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ORIGINAL ARTICLE

An epidemiological re-appraisal of the association between blood pressure and blood lead: a meta-analysis

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Studies on the possible association between blood pressure and blood lead have reached divergent conclusions. In a previous meta-analysis, a doubling of the blood lead concentration was associated with a 1.0/0.6 mm Hg increase in systolic and diastolic blood pressure (BP). This meta-analysis updates the analysis originally performed in 1994. Articles on the association between BP and blood lead were identified from computer searches from January 1980 to February 2001 using the Medical Literature Analysis and Retrieval System. Of the studies reviewed, 31 provided sufficient details to be considered. The meta-analysis included 58 518 subjects recruited from the general population in 19 surveys and from occupationally exposed groups in 12 studies. In all but four studies, the results were adjusted for age, and most studies took into account additional confounding factors such as body mass index and the use of alcohol and medication. Weighted joint *P*-values were calculated using Stouffer's procedure. The association between BP and blood lead was similar in both men and women. In the combined studies, a two-fold increase in blood lead concentration was associated with a 1.0 mm Hg rise in the systolic pressure (95% CI +0.5 to +1.4 mm Hg; $P < 0.001$) and with a 0.6 mm Hg increase in the diastolic pressure (95% CI +0.4 to +0.8 mm Hg; $P < 0.001$). On balance, this meta-analysis suggests that there can only be a weak association between BP and blood lead.
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Introduction

Environmental and occupational lead exposure is a common public health concern. Lead accumulates in the human body during life and has been implicated in the pathogenesis of renal dysfunction[1] and hypertension.[2–4] Several plausible pathophysiologic mechanisms for the involvement of lead in hypertension have been proposed, but the reports dealing with a positive and causal association between lead exposure and blood pressure elevation are not universally accepted. A meta-analysis of the available human studies in 1994 suggested that a two-fold increase in the blood lead concentration would be associated with a 1.0 mm Hg increase in systolic blood pressure (95% confidence interval (CI): +0.4 to +1.6 mm Hg) and a 0.6 mm Hg increase in diastolic blood pressure (95% CI: +0.2 to +1.0 mm Hg).[5] This weak positive relationship was attributed to confounding rather than to causation.

In view of continuing controversy[6,7] about the possible causal association between blood pressure and lead exposure, and the decrease of the blood lead concentrations in most western populations,[6] we updated our previous meta-analysis[5] to determine whether all the available data up to February 2001 support a positive association and how strong such a relationship between blood pressure and lead may be.

Methods

General design

The first step of this meta-analysis consisted of identification of relevant studies for inclusion. In accordance with current guidelines,[8,9] criteria determining the eligibility of studies for inclusion were established before the actual statistical analysis was undertaken. The effect of lead exposure on blood pressure, and its standard error, were then identified for each group of subjects included in

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individual studies. As a next step in the analysis, the estimates of the association size from the individual studies were expressed on a common scale in order to make the calculation of a combined association size possible. However, before pooling was undertaken whether the studies could reasonably be described as sharing a common association size, was first determined[8,9] by a statistical test of homogeneity. A combined association size and corresponding *P*-values were then computed, combining the evidence that from all studies both with and without weighting by the size of the groups included in the analysis. Finally, a sensitivity analysis was performed to ensure that the results from the combined data set were not critically dependent on only one or a few studies.

Data collection

Articles on the association between blood pressure and lead exposure were identified (1) from computer searches of the English, French and German literature from January 1980 to February 2001, using the Medical Literature Analysis and Retrieval System (MEDLARS), (2) from existing compilations of the literature,[4,10] and (3) via presentations at international meetings. Studies under the 50 subjects were excluded because they might not have had the power to detect a positive relation between blood pressure and blood lead. We excluded studies in children below the age of 10 years, because blood pressure in children is highly variable and correlates highly with height. Studies were further eligible for inclusion if both blood pressure and blood lead had been measured and presented with sufficient detail to estimate or calculate the size of the association. If a group published two or more papers describing the same study population, only the publication providing the most detailed information was included in the analysis. When possible, preference was given to blood pressure results adjusted for age, body mass index and additional factors of proven importance. Whenever possible, men, women, whites, and blacks were analysed as separate groups.

