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Blood lead levels in 2018/2019 compared to 1987/1988 in the German population-based KORA study

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ABSTRACT

Introduction: Lead exposure remains of continuing concern due to its known and suspected impacts on human health and has been designated as a priority substance for investigation in human biomonitoring studies by the EU. The aims of this study were to measure blood lead levels (BLL) in a population based cohort of middle-aged individuals without major current exposures to lead, and to compare these to historical blood lead levels obtained thirty years earlier.

Methods: The population-based KORA study from 1984 to 2001 included inhabitants of the Augsburg Region, Germany. During 2018 to 2019, a subsample of these participants (KORA-Fit) was invited for interview regarding demographic and lifestyle factors, physical examination and blood withdrawal. Blood samples were stored at −80C prior to measurement of BLL via graphite furnace atomic absorption spectroscopy (GF-AAS). Descriptive and multivariable analyses were performed.

Results: BLLs were measured in 3033 eligible persons aged 54 to 73, establishing a geometric mean (GM) BLL of 24.8 μg/l in 2018/19. Of these, 555 (18%) had BLL above proposed 95th percentile reference values of the German Environment Agency. Only small differences were found in BLL stratified by sociodemographic categories, however regular smokers had higher GM BLL (26.1 μg/l) compared to never smokers (23.7 μg/l), and an increasing BLL with increased wine consumption was noted. For 556 individuals, BLLs (GM: 54.0 μg/l) reduced by 35% in men and 50% in women compared to levels in 1987/88 with only 1.4% of individuals having an unchanged or increased BLL.

Discussion: KORA-Fit provided contemporary normative data for BLL in a Western European population without major current sources of lead exposure. Mean BLLs have fallen since the 1980s using historical BLL data which is likely linked to the ban of leaded gasoline. Nevertheless, BLLs in this population remain elevated at levels associated with morbidity and mortality.

Author contributions

James PK Rooney: Data visualization, preparation of the original draft, preparation of the final manuscript. **Stefan Rakete**: Laboratory analysis, writing - review & editing, preparation of the final manuscript. **Margit Heier:** Biosample and data acquisition, writing - review & editing. **Birgit Linkohr:** Methodology, data management, writing - review & editing. **Lars Schwettmann:** Methodology, writing - review & editing. **Annette Peters:** Conceptualization, methodology, funding acquisition, writing - review & editing, preparation of the final

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1. Introduction

Environmental exposure to lead has been associated with myriad health effects in humans. The Global Burden of Disease study (GBD) has included lead as exposure since 2003, and has associated lead exposure with intellectual disability, hypertension and cardiovascular outcomes, and with the development of chronic kidney disease (Shaffer et al., 2019). Even at low-levels (with levels increasing from 10 μg/l to 67 μg/l), clear associations of blood lead levels and all-cause mortality (Hazard ratio (HR) 1·37, 95% CI 1·17–1·60) as well as cardiovascular disease mortality (HR 1·70, 1·30–2·22) and ischaemic heart disease mortality (HR 2·08, 1·52–2·85) were observed (Lanphear et al., 2018). Furthermore, lead exposure has been linked with lower cognitive function and socioeconomic status in middle age (Reuben et al., 2017), and has been suggested as a risk factor for neurodegenerative diseases (Reuben, 2018; Wang et al., 2014). In addition, lead was classified as a probable human carcinogen (Rousseau et al., 2005). Sources of human exposure to lead are diverse, but for the majority of the population exposure is via inhalation or via ingestion (Agency for Toxic Substances and Disease Registry (ATSDR), 2020). Lead pollution from the environment was significantly higher until the mid 1990s, when tetraethyl lead was routinely added to fuels as an anti-knock agent and lead water pipes were common in old buildings in Europe. Today, leaded fuel is banned and most of leaded water pipes were replaced, therefore significantly reducing the exposure of the general population. Lead-based paint is still to date a major concern globally (O'Connor et al., 2018).

Lead has been identified as a priority substance for investigation by the HBM4EU project (https://www.hbm4eu.eu/the-substances/lead/). In a 2019 scoping review, the HBM4EU identified a lack of current data on blood lead levels (BLLs) in adults since the phasing out of leaded fuel in Europe. Therefore, the generation of new cross-sectional data is of current policy interest (Rudnai, 2019). The scoping review identified just 16 European countries that had reported phlebotomy surveys of BLL within the last 10 years, primarily in childhood populations, with just 7 reporting data within 5 years prior to the survey date (Rudnai, 2019).

Regarding individual characteristics associated with BLL, several cross-sectional studies have already identified important factors. In a Finnish birth cohort study, BLLs were measured in 249 subjects (126 males and 123 females) finding that men had a geometric mean (GM) of 17.1 μg/l, while women had a GM BLL of 9.1 μg/l (Abass et al., 2017). Lead concentrations were noted to be significantly higher in males, in those who consumed sugar-sweetened soft drinks, in smokers, in those with higher use of alcohol, and in those with lower educational level (Abass et al., 2017). In a separate multiple chemical exposures study of Danish women of reproductive age recruited from 2011 to 2014, a geometric mean BLL of 8.1 μg/l was found (Rosofsky et al., 2017). In Belgium, a follow-up study of a previously recognised site of industrial pollution measured blood metal concentrations in 278 adults (aged 40–60 years) and children in 2009 (Fierens et al., 2016). Amongst 52 men, the BLL geometric mean was 31.7 μg/l, while among 54 women a geometric mean of 21.4 μg/l was measured (Fierens et al., 2016). A higher BLL was found to be associated with male sex, alcohol consumption and age, while a lower concentration was associated with higher BMI (Fierens et al., 2016). In a Polish cohort of 594 pregnant mothers in their second trimester, a mean BLL of 12 μg/l was found (geometric mean 11 μg/l) and, after multivariable adjustment, higher BLL was found to be associated with age ($P = 0.02$), years of education ($P = 0.04$), and higher pre-pregnancy BMI ($P = 0.001$) (Polańska et al., 2014). Increased saliva cotinine level (used as a marker of smoking) was also positively associated with BLL ($P = 0.06$), while distance from a nearby copper smelter was negatively associated after multivariate adjustment (Polańska et al., 2014). A Spanish study with the aim to establish reference levels included 1880 nationally representative individuals aged over 16 and recruited between 2009 and 2010 (Cañas et al., 2014). A geometric mean BLL of 24.0 μg/l was found. After multivariable analysis, sex, age and occupational sector were found to be positively associated with BLL, with workers from the agriculture, construction and industry having significantly higher BLLs than service industry workers (Cañas et al., 2014).

