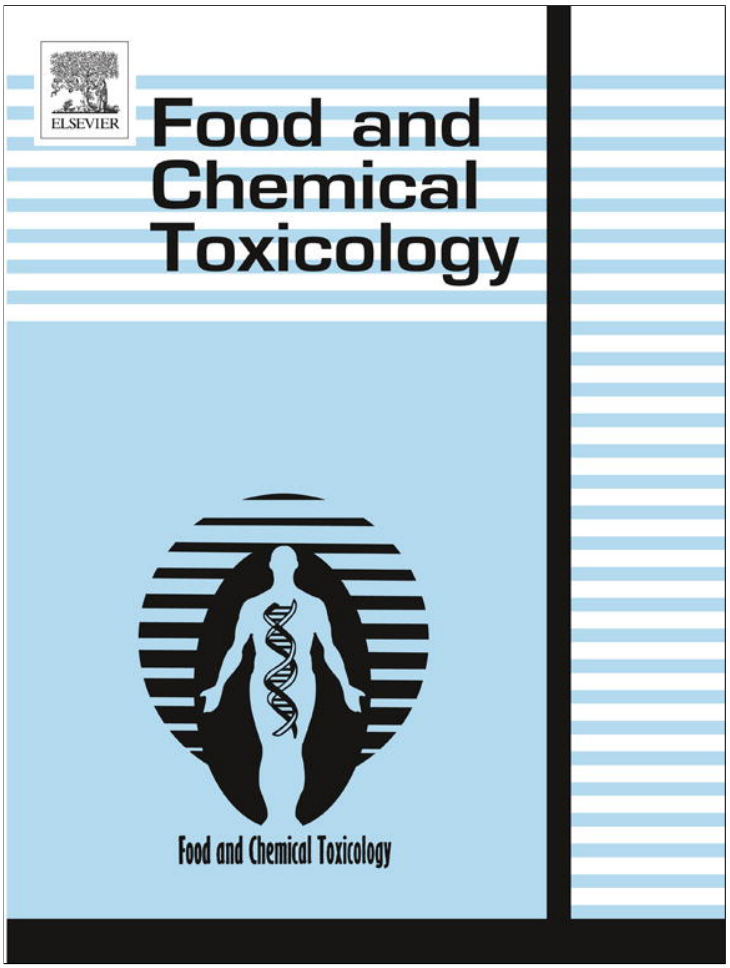

(This is a sample cover image for this issue. The actual cover is not yet available at this time.)

Food and Chemical Toxicology 50 (2012) 4180–4190

Contents lists available at SciVerse ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Potential health risks to adults and children in the UK from exposure to dietary lead in gamebirds shot with lead ammunition

R.E. Green [a,b,*], D.J. Pain [c]

[a] Conservation Science Group, Department of Zoology, University of Cambridge, Cambridge CB2 3EJ, United Kingdom
[b] RSPB, The Lodge, Sandy, Bedfordshire SG19 2DL, United Kingdom
[c] Wildfowl & Wetlands Trust, Slimbridge, Gloucestershire GL2 7BT, United Kingdom

ARTICLE INFO

Article history:
Received 7 May 2012
Accepted 15 August 2012
Available online 24 August 2012

Keywords:
Lead shot
Gamebirds
Food safety
Critical effects
Health risks

ABSTRACT

We estimate potential risks to human health in the UK from dietary exposure to lead from wild gamebirds killed by shooting. The main source of exposure to lead in Europe is now dietary. We used data on lead concentrations in UK gamebirds, from which gunshot had been removed following cooking to simulate human exposure to lead. We used UK food consumption and lead concentration data to evaluate the number of gamebird meals consumed weekly that would be expected, based upon published studies, to result in changes, over and above those resulting from exposure to lead in the base diet, in intelligence quotient (IQ), Systolic Blood Pressure and chronic kidney disease (CKD) considered in a recent opinion of the European Food Safety Authority (EFSA) to be significant at a population level and also in SAT test scores and in rates of spontaneous abortion. We found the consumption of <1 meal of game a week may be associated with a one point reduction in IQ in children and 1.2–6.5 gamebird meals per week may be associated with the other effects. These results should help to inform the development of appropriate responses to the risks from ingesting lead from ammunition in game in the UK and European Union (EU).