Estimation of the association size

The association size was estimated for each group of subjects as the blood pressure change that would be associated with a doubling of the blood lead concentration. For reports in which blood lead was expressed on a linear scale, the association size was calculated, assuming a two-fold increase of the mean blood lead concentration. For studies in which the association size was expressed on a logarithmic scale, the change in blood pressure associated with a doubling of the blood lead concentration was calculated by multiplying the regression coefficient by 0.30, if common logarithms had been used and by 0.69 for natural logarithms.

The standard error of the blood pressure difference associated with a given change in the blood lead concentration was not reported in all studies. In these instances, the standard error was estimated from the published association size and the test statistic corresponding with the reported *P*-value. If the parameters of a non-significant blood pressure effect were not reported, the authors of the paper were contacted in order to avoid bias resulting from the exclusion of non-significant studies, an important problem in any meta-analysis.[11] If no additional information was made available, according to the suggestion of Needleman and Gatsonis,[12] the non-significant effects were assumed to be zero and the non-significant *P*-values to be 0.50. Summary statistics were then calculated both with and without the studies for which these assumptions had to be made.

Statistical analysis

Statistical analyses were performed with the SAS software version 6.12 (The SAS Institute, Cary, NC, USA). Joint *P*-values were calculated by two different techniques, ie by Stouffer's method, as modified by Mosteller and Bush, and by Fisher's approach.[8] In Fisher's procedure, the logarithm of the product of the individual *P*-values was multiplied by −2. The resulting quantity follows a chi-square distribution with 2k degrees of freedom, where k refers to the number of combined groups. Fisher's procedure was not weighted, because weighting may produce computational instability.[8] Stouffer's procedure involved transforming each *P*-value to its corresponding normal score and then averaging these z-scores, using degrees of freedom (number of subjects −1) as weights. The weighted z-score average was employed to construct one-sided 95% CI for the combined association size. As a test of homogeneity, the z-scores of the individual studies were ranked and plotted to investigate whether they were on a straight line.

Results

Selection of studies

Of the studies reviewed[3,4,6,13–88] 22 reports were excluded. Two studies reported only on young children (<10 years),[25,37] two studies were case reports,[45,48] one[66] recruited less than 50 persons, in one[54] owing to missing information the analysis was performed in less than 50 subjects, five estimated exposure from other measurements than the blood lead concentration,[30,77,78,81,88] and 11 did not provide enough information to compute the association size.[17,19,22,26,27,36,39,62,63,67,86]

Characteristics of the selected studies

The 31 studies included in the meta-analysis are listed in chronological order in Table 1. Of these, 19