The aim of the current study is therefore two-fold. First, we aim to provide information on current BLLs in a population-based sample of middle-aged individuals in Southern Germany without major current sources of lead exposure based on data from the KORA-Fit study in 2018–2019 and thereby to add to current knowledge regarding BLLs in European populations. Second, we aim to compare current BLLs to corresponding values obtained from the same individuals thirty years earlier, building upon data collected in the KORA study in 1987–1988, at a time when sources of lead were more prevalent (Hense et al., 1992).

2. Methods

2.1. Study population

The population-based KORA cohort (Cooperative Health Research in the Region of Augsburg, Germany) consists of 4 cross-sectional baseline surveys (S1 1984/5, S2 1989/90, S3 1994/95 and S4 1999/2001) in the city of Augsburg and two surrounding rural counties Landkreis Augsburg and Land-kreis Aichach-Friedberg (https://www.helmholtz-muenchen.de/en/kora), Germany (Figs. 1 and 2). The KORA cohort is based on the WHO MONICA (MONitoring trends and determinants in CArdiovascular disease) project conducted from 1984 to 1995 in the Augsburg region and the additional survey S4 in 1999/2001. Details on the KORA study are provided in Holle et al. (2005). Briefly, the participants of the baseline surveys were randomly selected from population registries from all inhabitants with main place of residence and German nationality in the study region (Fig. 1). The sampling was sex- and age-stratified and included participants aged 25–74 years (64 years in S1) at baseline. Study participation was 4022 (79,3%) in S1, 4940 (76, 9%) in S2, 4856 (74,9%) in S3 and 4261 (66,8%) in S4. A follow-up study of the S1 participants was carried out in 1987–1988 ($N = 3753$ or 93,3% of S1) and included measurement of BLLs in 1703 men and 1661 women as described in Hense et al. (1992). Of these participants, 556 took part in the KORA-Fit study about 30 years later.

From January 2018 to June 2019 the KORA-Fit study was conducted. KORA-Fit is a follow-up study of all KORA S1–S4 participants born between 1945 and 1964, thus they were 53–74 years old at participation. Of the 6731 participants at baseline, 547 (8.1%) persons had died in the meantime, 919 (13.7%) lived outside the study region or were completely lost to follow-up, 471 (7.0%) had demanded deletion of their address data, and 46 (0.7%) withdrew consent. Of the remaining 4748 eligible persons, 365 could not be contacted, 394 were unable to take part because they were too ill or had no time, and 930 were not willing to participate in this follow-up resulting in a sample size of $n = 3059$. A flow diagram illustrating the study enrolment and inclusion is shown in Fig. 2.

At the KORA study center, an interview, physical examination and a blood withdrawal was performed. Self-reported information on demographic variables age and sex, lifestyle factors including smoking (never smoker, occasional and regular ex-smoker, occasional and regular smoker), alcohol consumption (g/day), physical activity based on leisure activity during summer and winter (Meisinger et al., 2005) (regularly >2 h/week, regularly about 1 h/week, irregularly about 1 h/week, almost none or none)and on socioeconomic factors including maximum education level reported at baseline, professional category, and net household income were collected in a standardized computer-assisted personalised interview. Alcohol consumption was assessed using a validated recall method in which participants were asked how much beer, wine, and spirits they consumed on the previous

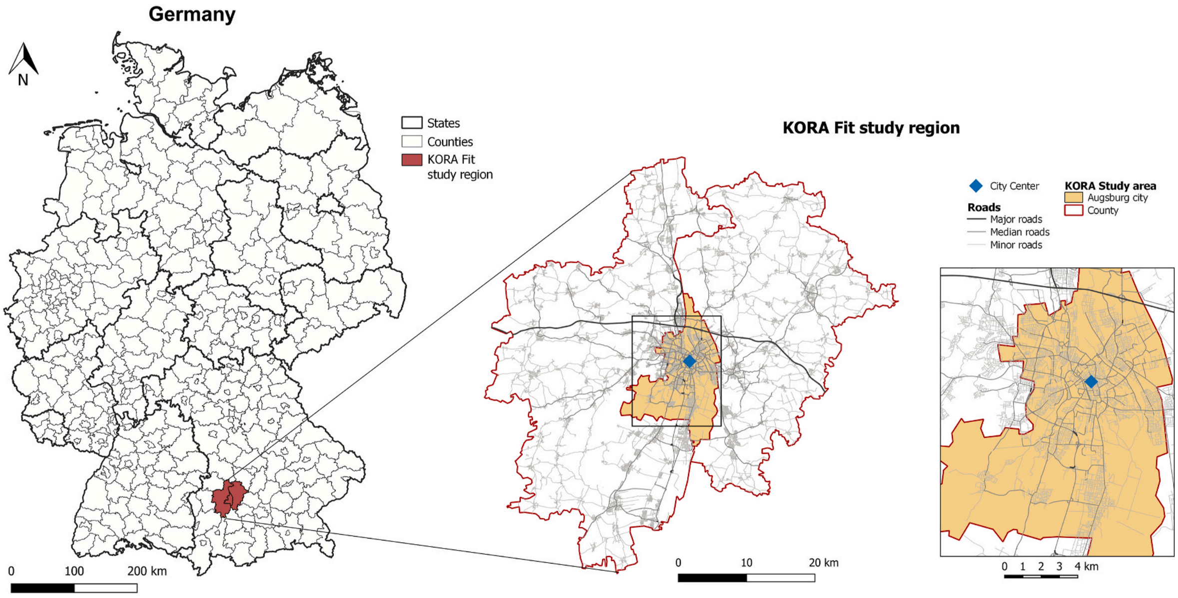

Fig. 1. Map of Augsburg city and surrounding counties included in the KORA study.