1. Introduction

Lead is a naturally occurring metal with many industrial uses which have resulted in it being widely distributed in the environment. Humans primarily absorb lead through the lungs and intestine. Absorption rates thorough the intestine depend upon the physical and chemical properties of ingested lead, the age of the person and on other dietary matter ingested (Barltrop and Khoo, 1975; Rabinowitz et al., 1980). Intestinal absorption of soluble lead is higher in newborn and young children than in older children and adults, decreasing significantly with age (Ziegler et al., 1978). Once absorbed, lead is transported in the bloodstream and transferred to soft tissues and to bone, where it accumulates over time, and from which it can be released again into the bloodstream. In adults bone generally contains over 90% of the body burden of lead, with a smaller proportion (>70%) in the bones of children (Barry, 1975). The half-life of inorganic lead in human tissues ranges from approximately 30 days in blood to decades, c.10–30 years, in bone (Rabinowitz et al., 1976; Rabinowitz, 1991; EFSA CONTAM, 2010). The concentration of lead in blood (B-Pb) is considered to be a good indicator of recent exposure, whereas lead in bone reflects long-term uptake and body burden. During pregnancy lead is mobilised from maternal bone and is transferred via the blood to the foetus through the placenta and to the infant through breast milk (Gulson et al., 2003).

Pathways of human exposure to lead include contaminated air, water, soil, house dust, food, tobacco smoke and consumer products. Drinking water may be contaminated because of lead plumbing in some older houses, especially in areas with acidic water, but this has decreased as alternative plumbing materials are used. Lead-containing paint can be a source of exposure in older houses where it was used for decoration. The addition of tetraethyl lead to vehicle fuel was formerly a major contributor to environmental lead exposure, but this source declined substantially across Europe and many other regions following the progressive removal of lead

Abbreviations: IQ, intelligence quotient; CNS, central nervous system; B-Pb, blood lead; NOAEL, no-observed-adverse-effect-level; JECFA, Joint Food and Agriculture Organisation/World Health Organisation Expert Committee on Food Additives; PTWI, Provisional Tolerable Weekly Intake; SCF, European Commission's Scientific Committee for Food; BMD, Benchmark Dose; BMR, Benchmark Response; CKD, chronic kidney disease; BMDL, Benchmark Dose Limit; EFSA, European Food Safety Authority; IEUBK, Integrated Exposure Uptake Biokinetic; WWT, Wildfowl & Wetlands Trust; VMD, Veterinary Medicines Directorate; TEE, Total Energy Expenditure; EU, European Union.

* Corresponding author at: Conservation Science Group, Department of Zoology, University of Cambridge, Cambridge CB2 3EJ, United Kingdom. Tel.: +44 1223 762840; fax: +44 1223 336676.

E-mail addresses: reg29@cam.ac.uk (R.E. Green), debbie.pain@wwt.org.uk (D.J. Pain).

0278-6915/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.fct.2012.08.032

from petrol from the 1980s onwards (e.g. Council Directive 85/210/EEC and subsequent amendments; Landrigan, 2002). In the European Union (EU), controls on other causes of environmental and occupational exposure to lead have resulted in the majority of lead exposure now being from the diet (EFSA CONTAM, 2010).

Lead is a non-essential and toxic metal that affects a wide range of body systems in humans and other animals. Effects range from reversible effects on the activity of some blood enzymes, to long-term and potentially irreversible effects on the development of the central nervous system (CNS) and IQ, and to death if exposure is sufficiently large or protracted (Kaufmann et al., 2003). Over the last 60 years, information on the human health effects of lead has increased steadily, especially from studies of humans with different occupational and environmental exposure levels. As a result, the risks to human health from lead are now well documented and well established. Formerly, measures to control the risks to human health from exposure to lead sought to maintain exposure below a no-observed-adverse-effect-level (NOAEL). However, as the availability of information and the sensitivity of assays have increased, the B-Pb concentrations demonstrated to be associated with adverse effects on human health have decreased. This has resulted in a progressive decrease in the B-Pb concentrations suggested as thresholds for action so that they are now one sixth or less of those thought to be protective of human health in the 1960s (Table 1).