Table 1 Characteristics of the study population

Author	*No.*	*Pop*	*Men (%)*	*HT*	*Age (years)*	*SBP*	*DBP*	*Lead (μmol/L)*	*QC*	*Scale*	*Info*
Pocock *et al*[59,71]	7379	GP	100	Y	49 (40–59)	145	82	0.73 (0.10–3.20)^{Ae}	BP, L	Log	S, C, R
Kromhout *et al*[46,47]	152	GP	100	Y	67 (57–76)	154	92	0.88 (0.52–1.35)^{Ac}	BP, L	Lin	0
Orssaud *et al*[50,51,56]	431	WC	100	Y	41 (24–55)	131	75	0.88 (0.43–2.41)^{Ae}	BP	Lin	S, C, R
Weiss *et al*[84,85]	89	WC	100	Y	47 (30–64)	122	83	1.18 (⟨0.9–⟩1.4)^{Mx}	BP	Lin (D)	0
de Kort *et al*[28,29]	105	BC	100	N	40 (25–80)	136	83	1.41 (0.21–4.02)^{Ae}	BP	Lin	S, C, R
Lockett and Arbuckle[14]	116	BC	100	Y	32 (?–?)	119	80	1.81 (0.72–4.61)^{Ae}	ND	Lin (G)	0
Parkinson *et al*[57]	428	BC	100	Y	36 (18–60)	127	80	1.35 (0.29–2.39)^{Ac}	BP	Lin	0
Rabinowitz *et al*[61]	3851	GP	0	Y	28 (18–38)	121	76	0.34 (0.18–0.49)^{Ac}	BP~0	Ln	S, R.
Elwood *et al* (1)[34,35]	1136	GP	100	Y	56 (49–65)	146	87	0.61 (0.29–1.26)^{Gc}	BP	Log	0
Elwood *et al* (2)[32,33]	1721	GP	50	Y	41 (18–64)	127	78	0.49 (0.22–1.12)^{Gc}	BP	Log	0
Gartside *et al* (3)[15,38,42,58,69]	6289	GP	53	Y	30 (10–74)	127	80	0.65 (0.10–4.63)^{Ge}	BP, L	Log	S, C, R
Neri *et al* (4)[55]	288	BC	100	?	? (?–?)	?	?	2.18 (0.29–3.14)^{Ae}	ND	Lin	S
Neri *et al* (5)[55]	2193	GP	?	Y	45 (25–65)	?	?	1.13 (0.00–2.27)^{Me}	ND	Lin	NA
Grandjean *et al* (6)[40,41]	1050	GP	48	Y	40 (40–40)	?	?	0.56 (0.19–2.90)^{Ae}	BP, L	Ln	0
Reimer and Tittelbach[63]	58	BC	100	?	32 (?–?)	134	81	1.93 (0.62–3.39)^{Ac}	ND	Lin (G)	0
Apostoli *et al*[13]	525	GP	48	Y	45 (21–60)	132	84	0.63 (0.10–1.36)^{Ae}	BP	Lin	S, C, R
Morris *et al*[52]	251	GP	58	Y	? (23–79)	?	?	0.36 (0.24–1.88)^{Ae}	BP	Ln	NA
Sharp *et al*[72,73,74]	249	WC	100	N	43 (31–65)	128	83	0.32 (0.10–0.72)^{Pe}	BP, L	Ln	0
Staessen *et al* (7)[78]	531	WC	75	Y	48 (37–58)	126	78	0.55 (0.20–1.70)^{Ge}	BP, L	Log	0
Møller *et al* (8)[53]	439	GP	100	Y	40 (40–40)	?	?	0.66 (0.24–2.90)^{Ae}	BP, L	Ln	0
Hense *et al*[43]	3364	GP	51	Y	48 (28–67)	129	80	0.38 (0.06–1.79)^{Ae}	BP, L	Lin	S, C, R
Maheswaran *et al*[14]	809	BC	100	Y	43 (20–65)	129	84	1.53 (0.00–4.73)^{Ae}	BP	Lin	S, C, R
Menditto *et al*[49]	1319	GP	100	Y	63 (55–75)	140	84	0.54 (0.30–1.19)^{K}	BP, L	Lin	NA
Proctor *et al* (9)[44,60]	798	GP	100	Y	66 (43–93)	134	80	0.27 (0.02–1.69)^{Pe}	BP, L	Ln	0
Staessen *et al* (10)[6,32,80]	728	GP	49.3	Y	46 (20–82)	130	77	0.44 (0.08–3.50)^{Ge}	BP, L	Log	0
Sokas *et al*[75,a]	186	BC	99	Y	43 (18–79)	130	85	0.36 (0.10–1.45)^{Pe}	BP, L	Lin	NA
Bost *et al*[20]	5326	GP	48	Y	48 (16–?)	135	75	3.08 (?–?)^{G}	BP	Log	R
Chu *et al*[24]	2800	GP	53	Y	44 (15–85)	123	78	0.31 (0.02–3.33)^{Ae}	BP, L	Ln	0
Rothenberg *et al*[64,65]	1627	GP	0	Y	27 (?–?)	110	59	0.11 (?–?)^{G}	BP, L	Ln	0
Schwartz *et al*[68]	543	BC	100	Y	58 (41–73)	128	77	0.22 (0.05–0.97)^{Ae}	BP, L	Lin	0
Den Hond *et al* (11)[31]	13781	GP	53.2	Y	48 (20–90)	125	73	0.15 (0.03–2.70)^{Ge}	BP, L	Log	S