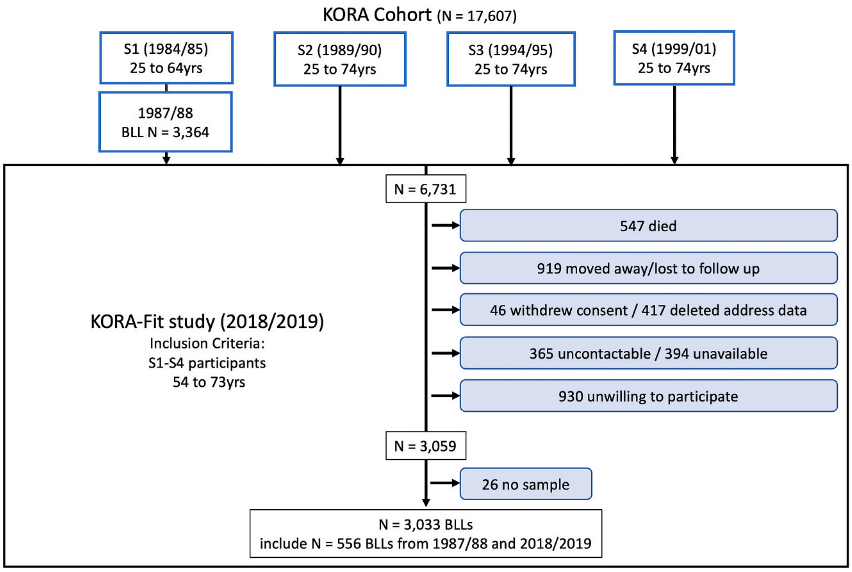

Fig. 2. Flow diagram of KORA-Fit study recruitment.

weekday and weekend (Schaeffler et al., 1991).

The educational level combines information on school education and vocational training, and from the codes of both sources of education, the highest code was taken. Occupational information is based on answers to the question “Which position do you have or did you have in your job?” Regarding income, respondents were asked to state their total household net income. Stated levels were weighted by the number of household members in different age-groups (i.e. equivalent household income). Finally, income was classified into nine groups according to per capita household income as percentage of the median income (viz. €1750).

An anthropometric measurement was performed to calculate the body mass index (BMI) as weight in kg divided by the squared height in meters. Finally, for each participant of the KORA-Fit study we searched for previous BLL data from the KORA 1987/88 study.

2.2. Sample collection

Blood samples were collected in 2.7 ml EDTA-Monovette (Fa. Sarstedt) according to a standardized protocol in a sitting position from the fasting participant after a minimum of 10 min rest in this sitting position. From the well-mixed sample 0.5 ml blood was transferred to 1 ml tubes stored in the refrigerator. After max. 6 h samples were frozen at −80 °C until analyzing blood lead concentration as described in the next section.

2.3. Laboratory methods

Pb in blood was analysed by graphite furnace atomic absorption spectroscopy (GF-AAS) at a detection wavelength of 193.7 nm. Blood samples were diluted tenfold with 0.05% Triton-X. 20 μl of this dilution were automatically pipetted into the graphite tube of the GF-AAS (AAnalyst 600, PerkinElmer, Rodgau, Germany). 50 μg $NH_4H_2PO_4$ and

3 μg $Mg(NO_3)_2$ were added as matrix modifiers. The furnace program was according to the recommendations of the manufacturer. Quantification based on the standard addition method. In detail, the same sample was spiked with 5 and 10 pg Pb, respectively, and then analysed as described above. The LOD was at 1.0 μg/l. All samples were at least analysed in duplicate after thawing on a roll mixer. For daily quality control, certified reference material for blood (ClinChek®, Recipe, Munich, Germany) was used. For external quality control, the authors' laboratory successfully participated in interlaboratory comparisons for the analysis of lead in blood.

2.4. *Statistical analysis*

Descriptive statistics were performed. Geometric and arithmetic means and percentiles (P05, P10, P25, P50, P75, P90, P95) were calculated for the full cohort and stratified by sub-groups. Where case counts in a given category were <5, data was censored for privacy reasons. For continuous variables quantile plots were drawn incorporating spline fits to allow for nonlinearity of log (BLL) vs explanatory variables (or log of the explanatory variable). To determine whether the exogenous exposures, i.e. cigarette smoking and alcohol consumption, had associations with BLL that were independent of demographic factors, a multivariable linear regression models with BLL as outcome was built including cigarette smoking and alcohol consumption with adjustment for age, BMI, educational level and professional category. Separate models were built for male and female participants. All statistical analyses were carried out using R Statistical Software version 4.0.5 and additional packages (Wickham, 2017; Pedersen, 2017). (Analysis code is available at: https://github.com/jpkrooney/KORA_lead_demographics_analysis and code is archived at: https://doi.org/10.5281/zenodo.7003131).

3. Results

In total, 3059 participants met the inclusion criteria for the KORA-Fit study in 2018/2019 (64.4% of all eligible participants). Supplementary Table S1 displays descriptive statistics for the cohort stratified by gender (1641 females and 1418 males). The distribution by 5-year age group is similar for males and females, however other variable show differences with 79% of men being pre-obese or obese vs 64% of women, 49% of women having never smoked vs 38% of men, 35% of women with no alcohol intake vs 15% of men. The numbers with BLL measurements did not differ by gender for the 1987/88 or 2018/19 groups (Supplementary Table S1). Blood lead levels for 3033 participants in the 2018–2019 KORA-Fit study for whom BLL was measured are shown in Table 1. The geometric mean (GM) blood lead level for the cohort as a whole was 24.8 μg/l. All individuals had BLLs above the limit of detection. Five hundred and fifty five women (34%) and 236 men (17%) were above the current 95th percentile reference values (30 μg/l in women and 40 μg/l in men) proposed by the German Environment Agency (Bundesamt, 2019). Two hundred and twenty nine (7%) of all participants were above the CDC reference level (for children) of 50 μg/l (CDC - Lead - Blood Lead Reference Value [Internet], 2020).

