also seem to experience adverse effects at lower blood Pb levels than adults. For children a blood level increase of 0.16 μg_{Pb}/dL per μg_{Pb}/day intake seems to be typical at low exposures; for adults the equivalent number is 0.04 μg_{Pb}/dL per μg_{Pb}/day intake (see e.g. Table 2.2.1 of EPA [2001b]). Converting the intake to mg_{Pb}/yr we find

$$\text{blood level increase/intake} = 0.438\ (\mu g_{Pb}/dL)/(mg_{Pb}/yr) \text{ for children} \quad (11a)$$

and

$$\text{blood level increase/intake} = 0.110\ (\mu g_{Pb}/dL)/(mg_{Pb}/yr) \text{ for adults} \quad . \quad (11b)$$

There seems to be no simple relation for bone lead. Therefore we are not able to quantify impacts for studies that report only associations with Pb_{bone}.

2.2. Mortality

Several recent studies have found very significant associations between Pb exposure and mortality. Weisskopf et al [2009] find that Pb in bones is associated with all-cause and cardiovascular mortality, but not cancer mortality; however, they found no association of Pb in blood with any mortality category. Schober et al [2006] and Menke et al [2006] analyze large samples (over 10,000 individuals) of the NHANES survey, where exposure is reported in terms of Pb in blood. The latter report that “After multivariate adjustment, the hazard ratio

(95% CI) for a 3.4-fold increase in blood lead level was 1.34 (CI 1.16 to 1.54) for all-cause mortality". Schober et al find similar results but the exposure information is less detailed. For these reasons we quantify the mortality impacts on the basis of Menke et al.

The RR of 1.34 found by Menke et al is for an increase of Pb in blood from 1.46 to 4.92 μg_{Pb}/dL, thus the risk increase is

$$\Delta RR \text{ for mortality} = 0.098\ \Delta RR/(\mu g_{Pb}/dL) \qquad \text{for all-cause mortality.} \tag{12}$$

By comparison the data of Schober et al imply an increase of 0.065 $\Delta RR/\mu g_{Pb}$/dL by comparing groups with >10 μg_{Pb}/dL and < 5 μg_{Pb}/dL. An earlier study by Lustberg and Silbergeld [2002] implies 0.023 $\Delta RR/\mu g_{Pb}$/dL by comparing groups with >20 μg_{Pb}/dL and < 10 μg_{Pb}/dL. Here, too, the ERF seems to be supralinear. Combining Eq.12 with Eq.11b for the blood level increase per intake and with the LE loss per ΔRR of 0.148 (YOLL/yr)/ΔRR of Eq.2 of Part 1 we obtain the ERF slope

$$s_{ERF} = 0.00159\ (YOLL/yr)/(mg_{Pb}/yr) \text{ for mortality.} \tag{13}$$

After multiplication by the IF of 183.8 mg_{Pb}/kg_{Pb} for adults we obtain a total population LE loss of 0.29 YOLL/kg_{Pb}; with VOLY = 84,000 €/YOLL the damage cost is 24,531 $€_{2010}/kg_{Pb}$.

2.3. Neurotoxic Effects

There are a variety of impacts on the nervous system, such as cognitive impairment in adults, hearing impairment in children, cognitive impairment in children, reduced IQ of children, effects on nerve conduction, amyotrophic lateral sclerosis (a degenerative motor neuron disease), and brain damage, see e.g. Chiodo et al [2004] and the review by Sanders et al [2009]. Bouchard et al [2009] find that in young adults with low levels of lead exposure, higher blood lead levels are associated with increased odds of major depression and panic disorders. A very interesting study by Nevin [2007] finds a strong association between preschool blood lead and subsequent crime rate trends over several decades in the USA, Britain, Canada, France, Australia, Finland, Italy, West Germany, and New Zealand.

There is considerable overlap between these endpoints and for most of them there are no monetary values. However, loss of IQ is a fairly good proxy for all of these and it can be measured, even for young children; furthermore the monetary valuation for this end point is relatively firm. Effects on the brains of children are far more severe than for adults because of the greater vulnerability of the brain during its development. For these reasons we base our valuation of neurotoxic impacts on IQ loss of children.

A meta-analysis by Schwartz [1994] found a decrement of 0.26 IQ points for a 1 µg/dL increase of Pb in blood, at the relatively high population exposures before the outlawing of leaded gasoline. A more recent international study designed to identify effects at the lowest doses found an even larger effect; not only was there no evidence of any threshold but the effect per exposure was supralinear, i.e. higher at low than at high levels of Pb_{blood} [Lanphear et al 2005]. Because of the nonlinearity it is a bit difficult to decide what the most appropriate slope of the ERF should be. WHO [2010] summarizes the results of Lanphear et al by saying "*An increase in blood lead level from less than 1 µg/dL to 10 µg/dL was associated with a six IQ point decrement*", in other words that the slope is 0.67 IQ points per 1 µg/dL. The low

exposure regime has been further investigated in a large study by Surkan et al [2007], and here we use the latter because it is the most precise at low exposures. We base the ERF slope on the loss of 6.04 IQ points between the reference group (whose mean blood Pb level is 1.38 μg/dL) and the highest exposure group (whose mean blood Pb level is 6.71 μg/dL), implying a loss of

$$\text{IQ loss} = 6.04/(6.71 - 1.38)\ \text{IQpoints}/(\mu g_{Pb}/dL) = 1.13\ \text{IQpoints}/(\mu g_{Pb}/dL) \quad . \qquad (14)$$