No.: Number of persons in whom relevant data were available.
Pop.: Study population: GP, sample from general population; BC, blue collar workers; WC, white collar employees.
Men.: Percentage of men.
HT.: Indicates whether the sample included (Y = yes) or did not include (N = no) hypertensive patients.
Age.: Mean age or midpoint of age span (range or approximate range given between parentheses).
SBP, DBP: Mean systolic and diastolic blood pressures.
Lead: Measure of central tendency: A = arithmetic mean, G = geometric mean, P = P_{50} (median), M = midpoint of range. The spread of blood lead is given between parentheses: e = extremes, c = P_5–P_{95} interval, P_{10}–P_{90} interval, or interval equal to 4 times the standard deviation, x = approximate limits of distribution.
QC: Quality control. BP indicates that the blood pressure measurements were well standardized; L stands for the explicit mention in the published papers of a quality control programme for the blood lead determinations; BP~0 means that the blood pressure readings were not standardized and ND that the published articles provided no details on the standardization of the blood pressure measurements nor on the quality control of the lead determinations.
Scale: The scale on which blood lead was expressed to compute the association size: lin = linear; log = common logarithm and in = natural logarithm. G indicates that the blood pressure was compared between groups with low and high exposure to lead and D that groups were contrasted in a regression model with use of dummy variables.
Info. Information provided by the authors: 0 = no information requested; NA = information requested, but no longer available; S = descriptive statistics; C = single (unadjusted) correlations.
R = multiple linear regression equations. Where available, the information provided by the authors was used rather than the often incomplete published data.
(1) Caerphilly Study (2) Welsh Heart Program, (3) NHANES II (National Health and Nutrition Examination Survey), (4) foundry workers, (5) Canadian Health Survey, (6) Glostrup Population Study, cross-sectional analysis (1976), (7) London Civil Servants, (8) Glostrup Population Study, longitudinal analysis (1976–1987), (9) Normative aging study, (10) PheeCad (Public Health and Environmental Exposure to Cadmium) Study, (11) NHANES III Survey.
[a]Because of missing information, only the effect in whites is included.

recruited participants from the general population, four included employees with clerical jobs and eight blue collar workers such as iron workers (Table 1). In 24 cross-sectional studies, and four prospective studies, the possible influence of lead exposure was investigated by regressing blood pressure on blood lead. In three studies[13,16,63] the blood pressure was measured in exposed and control groups with differing blood lead levels. The longitudinal Boston[84,85] and Glostrup[53] studies applied autoregression to investigate the correlation between lead at baseline and blood pressure during follow-up.

The blood lead concentration was expressed on a linear scale in 15 studies and on a logarithmic scale in 16 (Table 1). Only four studies,[13,16,34,63] calculated the association between blood pressure and blood

lead without any adjustment for possible confounders and one[49] reported only the unadjusted association size with sufficient detail to be included in the analysis. In all but six reports,[13,16,34,40,49,63] the results were adjusted for age. However, in one of these six reports all subjects were of the same age.[40] Body mass index or body weight was entered into the multivariate models of 22 studies.[6,13,14,24,31,38,40,43,46,53,55–57,59–61,65,68,72,75,79,84] Most studies also considered additional confounding variables, such as smoking,[13,14,24,31,38,40,53,57,60,61,68,79,84] alcohol consumption,[6,13,14,24,31,38,40,43,53,56,57,60,71,79,85] intake of caffeine,[65,72] milk, dietary calcium intake or serum calcium,[6,24,52,60,79] serum zinc,[55] exposure to cadmium,[28] the blood haemoglobin concentration[40,55,75] or haematocrit,[6,31,43,61] physical activity or fitness,[40,53,60] socio-economic status[38,57,71] and menopausal status.[6]

The 31 studies listed in Table 1 included 48 different groups of subjects. Of these groups, 32 consisted only of men or almost exclusively of men (99%),[75] 15 only of women, and one[55] comprised both men and women. The combined estimates involved 58518 subjects for systolic blood pressure and 58491 subjects for diastolic blood pressure. The association sizes for each of the groups involved in the meta-analysis were obtained for systolic (Figure 1) and diastolic (Figure 2) blood pressure.

Summary statistics

The z-scores for all the groups included in the meta-analysis represented a continuum with no evidence for a bimodal or other distribution. Thus, the hypothesis of homogeneity was not rejected.