Interestingly, absolute differences between BLLs of men and women were minor at just 4% on average in the 2018/2019 cohort (25.4 μg/l vs 24.4 μg/l and respectively, P = 0.021), although 34% of women and 17% of men were above proposed reference values from the German Environment Agency (30 μg/l in women and 40 μg/l in men) (Bundesamt, 2019). Similarly, GM blood lead level varied little across 5-year age ranges within the 54–73 year old age range included in the KORA-Fit cohort (P = 0.823). However, the differences by age group were greater in the older age categories (Table 1). Lead concentrations varied by smoking history with the lowest GM in never smokers and highest levels in current occasional and regular smokers (23.7 vs 26.0 μg/l, P < 0.001). Supplementary Table S2 shows BLLs for age and smoking categories stratified by gender. This did not reveal any additional pattern by age. However, male ex-smokers who smoked occasionally had higher BLLs (27.5 vs 23.8 μg/l). Other smoking categories were similar when compared by gender. Physical activity showed only minor changes across levels (P 0.038, Table 1), but with no clear pattern. Fig. 3 shows the relationship between log BLL and both BMI and log of daily alcohol consumption. BMI showed a roughly linear inverse relationship with log BLL with the lowest BMI individuals having on average higher BLL than high BMI individuals. The relationship with alcohol was

Table 1
Means and percentiles of lead concentrations by demographic and lifestyle factors in 3033 KORA-Fit participants 2018–2019.

	N (%)	Arithmetic mean	Geometric mean	P5%	P10%	P25%	P50%	P75%	P90%	P95%
Overall	3033	28.64	24.85	12.16	14.3	18.7	25.3	34.7	46.7	56.5
Sex (P = 0.021)										
Female	1627 (54%)	28.04	24.36	11.7	14.1	18.4	24.6	34.5	46	54.77
Male	1406 (46%)	29.34	25.42	12.5	14.55	19.125	25.75	35.075	47.6	57.88
Age (yrs) (P = 0.823)										
<55yrs	183 (6%)	28.37	25.35	12.7	14.34	19.15	26.1	33.2	45.92	52.73
55–59yrs	693 (23%)	28.12	24.45	12.06	14.4	18.8	24.6	34.2	43.66	51.46
60–64yrs	855 (28%)	28.61	24.86	12.2	14.2	18.4	24.9	34.55	47.04	56.79
65–69yrs	817 (27%)	28.95	25.29	12.64	14.7	19.1	25.4	34.8	47.4	56.24
≥ 70yrs	485 (16%)	29.04	24.50	11.5	14	18.2	25.4	36.7	49.82	59.3
Smoking history (P = <0.001)										
Never smoker	1339 (44%)	27.47	23.67	11.69	13.7	18.4	24.2	33.45	44.7	53.01
Ex-smoker who smoked occasionally	272 (9%)	29.13	25.33	12.84	14.7	18.5	25.4	34.8	49.16	63.37
Ex-smoker who smoked regularly	989 (33%)	29.02	25.77	12.3	14.48	18.8	25.8	36	47	56.22
Occasional smoker	53 (2%)	30.72	27.67	14.18	16.66	19.8	28.7	36	51.78	60.92
Regular smoker	375 (12%)	31.15	26.05	13.8	15.64	19.3	26.1	36.9	49.76	59.55
Missing smoking history	5 (~0%)									
Physical Activity (P = 0.038)										
Regularly >2 h/wk	1153 (38%)	29.67	25.49	12.36	14.52	19.4	25.6	35.5	48.32	59.44
Regularly ~ 1 h/wk	1026 (34%)	27.98	24.73	11.6	13.9	18.13	25.1	34.68	45.7	53.78
Irregularly ~ 1 h/wk	375 (13%)	28.29	23.83	12.8	14.7	18.6	24.9	34.55	45.68	51.96
Almost none or none	478 (15%)	27.86	24.38	11.79	13.97	17.63	24.4	33.18	46.96	56.6
Missing physical activity history	1 (~0%)									

ANOVA used to estimate P values.

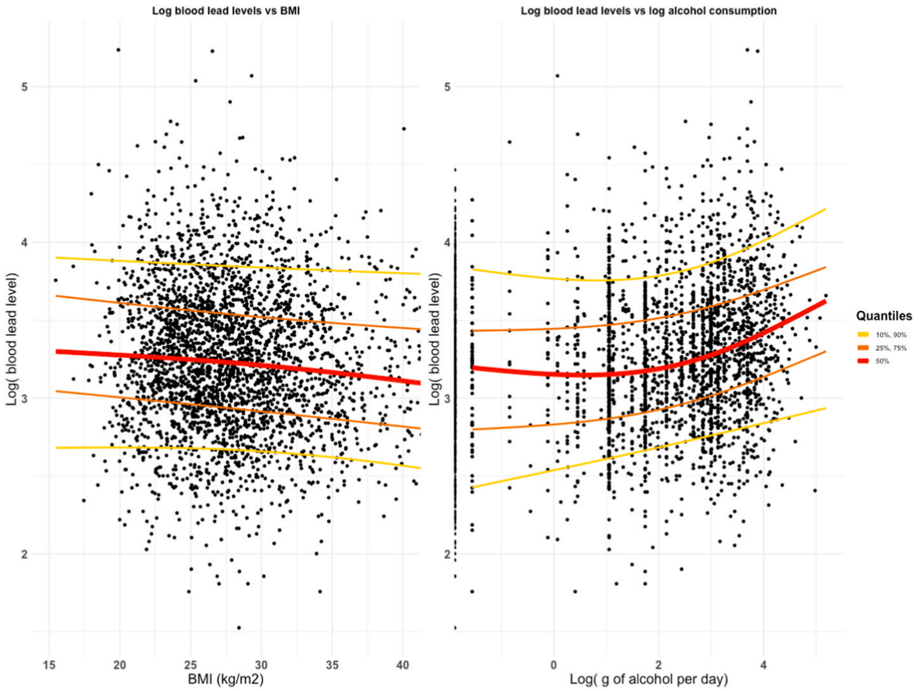

Fig. 3. Log blood lead level vs BMI and vs log daily alcohol consumption in N=3033 KORA-Fit participants (2018/19). Correlation of BMI and log BLL = −0.09. Correlation of daily alcohol consumption in grammes and BLL = 0.18.

non-linear with log BLL remaining relatively unchanged at log daily alcohol consumption and increasing with higher levels. By type of alcohol consumed, just 404 (13%) of respondents drank spirits, 1352 (44%) drank wine, and 1619 (53%) drank beer. Fig. 4 shows the trends of log BLL vs log daily alcohol intake by each subcategory. Beer and wine both show an increasing trend in log BLL with increased daily alcohol consumption, with wine showing a more sharply increasing trend. For spirits, a non-linear trend was evident that showed decreasing log BLL at higher levels of daily consumption of spirits. Supplementary Fig. 1 shows the relationship between log BLL vs log of grammes of daily wine consumption stratified by sex. No sex specific effect is apparent.

