REVIEW ARTICLE

Blood pressure and hypertension in relation to lead exposure updated according to present-day blood lead levels

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ABSTRACT

Lead is an environmental hazard that should be addressed worldwide. Over time, human exposure to lead in the Western world has fallen drastically to the levels comparable to those in humans living in the pre-industrial era, who were mainly exposed to natural sources of lead. To re-evaluate the health risks possibly associated with present-day lead exposure, a three-pronged approach was applied. First, we critically assessed the recently published population metrics describing the adverse health effects associated with lead exposure at the population level. Next, we summarized the key results of the Study for Promotion of Health in Recycling Lead (SPHERL; NCT02243904) and analyzed these results in the context of the published population metrics. Last but not least, we performed a brief literature review on the present-day lead exposure level in Poland. To our best knowledge, SPHERL is the first prospective study that accounted for interindividual variation in vulnerability to the toxic effects of lead exposure by assessing the participants' health status before and after occupational lead exposure, with blood pressure and hypertension as the primary outcomes. The overall conclusion of this comprehensive review on blood pressure and hypertension is that mainstream ideas about the public and occupational health risks related to lead exposure need to be urgently updated because a large part of the available literature has become obsolete given present-day exposure levels that sharply declined over the past 40 years.

Key words: blood pressure, environmental medicine, hypertension, lead, occupational medicine

INTRODUCTION

Lead is an environmental toxicant. At high exposure, as observed in the past in occupational settings or in the general population due to, for instance, the consumption of moonshine whiskey, lead causes hypertension and renal failure [1, 2]. However, the National Health Examination Survey (NHANES) demonstrated that mean blood lead levels in American adults have dramatically dropped from 13.1 µg/dl in NHANES II (1976–1980) [3] to 2.76 µg/dl in NHANES III (1988–1994) [3] and further to 1.64 µg/dl in NHANES IV (1999–2002) [4, 5]. Over time, increasingly tighter environmental regulations led to the prohibition on lead-containing paint (1976) [6], phasing out of leaded gasoline (1995) [6], elimination of lead as construction material, replacement of lead pipes in drinking water distribution, eliminating lead solder in food cans, and compulsory and systematic recycling of lead batteries and other lead waste. In developed nations, the average blood lead concentration in the general population currently approaches 1.5 µg/dl. As estimated by the Global Burden of Disease (GBD) Consortium [7], this level is close to the estimated blood lead concentration of 2 µg/dl in pre-industrial humans, who were only exposed to natural sources.

Our studies in the field of environmental medicine span over the past 40 years but did not provide convincing evidence supporting the thesis that environmental lead exposure is causally related to hypertension [8–10], renal dysfunction [11–13], or cardiovascular disease [14, 15]. Given this research track record, this review aimed to identify sources of bias in recent publications [16] associating adverse health outcomes with lead exposure, to summarize the key results of the Study for Promotion of Health in Recycling Lead (SPHERL; NCT02243904) [17], and to provide an overview on the contemporary lead exposure level in Poland. To our best knowledge, SPHERL is the first prospective study that accounted for individual variation in vulnerability to the toxic effects of lead exposure by assessing the participants' health status before and after lead exposure [17], which was an issue identified as a research priority in a meta-analysis published in 2002 [18]. As an introduction to the field, the toxicokinetics of lead in humans are first summarized.

TOXICOKINETICS OF LEAD IN HUMANS

Lead enters the body primarily through inhalation and ingestion. Today, adults are mainly exposed by breathing in lead-contaminated fine particulates and fumes in occupational settings or during leisure time activities. Exposure in the general population via ambient air is generally due to respirable particles capable of deep lung penetration and deposition [19]. Once the finest dust particles reach the lung alveoli, they readily pass the air-blood barrier and are subsequently system-wide distributed via the bloodstream. Occupational exposure entails coarser aerosols that deposit in the upper airways and then translocate to the gastrointestinal tract by mucociliary clearance, where gastrointestinal uptake kinetics prevail (5%–10% uptake). The lead in air to lead in blood slope is around 2 for ambient and 0.05 for occupational exposure [19].

Lead is a cumulative toxicant, 90%–95% of which is stored in bone, from where it is recirculated with a half-life of 20–25 years [20, 21]. Blood lead, in 99% carried by red blood cells, reflects recent exposure over the past 1–2 months and the amount of lead released and recirculated from bone stores [20]. Both bone [21, 22] and blood [11, 21, 22] lead levels increase with advancing age. Bone lead is associated with blood lead [21, 22] and explains around 20% of the variance in blood lead, depending on seasonality [21], hormonal, and other endogenous and environmental stimuli influencing the balance between bone formation and resorption [22]. Recirculation of lead from bone explains why there is a lag time for blood lead to decline when environmental [9] or occupational [20] lead exposure decreases.