Based upon evidence available at the time, the Joint Food and Agriculture Organisation/World Health Organisation Expert Committee on Food Additives (JECFA) set a Provisional Tolerable Weekly Intake (PTWI) of dietary lead of 25 μg/kg body weight. This was set for infants and children in 1982, extended to all age groups in 1993, confirmed by JECFA in 1999 and remained unchanged until its withdrawal in 2010/2011 (WHO, 2007; JECFA, 2010; WHO, 2011). The PTWI was endorsed in 1992 by the European Commission's Scientific Committee for Food (SCF, 1994). The European Commission carried out an updated lead exposure assessment in 2004 (SCOOP, 2004) and together with the SCF opinion this formed the basis of setting Maximum Levels of lead in foodstuffs in the EU (Regulation (EC) No 1881/2006). In 2007, the European Commission requested the European Food Safety Authority (EFSA) to produce a scientific opinion on the risks to human health related to the presence of lead in foodstuffs. In particular, EFSA was asked to consider new developments regarding the toxicity of lead, and to consider whether the PTWI of 25 μg/kg b.w. was still appropriate. EFSA was asked to include an updated exposure assessment for dietary and non-dietary lead and to consider the exposure situation for specific groups of the population (including infants and children and people following specific diets). EFSA's update included a call for the collection of new data on lead levels in food from 2003–2008 (DATEX-2008-0002), and its opinion was published in 2010 (EFSA CONTAM, 2010).

EFSA used the Benchmark Dose (BMD) approach to evaluate risk from exposure to lead in place of the NOAEL approach (Sand et al., 2008). The BMD is the dose of lead required to cause an increase in B-Pb associated with a pre-specified change in response, termed the Benchmark Response (BMR). Responses were defined as the most suitable 'critical endpoints' (sensitive, relevant and measurable responses to lead exposure). EFSA chose the following BMRs for their risk assessment: (1) a 1% change in outcome for IQ (equivalent to a one point change in IQ score), (2) a 1% change in systolic blood pressure (SBP; equivalent to a 1.2 mm Hg change), and (3) a 10% change in the prevalence of chronic kidney disease (CKD). A 1% change is described as a BMD_{01} (i.e. for IQ and SBP) and a 10% change a BMD_{10} and (i.e. for CKD). These were selected because such changes were within the range of observable values and were considered to have significant consequences for human health on a population basis. For example, the BMR for effects on IQ would impact the socioeconomic status of a population.

EFSA used information on lead concentrations in food and amounts of food eaten by individuals in participating countries to calculate mean ('average base diet') and 95th percentile ('high base diet') lead dietary exposures separately for each country. These exposure data were then modelled to produce corresponding B-Pb concentrations, and these were compared with the lower one-sided 95% confidence bound of the BMDs, i.e. the Benchmark Dose Limits (BMDLs) to evaluate risk. The data used for the EFSA opinion included measurements of lead concentration in a large number of samples of meat from game animals collected from across the EU, and EFSA examined exposure levels under certain specific diets, including the frequent consumption of game meat (defined as one 200 g meal per week of game). It was previously thought that consumption of meat from game shot with lead bullets and lead gunshot did not result in significant dietary exposure because nearly all of the mass of the projectile remained in large pieces, which either passed through the carcass or were removed during food preparation or at the table. However, it has recently been shown that lead bullets and lead gunshot fragment to some extent upon impact, so that many small lead fragments can often be found widely dispersed away from the wound canal (e.g. Dobrowolska and Melosik, 2008; Hunt et al., 2006, 2009; Pain et al., 2010; Knott et al., 2010). In subsistence and other hunting communities, B-Pb has been found to be correlated with the level of exposure to dietary lead from this source, and the amount of shot-game consumed (Dewailly et al., 2001; Bjerregaard et al., 2004; Johansen et al. 2006;Tsuji et al., 2008; Iqbal et al., 2009). EFSA calculated lead exposure levels in high game consumers by adding the lead concentration in one 200 g game meal per week to the average base diet.

Having considered both limitations of epidemiological data and health significance of observed changes associated with blood lead levels, EFSA concluded that the risk of clinically important effects on either the cardiovascular system or kidneys of adult consumers, at current levels of lead exposure in the general population in Europe is low to negligible. However, in infants, children and pregnant women, the CONTAM Panel concluded that there is potential concern at current levels of exposure to lead for effects on neurodevelopment. EFSA's analyses also indicated that the possibility of negative effects on health could not be excluded for some adult

Table 1
Action thresholds (CDC) and suggested action thresholds (other sources) for blood lead in children.