Table 2 displays the means and quantile data for BLLs of the KORA-Fit cohort (2018/2019) stratified by socioeconomic factors. By level of education only small differences were observed in the GM's and quantile levels across categories (P = 0.004), with only the general secondary school (in German "Hauptschule") category having lower GM BLL (20.4 μg/l), although this category contained only 92 individuals, and the category for technical college/technician/master craftsmen have the highest GM BLL (26.1 μg/l). Similarly, there were only small differences between categories of professions ranging from the lowest BLL for 'unpaid family workers' (GM 22.5 μg/l) to the highest for 'Other self-employed' (GM 25.9 μg/l). Differences across household income scales were also small. Boxplots of BLL by education level, professional category and household income are shown in Supplementary Figures S2, S3 and S4.

Five hundred and fifty-six individuals had BLLs measured in both 1987/88 and 2018/2019 (1987/88 overall GM BLL: 54.0 μg/l). Fig. 5 shows a boxplot of BLLs comparing both time periods for these 556 individuals, while arithmetic means, geometric means and quantile data are shown in Supplementary Table S3. In both men and women means and quantile levels are greatly reduced in 2018/2019 compared to 1987/88 with the geometric mean BLL in 2018/2019 in men reduced to 35% and in women to 50% of their respective 1987/88 levels. In 1987/88, 28 individuals had a BLL below the limit of detection at that time, however due to improved methodology in the 2018/2019 no individuals were below the limit of detection. Excluding those 28 individuals, 521 out 528 participants (98.6%), had a decreased BLL in 2018/2019 compared to 1987/88, leaving just 7 individuals (1.4%) with an unchanged or increased BLL. Fig. 6 displays the change of individual levels between both time-points.

Table 3 displays the parameter estimates from the multivariable regression models at both timepoints. In men after adjustment for age, BMI, education level and professional category, each gram of daily alcohol consumption was significantly associated with an increased BLL of 0.12 μg/l (95%CI: 0.08–0.15 μg/l, $P < 0.001$) and for smoking, being a current regular smoking was significantly associated with an increased BLL of 4.25 μg/l (95% CI: 1.37–7.14 μg/l, $P = 0.004$) compared to being a non-smoker, while other categories of smoking were not associated with BLL relative to being a non-smoker. In women, only daily consumption of alcohol was significant ($P < 0.001$) with each gram of alcohol associated with an increased BLL of 0.21 μg/l (95%CI: 0.15–0.27 μg/l).

4. Discussion

In this study, BLLs of 3033 KORA-Fit participants have been determined. For women, the GM BLL found in this study was higher to what has been reported in recent European studies, while lower and higher GM BLLs for men were found by other studies. Interestingly, absolute differences between BLLs of men and women were minor at just 4% on average in this cohort, although 34% of women and 17% of men were above proposed reference values from the German Environment Agency (Bundesamt, 2019). Similarly, differences were small across age groups, by maximum education level, by physical activity category, professional category and across equivalent household income scales.

Many of, though not all of, these results mirror previous results from the same catchment area during the KORA 1987/88 study, however overall BLLs are greatly reduced from that time (Hense et al., 1992). In contrast to the current study, the KORA 1987/88 study found large differences in BLL by gender (Tables 3 and S3), and cigarette smoking was found to be positively linearly associated with BLL (Hense et al., 1992). However, the earlier study found a non-linear relationship between BLL and daily alcohol consumption in particular in wine drinkers very similar to the current findings. This phenomenon has been already