SOURCES OF BIAS IN THE LITERATURE

Relevant publications are the NHANES III results and the articles published by the GBD consortium.

MORTALITY IN RELATION TO BLOOD LEAD IN NHANES III

The cross-sectional NHANES III survey (1988–1994) involved the collection of clinical variables, questionnaire data, and biochemical measurements, including blood lead, in a representative sample of the adult population of the United States (US) [23–25]. The method of blood lead measurement was graphite furnace atomic absorption spectrophotometry with the detection limit set at 1.0 µg/dl. For the 8% of participants with blood lead levels below the detection limit, a level of 0.7 µg/dl was imputed [23–25]. These NHANES III baseline data were linked with the National Death Index, using probabilistic matching based on 12 identifiers for each participant to ascertain vital status and cause of death. Follow-up (FU) was the time between the baseline examination date, date of death, or the participant's 90th birthday, whichever came first. The censoring date was 31 December 2011 in the latest NHANES III report [25].

In 1489 individuals (Table 1 [25]), the multivariable-adjusted hazard ratios expressing the risk of an increase in blood lead from the 10th to the 90th percentile (1.0 to 6.7 µg/dl) were 1.37, 1.70, and 2.08 for total, cardiovascular, and coronary mortality, respectively. From individual measures of blood lead and their associated hazard ratios, the population attributable fraction (PAF [26, 27]), i.e., the adverse health outcomes attributable to lead exposure, was then computed as the integral of the hazard ratios at each blood lead level weighted by the logarithmically transformed population distribution of blood leads over the total range from 0.70 to 56.0 µg/dl. The PAFs amounted to 18.0% (CI, 10.9%–26.1%) for total mortality, 28.7% (CI, 15.5%–39.5%) for cardiovascular mortality, and 37.4% (CI, 23.4%–48.6%) for coronary mortality. Given the overall annual mortality (n = 2 288 888), cardiovascular mortality (n = 891 896), and coronary mortality (n = 494 652) in the US and assuming that blood lead concentrations might be reduced to 1.0 µg/dl or less, the number of preventable deaths amounted to 412 000 (CI, 250 000–598 000) for total mortality, 256 000 (CI, 138 000–352 000) for cardiovascular mortality, and 185 000 (CI, 116 000–241 000) for coronary mortality.

That 2018 NHANES report (Table 1 [25]), based on historical blood lead from the year 1988 to 1994, has little relevance for public health policies in the third decade of the twenty-first century for the reasons listed below. First, the blood lead levels, as recorded in NHANES III, were not representative of current lead exposure. To a large extent, these levels reflected the recirculation of lead from earlier bone stores, which in many participants accrued from the first decades of the twentieth century onwards, when lead was still highly prevalent in the environment in the US. In our analyses of 12 725 NHANES IV participants examined from 2003 until 2010 [5], the geometric mean blood lead concentration in all participants was 1.41 µg/dl, with lower

Table 1. Mortality in 14 289 NHANES III participants followed up until December 31, 2011