Table 2 shows the combined *P*-values obtained via Fisher's method and via Stouffer's approach for both sexes combined and for men and women separately. The results in men and women were not significantly different with *P*-values of 0.4 and 0.9 for systolic and diastolic blood pressure, respectively (Table 2). For all groups and both sexes combined, a two-fold increase of the blood lead concentration was associated with a 1.0 mm Hg increase in systolic pressure (95% CI: +0.5 to +1.4 mm Hg; $P < 0.001$), and with a 0.6 mm Hg rise in the diastolic pressure (CI: +0.4 to +0.8 mm Hg; $P < 0.001$).

In four studies[31,38,65,74] the association size was reported separately for whites ($n = 15911$) and non-whites ($n = 6035$). For white subjects the association was 0.4 mm Hg (CI: −0.7 to +1.5 mm Hg; $P = 0.26$) for systolic pressure and 0.2 mm Hg (+0.1 to +0.3 mm Hg; $P < 0.001$) for diastolic pressure. For non-whites the corresponding estimates were 1.4 mm Hg (CI: +0.9 to +1.9 mm Hg; $P < 0.001$) and 0.7 mm Hg (+0.5 to +0.9 mm Hg; $P = 0.04$) for systolic and diastolic blood pressure, respectively.

In a further step of the analysis, subgroups were excluded for whom the association size was reported as non-significant, but for whom details of the statistical parameters were not available. This excluded two studies on systolic pressure[52,55] and two on diastolic pressure[52,61] in women. In this analysis doubling of the blood lead concentration was associated with an increase in systolic pressure by 1.0 mm Hg (CI: +0.5 to +1.5 mm Hg; $P < 0.001$), and with a rise in the diastolic pressure by +0.7 mm Hg (CI: +0.5 to +0.9 mm Hg; $P < 0.001$).

Sensitivity analysis

The sensitivity of the findings was examined by removing one study at the time from the analysis and recalculating the joint *P*-values, using Stouffer's method. For systolic pressure, the combined *P*-value dropped to 0.002 when a study in women at the end of pregnancy[61] was excluded. The 95% confidence limits of the association size (+1.0 mm Hg) for systolic pressure ranged from +0.4 to +1.6 mm Hg.

In the groups ($n = 31$) where the relationship between blood pressure and blood lead was studied on a logarithmic scale ($n = 49320$), the association size averaged +0.8 mm Hg (CI: +0.4 to +1.2 mm Hg; $P = 0.001$) for systolic pressure and +0.5 mm Hg (CI: +0.3 to +0.7 mm Hg; $P = 0.005$) for diastolic pressure. In the 17 other groups ($n = 9198$), in which the association was studied on a linear scale, these estimates were +1.9 mm Hg (+0.7 to + 3.2 mm Hg; $P = 0.006$) and +1.4 mm Hg (+0.5 to +2.2 mm Hg; $P = 0.003$), respectively.

Across the 48 groups there was no significant relationship between the association size and the mean blood lead concentration, the weighted correlation coefficient was 0.27 ($P = 0.07$) for systolic pressure and 0.17 ($P = 0.23$) for diastolic pressure.

Discussion

The present meta-analysis of 31 studies, with a combined total of 58518 subjects, assessed the association between blood pressure and blood lead. Our results showed that a doubling of the blood lead concentration is associated with an increase of 1.0 mm Hg in systolic blood pressure and a 0.6 mm Hg rise in diastolic pressure. These findings are in agreement with our previous meta-analysis published in 1994 which included 23 studies in 33141 subjects.[5]

These overall results must be cautiously interpreted. It was assumed in the analysis that all studies provided an estimate of a common association size. Although the evaluation of the homogeneity across studies did not refute this hypothesis, the various studies considered different factors as possible confounders. However, with the exception of age, there is no general agreement on the covariates that should be taken into account in estimating the relationship between blood pressure and blood lead. This may possibly have affected the estimate of the combined association size. A meta-analysis performed by Schwartz J *et al*[70] in 1995 included 15 studies and showed that a doubling of the blood lead