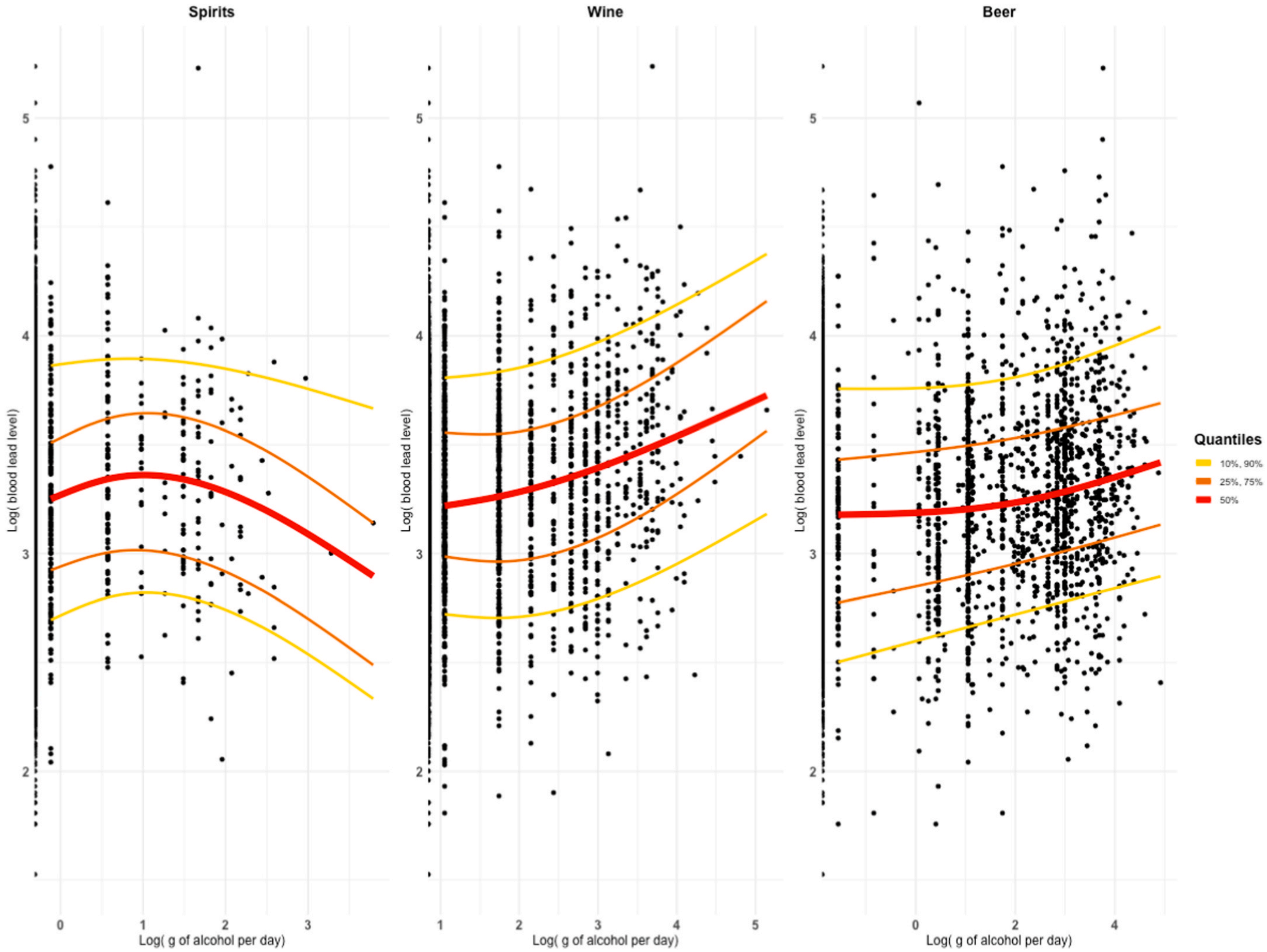

Fig. 4. Log blood lead level vs daily alcohol consumption stratified by alcohol type in N = 3033 KORA-Fit participants (2018/19). Correlation of daily alcoholic spirit consumption in grammes and BLL = 0.01. Correlation of daily wine consumption in grammes and BLL = 0.18. Correlation of daily beer consumption in grammes and BLL = 0.10.

observed in several studies (Abass et al., 2017; Fierens et al., 2016; Wennberg et al., 2017). One may speculate that alcoholic beverages such as wine may be a source of lead exposure, however, this has not been substantiated on a population-level to the best of our knowledge. BLLs were slightly elevated in ever-smokers compared to non-smokers. However, smoking behaviour did not show a clear association with BLLs across categories. However, after adjusting for confounders via multivariable regression modelling, both daily alcohol intake and being a current regular smoker were associated with increased BLL. Unfortunately, pack-years and smoking-related biomarkers (e.g. cotinine in urine) were unavailable for adjusted analyses. In the study by Abass et al. GM BLL was significantly higher in daily smokers (Abass et al., 2017). BLLs were slightly negatively correlated with BMI (Fig. 1) which has been observed previously and is likely due to larger blood volume and subsequent dilution (Abass et al., 2017; Fierens et al., 2016; Hense et al., 1992; Nisse et al., 2017).

For our study population, corresponding BLLs from the KORA 1987/88 study were available for 260 men and 296 women. As shown in Figs. 5 and 6, BLLs decrease for the vast majority of participants. In 1987/88, the GM BLL for men was 24.9 μg/l higher than the GM BLL in women. By 2018/19, this difference decreased to just 10% (2.3 μg/l). The KORA 1987/88 study concluded that BLLs were confounded by haematocrit levels and this might have in part explained differences in BLLs by gender (Hense et al., 1992). Unfortunately, we were unable to investigate the previously reported strong relationship between BLL and haematocrit as this variable was unavailable in the current study. Our findings contrast, in part, with studies from other regions of Europe (Table 4). Most studies, unlike ours, show clear differences between men and women. Furthermore, while our measured BLLs are considerably lower than the KORA 1987/88 study, they are moderately higher than many contemporary studies from around Europe for both men and women (Table 4). Of recent studies on BLLs amongst European adults, the studies of Swedish adults by Wennberg et al. and young German adults (<30 years) by Lermen et al. are the only ones to focus on changes of BLL over time (Wennberg et al., 2017; Lermen et al., 2021). In the first study, median BLL of randomly selected Swedish men (N = 619) across four time-points dropped from 25.1 μg/l in the 1990–1999 time period to 11.0 μg/l in the 2004 to 2014 time period. In women (N = 926), the median BBL dropped from 16.2 μg/l to 9.7 μg/l. However, the authors noted that this drop in concentration occurred prior to 2009 with levels remaining stable thereafter (Wennberg et al., 2017). In the second study, median BLL of young men living in Muenster, Germany dropped from 85.3 μg/l in 1981 to 11.0 μg/l in 2019. In young women, median BLL dropped from 72.2 μg/l to 8.4 μg/l. Again, the drop in BLLs levelled out after 2010 (Lermen et al., 2021).

Similarly, although BLL varied little by age group in our study, it has been reported to be positively correlated with age in a number of previous studies. For example, the IMEPOGE study of 2000 French adults

Table 2
Means and percentiles of lead concentrations by socioeconomic factors in 3033 KORA-Fit participants.