Variable	All participants	Results by thirds of the blood lead distribution			*P*-value
Blood lead range, µg/dl	0.7–56.0	<2.0	2.0–3.7	≥3.8	
Risk factors					
Black, %	10.2	9.1	9.2	12.1	0.0004
Men, %	47.9	24.6	49.2	68.3	<0.0001
Age, years	44.1	37.8	44.8	48.2	<0.0001
Body mass index					
<25 kg/m^2, %	44.6	49.4	42.8	42.0	<0.0002
25–29.9 kg/m^2, %	33.0	27.0	24.5	36.9	<0.0001
≥30 kg/m^2, %	22.4	23.6	22.7	21.1	0.13
Current smoking, %	34.9	23.0	33.0	47.8	<0.0001
Alcohol consumption, %					
<4 units per month, %	63.2	73.3	62.3	54.8	<0.0001
≥4 units per month, %	36.8	26.7	37.7	45.2	<0.0001
Hypertension, %	17.5	9.6	18.0	24.3	<0.0001
<$20 000 annual income, %	31.9	27.7	24.0	37.4	<0.0001
Total mortality					
Deaths, n (%)	4422 (30.9)	631 (13.2)	1340 (28.1)	2451 (51.5)	
Hazard ratios (95% CI)					
Primary analysis	1.37 (1.17–1.60)	–	–	–	–
Sensitivity analyses					
Blood lead <5 µg/dl	1.38 (1.15–1.66)	–	–	–	–
HT + treatment status	1.38 (1.18–1.61)	–	–	–	–
SBP + DBP (continuous)	1.36 (1.16–1.58)	–	–	–	–
Cardiovascular mortality					
Deaths, n (%)	1801 (12.6)	218 (4.6)	552 (11.6)	1031 (21.6)	
Hazard ratios (95% CI)					
Primary analysis	1.70 (1.30–2.22)	–	–	–	–
Sensitivity analyses					
Blood lead <5 µg/dl	1.95 (1.46–2.60)	–	–	–	–
HT + treatment status	1.73 (1.32–2.27)	–	–	–	–
SBP + DBP (continuous)	1.68 (1.28–2.19)	–	–	–	–
Coronary mortality					
Deaths, n (%)	988 (6.9)	112 (2.4)	284 (6.0)	592 (12.4)	
Hazard ratio (95% CI)					
Primary analysis	2.08 (1.52–2.85)	–	–	–	–
Sensitivity analyses					
Blood lead <5 µg/dl	2.57 (1.56–4.52)	–	–	–	–
HT + treatment status	2.13 (1.55–2.93)	–	–	–	–
SBP + DBP (continuous)	2.07 (1.55–2.84)	–	–	–	

HT, SBP, and DBP indicate hypertension, systolic blood pressure, and diastolic blood pressure, respectively. Data were extracted from reference [16]. Of 18 825 participants enrolled, 1795 had no medical examination or home visit, 1419 were excluded because of missing blood lead or urinary cadmium, 1314 because of missing covariables, and 8 because of missing identifiers to match with the national registry, leaving 14 289 for statistical analysis. Hazard ratios, given with a 95% confidence interval, represent the relative risk for an increase in blood lead from 1.0 to 6.7 µg/dl (10th–90th percentile interval). Hazard ratios accounted for ethnicity (White, Black, or Mexican-American), sex, the linear and squared terms of age, body mass index (categorical), hypertension (blood pressure ≥140 mm Hg or ≥90 mm Hg diastolic), smoking status (never, current, or former), alcohol consumption (<4 vs. ≥4 units per month), serum cholesterol, glycated hemoglobin, urinary cadmium (categorized), physical activity (categorized into none, 1–14 and ≥15 times in the previous month), annual income (< vs. ≥$20 000), and the healthy eating index (categorized). Sensitivity analyses were conducted by including only participants with blood lead <5 µg/dl (relative risk given for the 10th–80th percentile interval), considering treatment status in the definition of hypertension, and entering systolic and diastolic blood pressure as continuous covariables in the models to replace hypertension (categorical). To convert blood lead concentration from µg/dl to µmol/l, multiply by 0.0483. An ellipsis indicates that in reference [16], hazard ratios were not given for increasing categories of blood lead. Reproduced from reference [16], which was published as an open access article under the Creative Commons Attribution Non-Commercial-NoDerivs License

Abbreviations: DBP, diastolic blood pressure; HT, hypertension; SBP, systolic blood pressure

levels in women (1.25 µg/dl) than men (1.80 µg/dl) and in Whites (1.46 µg/dl) compared to Blacks and Hispanics (1.57 µg/dl). All blood lead levels were below 30 µg/dl [5]. Second, PAF was calculated as the proportional decline in mortality that would occur if the blood lead concentrations of all participants were reduced to a reference level of 1.0 µg/dl or lower [25], which is an unfeasible target, given lead exposure from natural sources and food. This very low null-effect blood lead concentration substantially inflated the hazard ratios and PAFs associated with blood lead. Third, hypertension as the causal pathway linking mortality to environmental or occupational lead exposure is a deeply rooted paradigm based on research dating back more than half a century ago [28, 29]. The NHANES III report itself [25] argued against this mechanistic pathway, given that models accounting for hypertension and hypertension treatment or adjusted for systolic and diastolic blood pressure (BP) as continuously distributed variables barely affected the hazard ratios (Table 1). Along similar lines, a meta-analysis of 31 studies published before