Year	Proposed or accepted (CDC) action threshold for children[a]	Reference
1960s	*60 μg/dl*	Chisolm and Harrison (1956)
1970	40 μg/dl	CDC (Centres for Disease Control and Prevention in the USA) 1991 cited in Kosnett (2009)
1975	30 μg/dl	CDC (1975)
1985	25 μg/dl	CDC (1985)
1991	10 μg/dl	CDC (1991)
2005	10 μg/dl but acknowledging effects below this level and stating that there is no no-effect level.	CDC (2005)
2011	*Elimination of term 'blood lead level of concern' 5 μg/dl recommended in January 2012 to CDC to identify children with elevated blood lead levels*	Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP, 2012)
2006	*5 μg/dl as a temporary measure that may need to be revised downward*	Declaration of Brescia (Landrigan et al., 2006)
2006	*2 μg/dl*	Gilbert and Weiss (2006)

[a] Recommended or proposed thresholds in italics.

consumers of game meat, because some of these consumers could incur an increased risk of cardiovascular and nephrotoxic effects as a result of exposure to lead. However, the EFSA analysis did not evaluate the impacts of game consumption on those eating a high base diet, or upon children or evaluate the potential effects of eating more than one meal of game meat per week.

In 2010, shortly before the publication of the EFSA opinion, we published an analysis of lead concentrations in meat from game animals in the UK, in which we estimated levels of game consumption that would result in the PTWI being exceeded (Pain et al., 2010). The publication of the EFSA opinion, with its replacement of PTWI, renders our conclusions obsolete. Based upon dose–response analyses, JECFA estimated that the PTWI of 25 μg/kg b.w. is associated with a decrease of at least 3 IQ points in children and an increase of approximately 3 mm Hg in SBP in adults, and concluded that the PTWI could no longer be considered health protective and withdrew it (JECFA 73/sc, 2010; WHO, 2011).

In this paper, we present revised estimates of the potential risks to human health in the UK from consumption of game meat, which follow the methods used by EFSA CONTAM (2010). We extend the EFSA analysis by using more recent and relevant (i.e. simulating human exposure) data on concentrations of lead in game meat in the UK than were available to them (from Pain et al., 2010), a new estimate of the bioavailability of lead derived from the meat of gamebirds shot with lead ammunition, a wider range of studies of the relationship between adverse effects on health and B-Pb, including one that was not published at the time of their analyses, and an evaluation of potential effects of game meat consumption on the intellectual development of children and on the rate of spontaneous abortion.

2. Methods

2.1. Diet composition and dietary lead intake of UK consumers

We obtained the average quantity by mass (kg) of various food types eaten by consumers in the UK per day from Table 1 of FSA (2009), which reports results of the Expenditure and Food Survey. We took the amount of this food which was meat to be the totals given for carcass meat, offals, meat products and poultry. We multiplied these quantities by the concentration of lead (μg/kg) in each food type from data from the 2006 UK Total Diet Study in Table 3a of FSA (2009) to give the daily mass (μg) of lead ingested from each food type. Where the table indicated a quantity below the limit of quantification (LOQ), we assumed that the concentration was the mean of the LOQ and zero (=LOQ/2). We summed these quantities to obtain the average total daily mass of lead ingested and the subtotal for meat. These calculations gave an estimated total mass of food eaten per person per day of 2.425 kg, of which 0.101 kg was meat, and a total of 5.007 μg of lead ingested per person per day from the whole diet, of which 0.276 μg (5.5%) came from meat. The quantity of lead ingested in the non-meat components of the diet was 4.731 μg per person per day.

Data from the UK given in the EFSA Concise European Food Consumption Database (used for the scientific opinion on lead of EFSA CONTAM, 2010) is from the UK Diet and Nutrition Survey 2000–2001 for adults only. This gives total food consumption figures of 2.717 kg of food eaten per person per day of which 0.161 kg is meat.

The data on UK diet and lead intake in FSA (2009) are averages for consumers of all ages and we took them as applying to adults. This was necessary because dietary exposure to lead is not evaluated separately in FSA (2009) for different age groups for the meat and non-meat components of the diet. We believe this to be a reasonable approximation because over 80% of people in the UK are adults [UK Office for National Statistics http://www.statistics.gov.uk/cci/nugget.asp?ID = 949]. In addition, a comparison of the average mass of food ingested per person per day in the UK between the SCOOP (2004) report (adults only) and the Expenditure and Food Survey (FSA 2009: all ages) shows that the results for the adults only survey were unexpectedly somewhat lower than from the survey of adults and children combined (2.075 kg person/day cf. 2.425 kg person/day). We avoided using results from SCOOP (2004) for this assessment, even though it refers to adults only, because the data were collected a considerable time ago when lead concentrations in most foods were higher than they have been more recently (FSA 2009). In addition, the categories of foods used in SCOOP (2004) and FSA (2009) are different, which would give rise to uncertainty in the correct lead concentration to use for each food category if we had attempted to combine SCOOP (2004) diet data with FSA (2009) lead concentrations.