	N (%)	Arithmetic mean	Geometric mean	P5%	P10%	P25%	P50%	P75%	P90%	P95%
Education level* (P = 0.004)										
Did not finish	1 (<0.1%)	–	–	–	–	–	–	–	–	–
General secondary school (“Hauptschule”)	91 (3%)	23.67	20.44	10.1	11.7	15.6	20.4	29.1	37.7	52.55
Vocational school/apprenticeship (“Berufsschule/Lehre”)	1124 (37%)	28.17	24.79	11.92	14.3	18.2	24.6	34.3	46.2	56.49
Intermediate secondary school (“Realschule, mittlere Reife”)	598 (20%)	28.52	25.20	12.69	14.5	19.425	25.6	35.675	45.7	51.48
Technical college/Technician/Master craftsmen (“Fachschule/Techniker/Meister”)	485 (16%)	30.36	26.13	12.32	14.64	19.2	26	35.6	49.56	60.62
High School Diploma (Abitur)	203 (7%)	27.52	24.47	12.5	13.8	18.65	24.7	32.45	44	49.17
University degree	531 17%)	29.49	24.41	12.1	14.2	18.7	25.8	34.85	48.6	57.15
Professional category (P = 0.028)										
Worker	501 (16%)	27.68	24.45	12.2	14	17.7	24.1	33.8	45.3	54.8
Employee	1768 (58%)	28.34	24.65	11.8	14.27	18.7	24.9	34.425	46.2	54.2
Civil servant	332 (11%)	29.40	25.76	12.86	14.6	19.425	25.95	34.8	46.68	57.05
Self-employed farmer	47 (2%)	26.64	24.21	12.82	13.3	17	26.1	33.9	40.18	44.73
Other self-employed	318 (11%)	31.20	25.85	12.59	14.71	19.85	27.05	38.375	53.83	64.8
Unpaid family workers	36 (1%)	26.51	22.47	12.55	15.45	19.325	25.35	34.525	37.3	40.43
Something else	20 (1%)	27.33	25.13	14.64	15.44	19.375	24.7	34.1	43.09	48.41
Missing	11 (<1%)									
Equivalent household income** (P = 0.583)										
up to 875 EURO (50%)	165 (5%)	30.01	24.84	10.64	12.7	17.3	25.4	37.7	52.02	63.62
875–1207.5 (69%)	265 (9%)	27.73	23.73	11.98	14.28	18.1	23.5	33.4	44.28	57.74
1207.5–1557.5 (89%)	828 (27%)	28.11	24.90	12.24	14.6	18.675	25.25	33.825	45.82	55.17
1557.5–1907.5 (109%)	524 (17%)	29.48	25.03	11.7	14.13	19.175	25.45	35.325	46.77	58.25
1907.5–2257.5 (129%)	317 (10%)	28.10	25.06	12.9	15.22	19.2	24.6	33.3	46.2	54.66
2257.5–2607.5 (149%)	189 (6%)	27.91	25.02	12.9	14.1	17.4	24.6	33.6	46.2	54.62
2607.5–2957.5 (169%)	225 (7%)	28.90	24.70	12.2	14.2	18.4	25.7	35.3	45.96	56.06
2957.5–3307.5 (189%)	120 (4.0%)	28.18	24.58	11.88	14.56	18.3	24.1	34.65	47.79	55.53
>3307.5 (>189%)	158 (5%)	29.75	25.78	12.57	14.27	20.625	27.2	35.775	45.17	54.38
Missing	242 (8%)									

* Original German educational levels are given in brackets. ** Income is based on self-stated total household net income and weighted by the number of household members in different age-groups (values in brackets indicate percentage of the median income, viz. €1750).
ANOVA used to estimate P values.

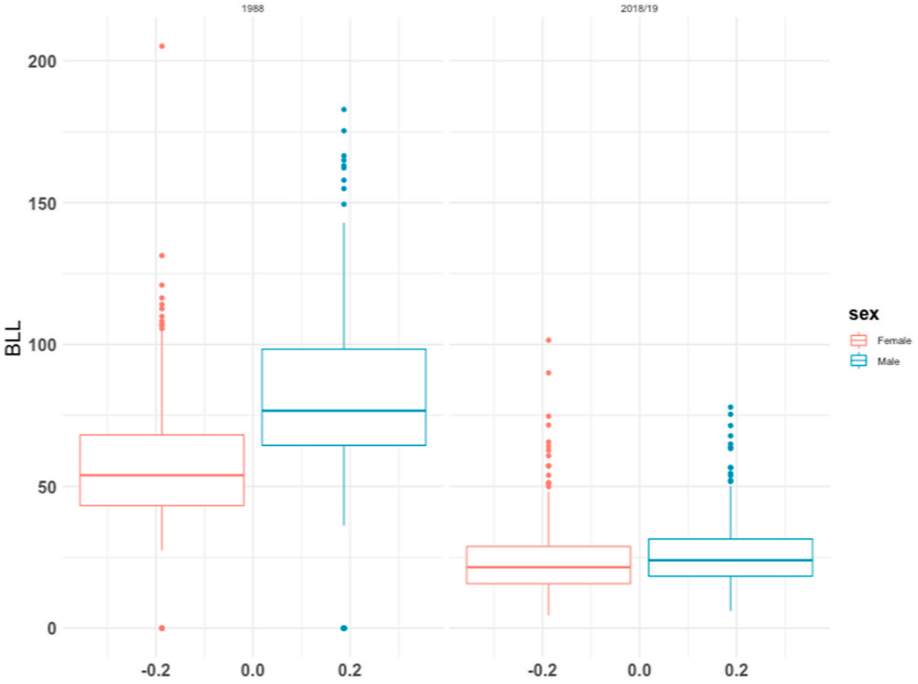

Fig. 5. Boxplot of blood lead level by year and gender for 528 participants of both the KORA 1987/88 and KORA-Fit (2018/19) studies.

Fig. 6. Individual blood lead levels for 528 participants of both the KORA 1987/88 and KORA-Fit (2018/19) studies.

Table 3
Parameter estimates for cigarette smoking and alcohol consumption after multivariable linear regression modelling in N = 3033 KORA-Fit (2018/19) participants.

Variable[a]	Parameter estimate	95% CI	P value (Wald)
Males			
Daily alcohol consumption in grams	0.12	0.08 to 0.15	<0.001
Smoking category:			
Never smoked (reference level)	0	–	–
Ex-smoker who smoked occasionally	2.90	−0.37 to 6.17	0.082
Ex-smoker who smoked regularly	0.81	−1.16 to 2.78	0.421
Occasional smoker	3.73	−2.44 to 9.90	0.236
Regular smoker	4.25	1.37 to 7.14	0.004
Females			
Daily alcohol consumption in grams	0.21	0.15 to 0.27	<0.001
Smoking category:			
Never smoked (reference level)	0	–	–
Ex-smoker who smoked occasionally	−0.47	−3.03 to 2.09	0.718
Ex-smoker who smoked regularly	1.29	−0.48 to 3.06	0.153
Occasional smoker	2.33	−3.81 to 8.48	0.456
Regular smoker	1.73	−0.56 to 4.03	0.139

[a] Daily grams of alcohol is modelled as a continuous variable, therefore the parameter represents the increase of BLL in μg/l per gram of daily alcohol consumption adjusted for smoking, age, BMI, education level and professional category. For smoking categories the parameter represents the difference in BLL relative to the reference level (never smoked) adjusted for alcohol consumption, age, BMI, education level and professional category.