February 2001 involving 58518 participants [30] indicated the doubling of blood lead was only associated with a marginally higher BP. The pooled estimates averaged 1.0 mm Hg (confidence interval [CI], 0.5–1.4 mm Hg) systolic and 0.6 mm Hg (CI, 0.4–0.8 mm Hg) diastolic. Furthermore, in a prospective population study of 728 individuals (50.7% women; age range, 20–82 years), BP was measured conventionally at baseline (1985–1989) and at FU (1991–1995), and by 24-hour ambulatory BP monitoring at FU [9]. Over a median FU of 5.2 years (range, 3.5–8.4 years), the geometric mean blood lead concentration dropped by 32% from the baseline level of 8.7 µg/dl (range, 1.7–72.5 µg/dl). The small changes in systolic/diastolic BP on conventional measurement (–1.5/+1.7 mm Hg) were unrelated to the blood lead concentration at baseline or to the changes in this exposure biomarker over FU. Similarly, 24hour ambulatory BP was not associated with blood lead at baseline or FU [9]. A recent NHANES report covering the data from 1999 to 2016 [31] included 30 467 participants at the age range of 20-79 years. Non-Hispanic Black men (n = 3006) had the highest mean blood lead level (2.20 µg/dl), compared to 3 814 Hispanic men (2.18 µg/dl), and 6989 non-Hispanic White men (1.89 µg/dl). A similar ethnic gradient in blood lead was observed in women: 1.49 µg/dl in 3256 non-Hispanic Black women, 1.30 µg/dl in 4130 Hispanic women, and 1.30 µg/dl in 7078 non-Hispanic White women. In the multivariable-adjusted logistic regression models [31], hypertension was not associated with blood lead (odds ratio, 1.002; CI, 0.983–1.021).

The percentage of all-cause mortality was 55.4% in the top third of the NHANES III blood lead distribution (Table 1) [25]. The 2011 National Vital Statistics Report [32] listed cause-specific mortality corresponding in time with the end of the 20-year FU of the NHANES III participants [25]. Malignancies, standardized per 100 000 deaths from 45 up to 84 years, contributed 434 more deaths to all-cause mortality than cardiovascular disease, whereas from the age of 85 onwards, heart disease overtook malignant disease, contributing 2435 extra deaths. The NHANES III models [25] did not account for the competing risks of fatal cardiovascular and non-cardiovascular diseases, both contributing to all-cause mortality [33, 34]. Finally, a major limitation of the NHANES III studies [23–25] was their focus on mortality. The introduction of stroke units and the wide availability of invasive coronary care, thrombolysis, and percutaneous vascular interventions have reduced the case-fatality rate of most cardiovascular complications of hypertension. Not accounting for nonfatal events, therefore, limits the generalizability of the NHANES III reports [23–25].

THE GLOBAL BURDEN OF DISEASE REPORTS

A disability-adjusted life year (DALYs) is a summary metric that reflects the sum of years lived with a disability and the years of life lost. It, therefore, reflects both quality of life and premature mortality [35]. From the age of 25 years onwards, there is a causal association between systolic BP and lead exposure, as proposed by the GBD consortium [36, 37]. Mediated-via-BP lead exposure was unrealistically assumed to cause a wide range of cardiovascular diseases, including right heart disease; ischemic heart disease; ischemic, hemorrhagic, and other non-ischemic strokes; hypertensive heart disease; aortic aneurysm; the aggregate of cardiomyopathy, myocarditis, and endocarditis; the aggregate of atrial fibrillation and flutter; pulmonary vascular disease; other cardiovascular diseases; and chronic kidney disease [38]. If evidence was only available for the relative risk of either morbidity or mortality, the assumption was that estimates of relative risk would equally apply to both fatal and nonfatal outcomes. In 2010, high BP was the leading single risk factor globally, accounting for 9.4 million deaths (95% uncertainty interval [UI], 8.6–10.1 million) and 7.0% (UI, 6.2%–7.7%) of global DALYs [35]. For environmental lead exposure, these estimates were 0.67 million deaths (UI, 0.58–0.78 million) and 0.56% of DALYs lost (UI, 0.47%–0.66%) [35]. Worldwide, for both sexes and all ages combined, high BP moved up in the global risk factor ranks from rank 4 in 1990 to rank 1 in 2010 and environmental lead exposure from rank 30 to rank 25 [35].