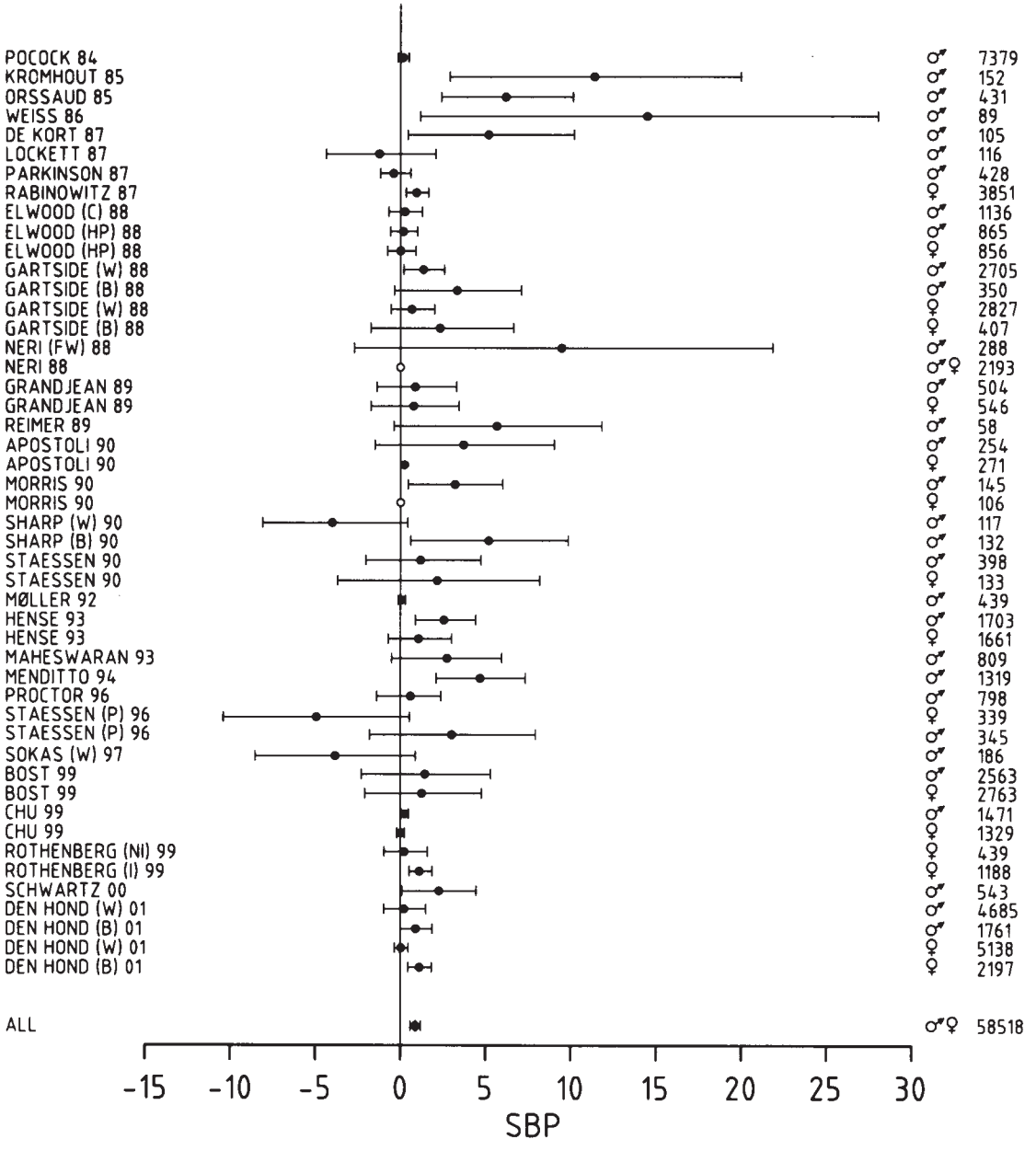

Figure 1 Change in the systolic pressure (association size in mm Hg with 95% confidence interval) associated with a doubling of the blood lead concentration. Circles represent individual groups and squares the combined association sizes. Open circles denote groups for whom a non-significant systolic[52,55] association size was assumed to be zero. C: Caerphilly Study; HP: Welsh Heart Program; W: Whites; B: Blacks; NI: Non-immigrants; I: Immigrants; FW: Foundry Workers; CS: Civil Servants; P: PheeCad (Public Health and Environmental Exposure to Cadmium) Study.

concentration was associated with a significant increase of 1.25 mm Hg in systolic blood pressure, which was 0.25 mm Hg higher than in the present analysis.