2.2. Lead intake rates of UK children from foods other than meat

We required estimates of average rates of ingestion of lead from foods other than meat for children of two ages. These ages are 2.5 years, which is the average age at which blood lead was measured in the children whose later academic performance was analysed by Chandramouli et al. (2009), and 6.9 years, which is the average age at which IQ and blood lead concentration were measured in the studies analysed by Lanphear et al. (2005) and used to assess developmental neurotoxicity by EFSA CONTAM (2010).

We calculated dietary exposure to lead from sources other than meat of UK children by using data on the food consumption and dietary exposure to lead of UK consumers from FSA (2009) as a starting point (see above). Because we did not have recent lead intake rates for UK children, we then multiplied these UK data by the ratio of daily lead intake rates for children in Germany, relative to intake rates for adults in Germany. Tables 4.2 and 4.5 of SCOOP (2004) give daily lead intake from foods other than meat and offal of 4–6 and 10–12 year old children and of adults in Germany as 20.741, 25.621 and 36.120 μg/day, respectively. These were the most detailed European data available to us, with respect to age. The ratio of non-meat lead intake for 4–6 year old children to that of adults in Germany is 0.574 and the equivalent figure for 10–12 year olds is 0.709. Assuming these ratios apply to the

Table 2
Daily dietary lead exposure and expected effects on blood lead concentration (B-Pb) of adults under eight scenarios of weekly consumption of meat from UK gamebirds.

Parameter	Units								
Gamebird meal consumption scenario	Number/week	0	1	2	3	4	5	6	7
Non-gamebird meat meals per week	Number/week	3.54	2.54	1.54	0.54	0.00	0.00	0.00	0.00
Daily Pb dietary intake from gamebird meat	μg/d	0.0	33.7	67.5	101.2	135.0	168.7	202.5	236.2
Daily Pb dietary intake from non-gamebird meat	μg/d	0.3	0.2	0.1	0.0	0.0	0.0	0.0	0.0
Daily Pb dietary intake from non-meat foods	μg/d	4.7	4.7	4.7	4.7	4.7	4.6	4.6	4.5
Total daily Pb dietary intake	μg/d	5.0	38.7	72.3	106.0	139.7	173.4	207.0	240.7
Bioavailability coefficient (weighted mean)	Ratio	0.0400	0.0265	0.0255	0.0252	0.0250	0.0249	0.0248	0.0248
B-Pb (default bioavailability coefficient)	μg/dL	0.2	1.5	2.9	4.2	5.6	6.9	8.3	9.6
B-Pb (weighted mean bioavailability coefficient)	μg/dL	0.2	1.0	1.8	2.7	3.5	4.3	5.1	6.0

Table 3
Modelled effects of dietary lead exposure on aspects of the health of adults under seven scenarios of weekly consumption of meat from UK gamebirds. Values shown are increases relative to the expected value when no gamebird meals are consumed.