The GBD investigators listed among possible limitations of their results: (1) residual confounding; (2) uncertainty as to the extent to which effect sizes were generalizable; (3) and the impossibility to account for temporal changes in the exposure to risk factors. Thus, the GBD statistics fell short of accounting for the steady global decline in environmental lead exposure. This might explain why globally, regardless of declining environmental exposure [3–5, 9], environmental lead exposure moved up in the risk factor ranks from rank 30 in 1990 to rank 25 in 2010 [35]. Furthermore, PAF for clusters of risk factors, rather than for a single risk indicator, has to be calculated because of the issue of residual confounding. Indeed, cardiovascular risk factors [39–41] and exposures to various environmental pollutants [8, 12, 42] cluster within individuals, such as, for instance, poverty, unhealthy lifestyle habits, poor housing conditions, and lead exposure in the NHANES surveys. The GBD estimates did not account for co-exposures to risk factors and environmental pollutants. According to the World Health Organisation demographic data, in 2010, the population of the US (309 million) represented approximately 4.5% of the world's population (6.9 billion). Interestingly, if the statistics of the 2012 GBD report are truly generalizable (PAF, 0.67 deaths worldwide [35]), preventable deaths related to environmental lead exposure in the US would amount to approximately 30 150 per year, an estimate more than 10-fold smaller than that proposed in the NHANES III report [25].

SPHERL

SPHERL is a longitudinal study of newly hired lead workers without known previous occupational exposure. They were employed at battery manufacturing and lead recycling plants in the US. SPHERL complies with the Helsinki Decla-

ration for investigations in humans. The Ethics Committee of the University Hospitals Leuven (Belgium) approved the study protocol (Nº B322201421631), which has been published in detail [17]. The co-primary endpoints for which SPHERL was powered [17] were the changes in BP and renal function. The secondary endpoints included the autonomous nervous regulation of the cardiovascular system, as captured by heart rate variability (HRV), neurocognitive function, and peripheral nerve conduction.

The workers underwent FU visits 1 and 2 years after enrollment. Detailed diagrams describing the flow of participants and the number of workers excluded from the statistical analyses have been published for BP and hypertension [43]. In the most recently published SPHERL article focusing on BP [43], the geometric mean blood lead concentration was 4.1 µg/dL (interquartile range [IQR], 2.3–8.1 µg/dl) at baseline, and 13.5 µg/dl (IQR, 10.1–22.8 µg/dl) at last FU in the office BP cohort (n = 267). The last follow-up-to-baseline blood lead concentration ratio averaged 3.3 (IQR, 3.0–3.8; $P = 0.036$; Figure 1). Changes in the blood lead concentration were similar in the ambulatory BP cohort (n = 137).

At the study sites, office BP was measured at the brachial artery by trained nurses according to the current guidelines [44]. After the workers had rested for 5 minutes in the sitting position, the nurses obtained five consecutive BP readings to the nearest 2 mm Hg by auscultation of the Korotkoff sounds, using standard mercury sphygmomanometers. For analysis, the five readings were averaged. Ambulatory BP was recorded on the same arm as office BP with similarly sized cuffs, using validated [45] oscillometric Mobil-O-Graph 24-h PWA monitors (I.E.M. GmbH, Stolberg, Germany). The monitors were programed to obtain readings at 15-minute intervals during waking hours and every 30 minutes during sleep. Mean 24-hour BP was the average of the awake and asleep BPs weighted for the duration of the awake and asleep periods. Office and ambulatory BP were categorized according to the 2017 American College of Cardiology/American Heart Association (ACC/AHA) guidelines [44].

Office BP was measured in 267 participants (11.6% women, mean baseline age, 28.6 years) and 24hour ambulatory BP in 137 participants at two FU visits. Fully adjusted changes in systolic/diastolic BP associated with a doubling of the blood lead ratio were 0.36/0.28 mm Hg (CI, 0.55 to 1.27/0.48 to 1.04 mm Hg) for office BP and 0.18/0.11 mm Hg (CI, 2.09 to 1.74/1.05 to 1.27 mm Hg) for the 24-hour ambulatory BP. The adjusted hazard ratios for moving up hypertension categories associated with a doubling of the blood lead concentration were 1.13 (CI, 0.93–1.38) for office BP and 0.84 (CI, 0.57–1.22) for the 24-hour ambulatory BP. Heat maps demonstrated, in line with all clinical measurements [46], that baseline BP was the main determinant of BP at FU (Figure 2). Due to regression to the mean, workers with low BP at enrollment were more likely to experience an increase in their office and ambulatory BP or to move up across hypertension categories according to the ACC/AHA