Since this effect is for children, we use Eq.11a to relate the blood level to the intake rate

$$\text{IQ loss} = 0.496\ \text{IQpoints}/(mg_{Pb}/yr) \qquad (15)$$

Since this loss is incurred once for each birth cohort, we multiply by the birth rate, 0.0104 births/yr to obtain the ERF slope

$$s_{ERF} = 0.00516\ (\text{IQpoints/yr})/(mg_{Pb}/yr) \quad . \qquad (16)$$

Adjusting the IF for adults for the food intake of children we find an IF for children of 52.8 mg_{Pb}/kg_{Pb}. Combining these numbers with the cost per IQpoint we find a damage cost contribution of 3,948 $€_{2010}/kg_{Pb}$.

2.4. Other effects

An increase of childhood anemia due to Pb has been found by Jain et al [2005] by comparing a group with <10 μg_{Pb}/dL and a group with >10 μg_{Pb}/dL; the risk of moderate anemia is a factor 1.3 higher in the latter group. Estimating very roughly the mean difference between the groups as 10 μg_{Pb}/dL, the risk increase is

$$\text{Risk increase} = 0.030\ \Delta RR/(\mu g_{Pb}/dL) \qquad \text{for childhood anemia.} \qquad (17)$$

The prevalence of moderate childhood anemia is about 2% [CDC 1998]. We estimate the incidence as prevalence times birthrate. Combining these numbers with Eq.11a we obtain an ERF slope of

$$s_{ERF} = 2.73\text{E-}06\ (\text{cases/yr})/(mg_{Pb}/yr)\ \text{ of childhood anemia.} \qquad (18)$$

Let us assume that such anemia is incurable and lasts an average of 70 yr. Multiplying Eq.18 by 70 years, by the IF for children of 52.8 mg_{Pb}/kg_{Pb}, by the DALY score of 0.058 DALY/yr of moderate anemia [Salomon et al 2012] and VOLY we find a damage cost of 49.2 $€_{2010}/kg_{Pb}$.

Several studies have found impacts of Pb on kidney function [e.g. Yu et al 2004, Tsaih et al 2004, Navas-Acien et al 2009], but they measure the effects in terms of indicators such as excretion of albumin or creatinine. Unfortunately we do not know how to relate such indicators to concrete manifestations of kidney disease.

Hypertension has also been identified as effect of Pb [e.g. Nawrot et al 2002]. It is a precursor or concomitant of heart disease, but difficult to evaluate in terms of damage costs because there is no DALY score for hypertension. Since hypertension is correlated with reduced life

expectancy [Franco et al 2005] one could try an indirect valuation via an estimation of the LE loss due to hypertension, but that would amount to double counting since we have already evaluated to damage cost due to all-cause mortality.

2.5. Thresholds and Summary

For Pb the ERFs for mortality and for IQ loss seem to be supra-linear, i.e. above the straight line from higher exposures to the origin. If that is indeed correct, the existence of a no-effect threshold is most unlikely. Such absence of a threshold seems to be generally accepted. Even if there is a threshold for anemia, its contribution is so small that it would hardly change to overall result, and so we take the simple sum in Table 2 as damage cost of Pb, namely 20,553 $€_{2010}/kg_{Pb}$, as damage cost. Mortality contributes 81% of the total discounted damage cost.

Table 2. Summary of damage costs contributions for Pb, in $€_{2010}$ per kg emitted into air. The entire population is assumed to be above threshold, if any. The units for cases are YOLL for mortality and IQ points for IQ loss. Threshold = 0 and f_{thr} = 1 for all endpoints.

Endpoint	Cases/kg_{Pb}	Undiscounted, no threshold	Lag [yr]	Discount factor	Discounted, no threshold
Mortality	0.27	24,531	10	0.68	16,572
IQ loss	0.29	3,948	0	1	3,948
Anemia	1.44E-04	49	10	0.68	33
Total $€_{2010}/kg$		**25,528**			**20,553**

Finally we note that there are several endpoints, for Hg or for Pb, for which the epidemiological evidence is fairly strong but for which we have been unable to provide estimates, for instance kidney damage, non-fatal heart attacks or hypertension, for various reasons: lack of a relation between intake and the specific biomarker used in a study, lack of monetary valuation, or risk of double counting (if the endpoint is associated with a loss of life expectancy). However, in view of the high valuation of mortality this study, like other studies of air pollution, has found the contribution of mortality to dominate the result. Thus the underestimation due to omitted endpoints is unlikely to be very important.

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Abbreviations and symbols: see Part 1 of this series.

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