Health effects for these numbers of gamebird meals per week									
Health effect	B-Pb - effect model	Health effect units	1	2	3	4	5	6	7
Bioavailability coefficient = 0.04									
Systolic blood pressure	Glenn et al. (2003)	mm Hg	0.1	0.2	0.4	0.5	0.6	0.7	0.8
Systolic blood pressure	Vupputuri et al. (2003)	mm Hg	0.4	0.9	1.3	1.7	2.2	2.6	3.0
Systolic blood pressure	Nash et al. (2003)	mm Hg	0.6	1.3	1.9	2.5	3.2	3.8	4.4
Systolic blood pressure	Glenn et al. (2006)	mm Hg	0.3	0.7	1.0	1.3	1.7	2.0	2.4
Systolic blood pressure	Mean	mm Hg	0.4	0.8	1.1	1.5	1.9	2.3	2.7
Chronic kidney disease	EFSA CONTAM (2010)	Percent with CKD	8.6	15.1	20.2	24.4	28.0	31.0	33.8
Chronic kidney disease	Navas-Acien et al. (2009)	Percent with CKD	5.1	7.3	8.8	10.0	11.0	11.9	12.6
Spontaneous abortion	Borja-Aburto et al. (1999)	Percent aborted	0.3	0.7	1.1	1.6	2.1	2.8	3.5
Bioavailability coefficient = weighted mean									
Systolic blood pressure	Glenn et al. (2003)	mm Hg	0.1	0.1	0.2	0.3	0.4	0.4	0.5
Systolic blood pressure	Vupputuri et al. (2003)	mm Hg	0.3	0.5	0.8	1.1	1.3	1.6	1.8
Systolic blood pressure	Nash et al. (2003)	mm Hg	0.4	0.8	1.2	1.5	1.9	2.3	2.7
Systolic blood pressure	Glenn et al. (2006)	mm Hg	0.2	0.4	0.6	0.8	1.0	1.2	1.4
Systolic blood pressure	Mean	mm Hg	0.2	0.5	0.7	0.9	1.2	1.4	1.6
Chronic kidney disease	EFSA CONTAM (2010)	Percent with CKD	5.6	10.2	14.2	17.5	20.5	23.1	25.4
Chronic kidney disease	Navas-Acien et al. (2009)	Percent with CKD	3.8	5.7	7.0	8.0	8.9	9.7	10.3
Spontaneous abortion	Borja-Aburto et al. (1999)	Percent aborted	0.2	0.4	0.6	0.8	1.1	1.4	1.7

Table 4
Modelled effects of dietary lead exposure on blood lead concentration (B-Pb) in children sampled at an average age of 6.9 years and their IQ under eight scenarios of weekly consumption of meat from UK gamebirds. Values shown for IQ points are decreases relative to the expected value when no gamebird meals are consumed.

Parameter	Units	Gamebird meal consumption scenario							
Gamebird meal consumption scenario	Number/week	0	1	2	3	4	5	6	7
Non-gamebird meat meals per week	Number/week	3.54	2.54	1.54	0.54	0.00	0.00	0.00	0.00
Daily Pb dietary intake from gamebird meat	μg/d	0.0	19.9	39.8	59.7	79.6	99.5	119.3	139.2
Daily Pb dietary intake from non-gamebird meat	μg/d	0.2	0.1	0.1	0.0	0.0	0.0	0.0	0.0
Daily Pb dietary intake from non-meat foods	μg/d	2.9	2.9	2.9	2.9	2.9	2.9	2.9	2.8
Total daily Pb dietary intake	μg/d	3.1	22.9	42.8	62.6	82.5	102.3	122.2	142.1
Bioavailability (weighted mean)	Proportion	0.500	0.332	0.320	0.315	0.313	0.311	0.311	0.310
B-Pb (IEUBK default biovailability)	μg/dL	1.0	3.6	6.0	8.2	10.2	12.1	13.8	15.5
B-Pb (weighted mean bioavailability)	μg/dL	1.0	2.6	4.1	5.6	7.0	8.3	9.5	10.7
Decrease in IQ due to game: bioavailability = 0.5	IQ points	0.00	2.25	3.38	4.12	4.65	5.07	5.40	5.70
Decrease in IQ due to game: bioavailability = weighted mean	IQ points	0.00	1.59	2.53	3.22	3.74	4.15	4.48	4.77

midpoints of the children's age ranges (5 and 11 years) and that the ratio changes linearly with age we take the relationship of this ratio to age to be 0.461673 + 0.022518*age(years). Hence, the expected ratio for 2.5 year old children is 0.518 and that for 6.9 year old children is 0.617. We then take the average daily intake of lead from non-meat foods for UK consumers from FSA (2009) (4.731 μg/day, see above) and multiply this by these ratios to get the daily intake of lead from non-meat foods for 2.5 year old UK children of 2.450 μg/day and the daily intake of lead from non-meat foods for 6.9 year old UK children of 2.919 μg/day.