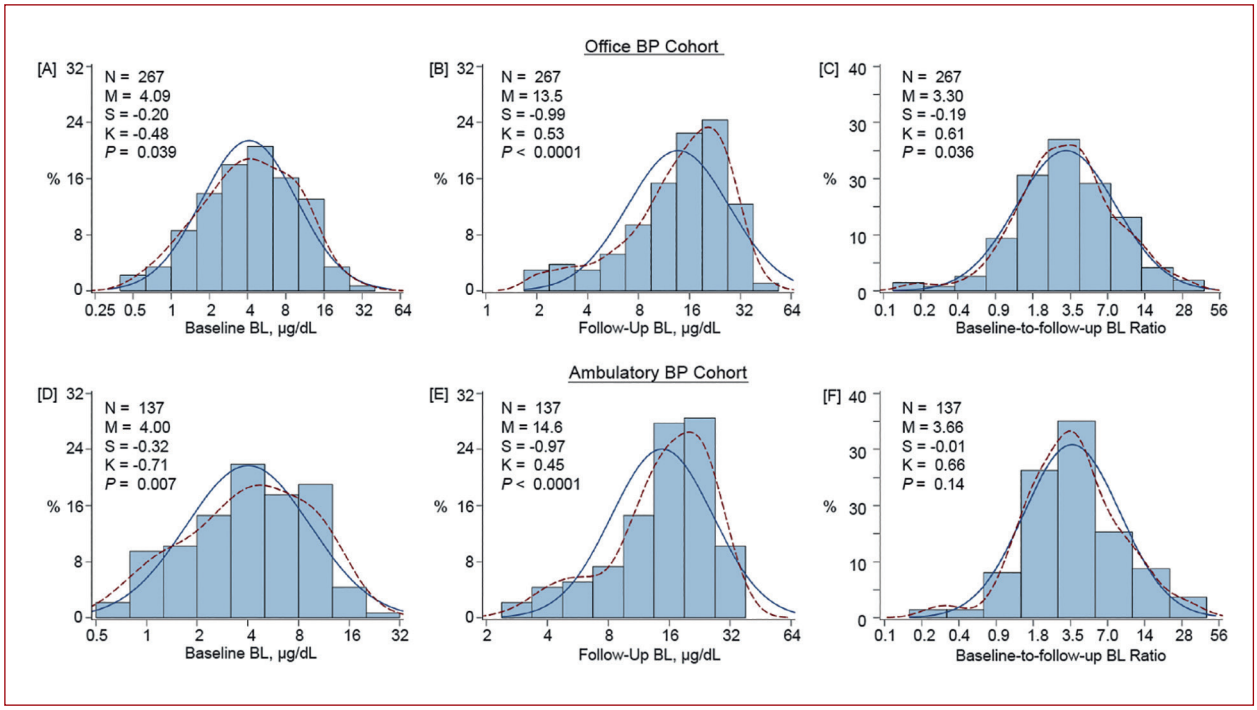

Figure 1. Distributions of the blood lead concentration at baseline (**A, D**), at the last follow-up visit (**B, E**), and the last-follow-up-to-baseline blood lead ratio (**C, F**) in the office (**A–C**) and ambulatory (**D–E**) blood pressure cohorts. N, M, S, and K indicate the number of workers, geometric mean, and coefficients of skewness and kurtosis. The solid and dotted lines represent the normal and kernel density distributions. The *P*-values are for departure of the observed distribution from normality according to the Shapiro-Wilk statistic.

Abbreviations: BP, blood pressure; BL, blood lead

guidelines, whereas the opposite was true for workers in the top tail of the baseline BP distribution. However, there was no systematic shift in BP distributions from baseline to last FU. During the 2-year FU, there was not a single case of the wide array of cardiovascular diseases to be associated with lead exposure, according to the 2012 GBD report [38].