The change in blood pressure associated with a doubling of the blood lead concentration was calculated for all groups included in the present meta-analysis. A two-fold increase in blood lead was selected since it was less than or equal to the range of the non-industrial population means of blood lead for the studies included here. Moreover, within the groups included in each study, more than a doubling of blood lead concentration was observed as evidenced by the measures of central tendency and the ranges of the blood lead concentrations.

According to the Science Citation Index, studies considered as supportive of a hypothesis are cited almost six times more frequently than negative studies.[89] To exclude bias the present analysis estimated the overall blood pressure effects both with and without the studies,[52,55,61] for which the non-significant associations had been assumed to be zero. In addition, for 13 studies detailed information was made available by the authors.

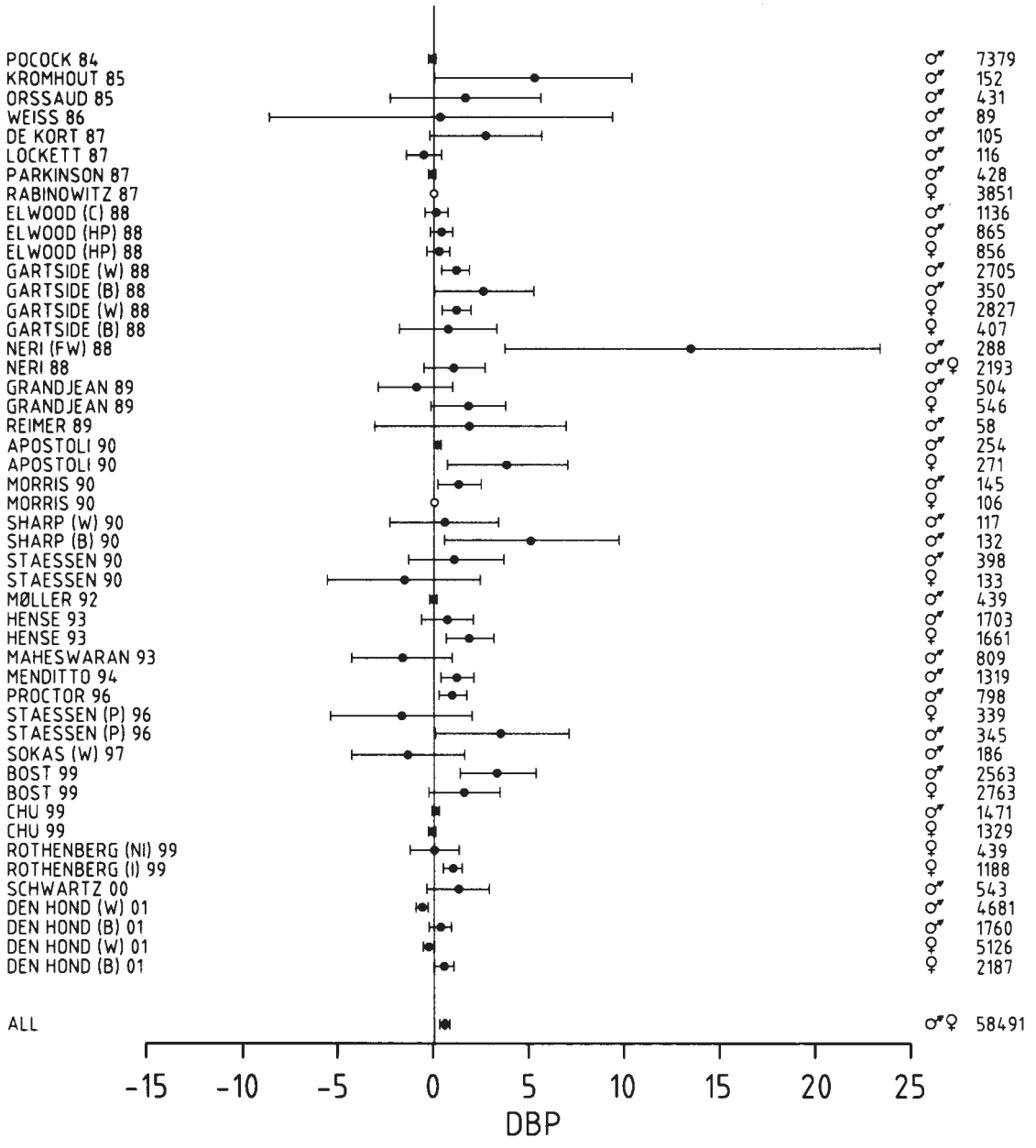

Figure 2 Change in the diastolic pressure (association size in mm Hg with 95% confidence interval) associated with a doubling of the blood lead concentration. Open circles denote groups for whom a non-significant diastolic[52,61] association size was assumed to be zero. For further details see caption to Figure 1.

It is noteworthy that some large studies, which supported a positive relationship between blood pressure and blood lead, based their conclusions on a single blood pressure reading.[42,58] Some reports based on the NHANES II Study (1976–1980) showed a relationship between blood pressure and blood lead concentration that was particularly strong among white middle-aged men.[69] However, the quality of the blood pressure measurements was questionable.[38] The NHANES III investigators (1988–1994) recognised this problem and measured seated blood pressure three times.[31] Twenty-four hour ambulatory blood pressure recordings are characterised by high reproducibility, are not subject to digit preference or observer bias and minimise the transient rise of a person's blood pressure in response to the observer, the so-called white-coat effect.[90] Only one study[6] used this new technique of blood pressure measurement but did not support the hypothesis of a consistent positive relationship between blood pressure and blood lead concentration.

Successful conduct of a meta-analysis is predicated upon there being similar effects in different sub-groups. Pooling data from many different studies could mask impacts in susceptible populations

Table 2 Combined *P*-values and overall association sizes between blood pressure and blood lead.