found and increasing trend of BLL from a GM BLL of 13.6 μg/l in 20–29 year olds to 29.1 μg/l in 50–59 year olds (Nisse et al., 2017). Two large studies from Spain, one in a nationally representative sample of the population (n = 1880), the other in a survey of hospital workers (n = 951), both found that BLL increased with older age (Cañas et al., 2014; González-Estecha et al., 2009). Age differences may be explained by elevated total exposure to leaded fuel when it was still in use, therefore having an increased lead body burden. Participants of KORA-Fit ranging in age from 53 to 74 years, born between 1945 and 1965. They spent a significant portion of their lives in the leaded petrol era and are likely to have had similar exposures as young adults as documented by the German Environmental Specimen Bank (Lermen et al., 2021). In 1987/88, leaded fuel was still available in Germany and its emissions therefore were the major environmental source of lead exposure. In fact, lower BLLs were found in young German adults that were born in the late 1980s and later (Lermen et al., 2021). As discussed by Lermen and colleagues, other external sources such as lead paint, occupational or dietary exposures were of lesser importance on a population-level thirty years ago (Lermen et al., 2021). Additionally, it is known that BLL can rise in menopausal and post-menopausal women (Nash, 2004; Lee and Kim, 2012). Lead has a particularly long half-life in bone (on the order of decades) and it is thought that the bone remodelling that occurs in menopause leads to the release of long stored lead into the blood (Nash, 2004; Lee and Kim, 2012). In this context, with the disappearance of leaded fuel emission and possibly endogenous hormonal factors, BLLs of men and women have converged on our study.

Our analysis benefits from a large sample size in a well-studied cohort with high response rates at baseline and during follow-ups (Holle et al., 2005). In addition, we were able to link, compare and contrast BLLs from 556 individuals in 2018/19 to BLL measurements from the same individuals in 1987/88 and demonstrate marked decrease in BLL since that time. Our study is limited to a 20 year age-range (i.e. 53–74 years), and given the phasing out of leaded petrol younger generations would have experienced lower exposures (on average). Therefore, the generalisability of our results to other age groups is limited. Although we described the distribution of blood lead levels across a range of demographic and social factors, we did not have data on individual occupations or hobbies linked to lead exposure. Similarly, we did not have data on other potential confounders such as calcium, iron, zinc, selenium, and vitamin D nutritional status. One may wonder about a spatial distribution of blood lead levels. However, we do not have a priori knowledge of any point source such as a polluting factory that would produce potentially strong spatial patterns. Given that blood lead levels are reflective of individual exposures accrued over time – potentially decades, and that individuals may have moved home several times in that timescale, it is again not clear that we should expect a strong spatial pattern with regard to current home address.

In conclusion, BLLs of the KORA-Fit participants are broadly independent of gender, age, socioeconomic status, and other parameters collected in this study. On an individual level, BLLs have consistently decreased over the past 30 years. While individual factors (e.g. alcohol consumption, smoking) may feed into lead exposure, BLLs found for this population are likely connected to leaded fuel emissions before its ban in Germany in late 1980s and early 1990s, respectively. In the absence of major current sources of exposures, BLLs in middle aged and older men and women are still elevated at levels associated with morbidity and mortality and requires further investigations.

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Table 4
Comparison to blood lead levels in other European studies and the NHANES study.

Country	Year	Sample size	Age Range	GM	5th centile	50th centile	95th centile	Ref
Men								
Germany	2018–2019	1418	54–73	25.4	12.5	25.8	57.9	This study
Germany	1987–1988	1703	28–67	–	–	83.0	–	KORA 1987/88 study (Hense et al., 1992)
Belgium	2009	52	40–60	31.7	–	–	–	Fierens et al. (2016)
Finland	1997	126	31	17.1	–	17.6	41.3	Abass et al. (2017)
France	2008–2010	982	20–59	22.8	–	22.8	56.7	Nisse et al. (2017)
Germany	2010–2019	2310	20–29	12.7	–	12.4	26.1	Lermen et al. (2021)
Spain	2008–2009	229	[b]	–	–	20.0	–	González-Estecha et al. (2009)
Spain	2009–2010	962	18–65	28.3	–	27.3	64.0	Cañas et al. (2014)
Sweden	2004–2014	169	49–61	–	10.9	14.2	21.8	Wennberg et al. (2017)
United States	2015–2016	2488	Total	9.2	–	8.6	29.3	Fourth (2019)
Women								
Germany	2018–2019	1641	54–73	24.4	11.7	24.6	54.8	This study
Germany	1987–1988	1661	28–67	–	–	60.0	–	KORA 1987/88 study (Hense et al., 1992)
Belgium	2009	54	40–60	21.4	–	–	–	Fierens et al. (2016)
Denmark	2011–2014	73	18–40	8.1	–	–	15.8	Rosofsky et al. (2017)
Finland	1997	123	31	9.1	–	9.4	21.9	Abass et al. (2017)
France	2008–2010	1018	20–59	15.6	–	15.1	41.3	Nisse et al. (2017)
Germany	2010–2019	2626	20–29	10.5	–	10.2	21.8	Lermen et al. (2021)
Poland	2007–2011	594	[a]	11.0	–	–	–	Polańska et al. (2014)
Slovenia	–	127	50–60	26.7	–	–	–	Tratnik et al. (2013)
Spain	2009–2010	918	18–65	19.5	–	18.7	36.0	Cañas et al. (2014)
Spain	2008–2009	704	[b]	–	–	15	–	González-Estecha et al. (2009)
Sweden	2004–2014	302	49–61	–	10.1	13.7	19.0	Wennberg et al. (2017)
United States	2015–2016	2500	Total	7.4	–	7.2	23.9	Fourth (2019)

[a] Childbearing age – range not specified.
[b] Hospital workers of mean age 44.8 years.

Ethics

The KORA-Fit study methods were approved by the Ethics Committees of the Bavarian Chamber of Physicians (KORA-Fit EC No 17040). Written informed consent was obtained from all participants.

Consent to participate

Written informed consent was obtained from all participants.

Code availability

Analysis code is available at: https://github.com/jpkrooney/KORA_lead_demographics_analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The informed consent given by KORA study participants does not cover data posting in public databases. However, data are available upon request by means of a project agreement from KORA (https://helmholtz-muenchen.managed-otrs.com/external). Requests should be sent to kora.passt@helmholtz-muenchen.de and are subject to approval by the KORA Board.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.114184.

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