LEAD EXPOSURE IN POLAND

We performed a literature review on lead exposure in Poland by searching PubMed from January 2018 to June 2023, using "lead", "lead poisoning", "occupational exposure", "environmental exposure", and "Poland" as keywords and MeSH (Medical Subject Headings) terms. After excluding the articles unrelated to humans, 9 articles were left, including 5 studies in adults, 2 studies in children, 1 in-vitro experiment, and 1 literature review. We did not find any recently reported Polish occupational lead exposure study. In the studies conducted in Polish adults, the mean blood lead levels ranged from 1.16 to 7.25 µg/dl in the general population under environmental exposure [47–50]. Blood lead was significantly and positively associated with the severity of anxiety in healthy postmenopausal women [47] and the percentage of monocytes and cortisol levels in blood in women with metabolic syndrome [48]. However, given their observational nature, these studies cannot establish a causal relation with lead exposure. A cross-sectional study [51] recruited 1141 schoolchildren (551 boys and 590 girls, at average age of 10.79 years) in an industrialized mining area in southwestern Poland. The mean blood lead level was 3.76 µg/dl (range, 1.7–15.2 µg/dl). The boys with a blood lead level above median (>3.7 µg/dl) had significantly lower body mass index, mid-upper arm circumference, and skinfold thickness (P <0.01), while these associations were not significant in girls (P >0.05) [51]. However, nutritional status was not accessed, and the co-exposure to other heavy metal pollutants in the industrialized area could