		No.	*Chi-square*	*Z-score*	*Association size*
Both sexes[a]					
All studies	SBP	58518	210 (<0.001)	6.6 (<0.001)	+1.0 (+0.5 to +1.4)
	DBP	58491	229 (<0.001)	5.3 (<0.001)	+0.6 (+0.4 to +0.8)
Men[b]					
All studies	SBP	32268	210 (<0.001)	6.6 (<0.001)	+1.2 (+0.6 to +1.7)
	DBP	32263	143 (<0.001)	5.5 (<0.001)	+0.6 (+0.4 to +0.8)
Women					
All studies	SBP	24057	63 (=0.003)	2.7 (=0.004)	+0.8 (+0.2 to +1.4)
	DBP	24035	83 (<0.001)	4.9 (<0.001)	+0.6 (+0.3 to +0.9)

No.: Number of subjects included in the analysis.
Chi-square. Statistic derived by Fisher's method with unweighted *P*-value between parentheses.[8]
Z-score. Statistic derived by Stouffer's method with one-sided *P*-value between parentheses.[8] The combined z-scores were weighted by the number of subjects in each group.
Association size. Increase in the blood pressure (mm Hg) associated with a twofold increase in the blood lead concentration (with 95% confidence interval between parentheses).
[a]Includes also one study[55] in which the effects in men and women were not reported separately.
[b]Includes Sokas *et al*[75] (99% men).

unless care is taken to ensure this is not occurring. No significant differences between genders were observed but there seems a trend that blacks are more susceptible than whites. Differences in genetic and socio-economic background might make blacks more susceptible to the possible rising effects of blood lead on blood pressure.

The biologic plausibility of a causal relationship between an increased blood pressure and lead exposure has been mainly investigated in animal experiments. The most likely mechanisms include impairment of renal function,[1] interference with the balance between the renin-angiotensin-aldosterone axis and the renal kallikrein system,[48,66,91] direct actions at the level of the vascular smooth muscle cells,[92] alternations of the transport of ions across the cellular membranes,[51] potentiation of sympathetic stimulation[93] and nitric oxide inactivation.[94,95] Notwithstanding these biological mechanisms of actions, in the majority of the population studies, the association between blood pressure and blood lead concentration did not reach statistical significance. On the other hand epidemiological studies can only show associations but not prove causation or lack thereof. On balance across all human studies the relationship between blood pressure and blood lead concentration is inconsistent based on the observation that many studies did not reach the level of significance. The present meta-analysis shows an overall statistically significant positive relationship, which is weak in biological terms.

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