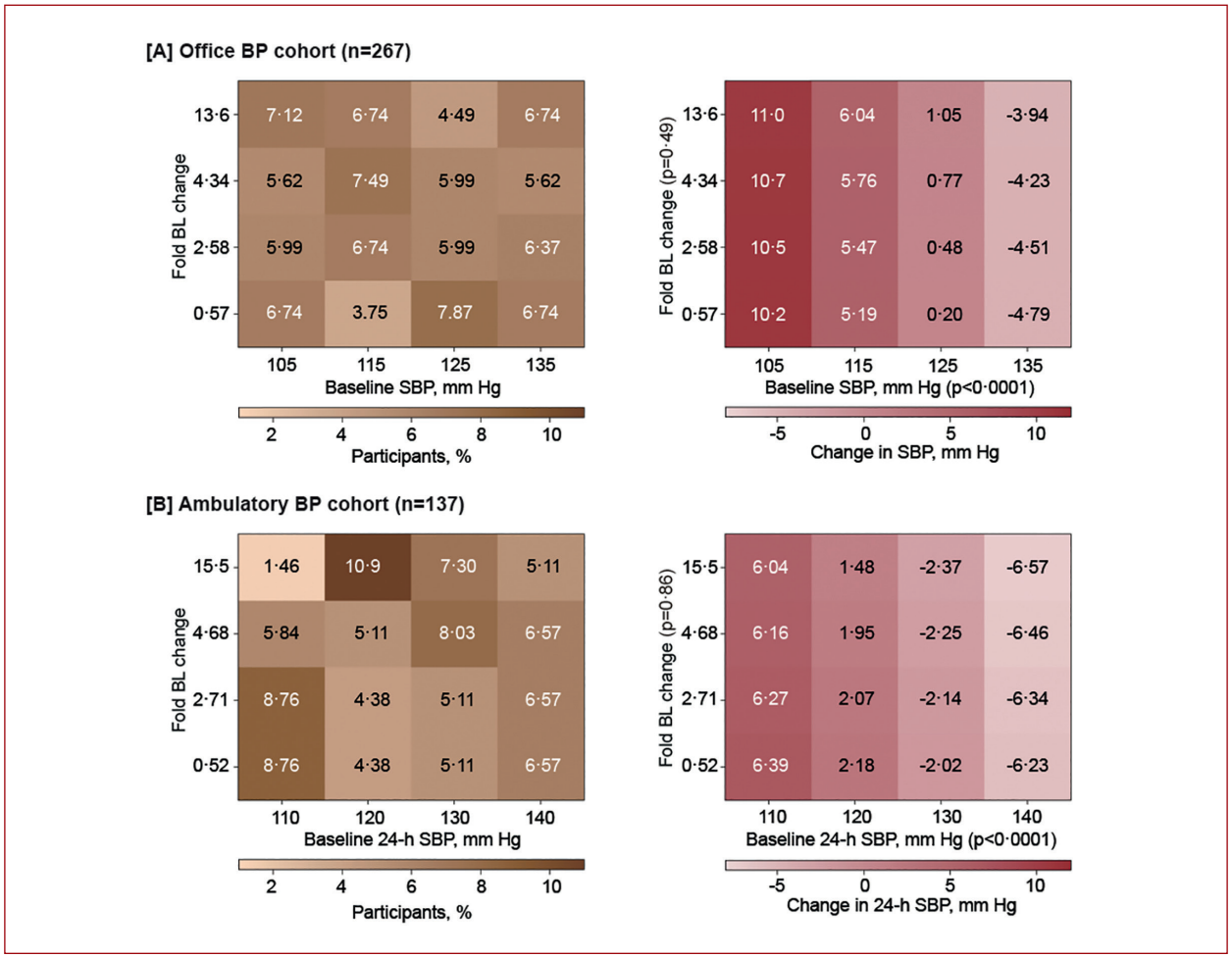

Figure 2. Heat maps relating the change in office (**A**) and 24-hour ambulatory (**B**) systolic blood pressure to the change in blood lead multiple from baseline to last follow-up. SBP refers to systolic blood pressure. Associations were derived by mixed models, including the individual as a random effect. Models were adjusted for ethnicity (white vs. other), sex, age, body mass index at baseline, change in body weight during follow-up, the baseline value of blood lead, and the baseline values of and changes during follow-up in heart rate, smoking status, total-to-HDL serum cholesterol ratio, γ-glutamyltransferase, and serum creatinine. The percentage of workers contributing to the cross-classification between the baseline blood pressure (horizontal axis) and the fold change in blood lead was given for each analysis run. Reproduced from reference [43], which was published as an open access article under the Creative Commons Attribution Non-Commercial-NoDerivs License

Abbreviations: see Table 1 and Figure 1

not be excluded [51]. Another study reported geometric mean blood lead levels of 2.54 and 2.39 µg/dl in 3–7 year-old environmentally exposed boys and girls, respectively [52]. The blood lead level was significantly higher in the children whose fathers had higher education attainments, whose mothers smoked cigarettes, and those living in the neighborhood with some environmental hazards [52]. In a society with a life expectancy of more than 74 years, biomarkers in young people show recent exposure, which is particularly relevant for pollutants, such as lead, a heavy metal accumulating during life [12, 53]. Although lead exposure is still a contributor to adverse health outcomes, the aforementioned studies demonstrated a substantially lower blood lead level in the environmental setting compared with the historic high exposure levels in Poland (the year 1997, blood lead ranged from 1.9 to 28.1 µg/dl in 155 children aged 4–14 years) [54]. The blood lead levels in Polish children reflected the current environmental exposure level in Poland and were lower than 5 µg/dl, the target level as suggested by the Centers for Disease Control and Prevention (CDC) [55].

PERSPECTIVES

Lead exposure represents an environmental risk that should be addressed worldwide. To re-evaluate the health risks possibly associated with present-day lead exposure, a three-pronged approach was applied, first assessing recently published population metrics [23–25], next summarizing the SPHERL results on BP and hypertension [43, 56–58], and third performing a brief literature review on the present-day lead exposure in Poland. Considering health preservation at the population level, health metrics might gain credibility by addressing the following issues: (1) ensuring use of health data (e.g., BP) in relation to present-day lead exposure levels; (2) retesting the presumed pathogenic pathway leading from hypertension to both fatal and nonfatal adverse health outcomes; (3) narrowing the range of cardiovascular complications potentially associated with lead exposure; (4) developing risk models accounting for multimodal exposure to risk factors and pollutants, thereby reducing residual confounding; and (5) setting no-risk thresholds at blood lead levels that are not lower than what is achievable given the naturally occurring background sources of lead exposure.

SPHERL was an ethically endorsed real-world experiment. The major strength of that cohort study was that it accounted for interindividual variability in the responses to an over 3-fold blood lead increase with full documentation of the baseline values in the biomarkers of effect and exposure. Additionally, although residual confounding by unmeasured risk factors can never be excluded in observational studies, SPHERL did address a wide array of potential confounders. Nevertheless, the limitations of SPHERL should be addressed in future research. First, the attrition rate among the workers who participated in the baseline examination but defaulted from FU amounted to over 40% mainly because they left employment. According to the published SPHERL protocol [17], the anticipated attrition rate was 50%. To meet the sample size required to address hypertension and renal dysfunction as the primary endpoint, 500 workers were enrolled. Second, the small sample size and limited 2-year FU of the current SPHERL cohort warrant a cautious interpretation of the findings. Third, the healthy worker effect [59] might partially account for the nonsignificant results in relation to lead exposure in this occupational cohort, as the mean age of the workers was 28.6 years. The current observations should not be unthinkingly generalized and might, therefore, not apply to older individuals or patients with comorbidities, such as diabetes [60], in whom renal function is more vulnerable. Finally, co-exposure to other metals, such as cadmium, is common in lead recycling plants. Lead accumulates in the kidneys, with a half-life exceeding 30 years [61]. Cadmium is an established renal toxicant, adversely affecting renal tubular and glomerular function [62], which would affect BP and hypertension.

Article information

Conflict of interest: None declared.

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