2.3. Lead concentration in meals prepared from UK gamebird meat

We took the average concentration of lead in meals prepared using gamebird meat eaten by UK consumers to be the arithmetic mean concentration of lead in prepared meals per unit mass of meat across 122 samples from six gamebird species obtained in the UK by the Wildfowl & Wetlands Trust (WWT) and reported in Table 5 of Pain et al. (2010). This includes a few birds known to have been killed using non-lead ammunition. This gave a mean concentration of 1181 μg/kg. We did not use concentrations

Table 5
Modelled effects of dietary lead exposure on blood lead concentration (B-Pb) in children sampled at an average age of 2.5 years and their Key Stage 1 writing test SATs scores at 7–8 years of age under eight scenarios of weekly consumption of meat from UK gamebirds. Values shown for SATs scores are decreases relative to the expected value when no gamebird meals are consumed.

Parameter	Units	Gamebird meal consumption scenario							
Gamebird meal consumption scenario	Number/week	0	1	2	3	4	5	6	7
Non-gamebird meat meals per week	Number/week	3.54	2.54	1.54	0.54	0.00	0.00	0.00	0.00
Daily Pb dietary intake from gamebird meat	μg/d	0.0	16.8	33.6	50.4	67.1	83.9	100.7	117.5
Daily Pb dietary intake from non-gamebird meat	μg/d	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0
Daily Pb dietary intake from non-meat foods	μg/d	2.5	2.5	2.5	2.5	2.4	2.4	2.4	2.4
Total daily Pb dietary intake	μg/d	2.6	19.3	36.1	52.8	69.6	86.4	103.1	119.9
Bioavailability (weighted mean)	Proportion	0.500	0.332	0.319	0.315	0.313	0.311	0.311	0.310
B-Pb (IEUBK default biovailability)	μg/dL	1.2	4	6.5	8.8	10.8	12.6	14.3	15.9
B-Pb (weighted mean bioavailability)	μg/dL	1.2	3	4.6	6.1	7.6	8.9	10.1	11.3
Decrease in KS1 score: bioavailability = 0.5	SATs score	0.00	0.09	0.39	0.43	0.45	0.46	0.48	0.49
Decrease in KS1 score: bioavailability = weighted mean	SATs score	0.00	0.00	0.16	0.34	0.42	0.43	0.44	0.45

calculated separately for each gamebird species or attempt to adjust the mean concentration for the relative amounts of meat from the different species eaten by consumers because the analysis of Pain et al. (2010) showed that there was no significant variation in lead concentration among gamebird species. We used the concentration from WWT samples in preference to the higher values found in pheasants and partridges collected by the Veterinary Medicines Directorate (VMD) and reported by Pain et al. (2010) because visible fragments of lead shot were removed by WWT during preparation of the meal, whereas the VMD sample preparation protocol did not involve removal of shot and therefore does not simulate dietary exposure of consumers resulting from normal culinary practice. We avoided any calculation of lead ingestion from meat from wild-shot deer because of this problem: the only large sample of lead concentration data we know of from UK wild-shot deer meat was collected by VMD using the same preparation protocol as that for gamebirds. The mean lead concentration in 2521 samples of game from EU countries presented in Table 14 of EFSA CONTAM (2010) was about three times the concentration we use here based upon UK gamebird meals (Pain et al. 2010). This may be at least partly because of the inclusion in the EFSA report of samples from which visible shot fragments were not removed prior to chemical analysis. Not all member states supplying data to EFSA recorded whether or not visible shot fragments were removed, and we were therefore unable to fully evaluate this possibility.

2.4. Scenarios of gamebird meat consumption and their effect on exposure to dietary lead

We assumed for the purposes of our scenarios that consumers might feasibly eat from 0 to 7 gamebird meat meals per week. This range was considered to be plausible because it is consistent with one study from Switzerland (Haldimann et al., 2002), which reported that hunters ate an average of 2.2 meals of game per week during the hunting season. We followed EFSA CONTAM (2010) in assuming that an average meat meal for adults contained 0.2 kg of meat. Hence, given that an average of 0.101 kg of meat is eaten per person per day by UK consumers (FSA, 2009), the average number of meat meals per adult per week was 3.535. In calculating the consequences of gamebird meat consumption for the overall mass of lead ingested per consumer per week, we assumed that gamebird meat replaced non-game meat in the diet up to a total of 3.535 meals per week. For example, if two gamebird meals were eaten per week, then 1.535 meals per week of non-game meat were eaten. For gamebird meal consumption rates greater than 3.535 meals per week it was assumed that all the meat eaten came from gamebirds and that each additional gamebird meal replaced 0.2 kg of non-meat food containing the average lead concentration in non-meat foods. Assuming that the presence of lead contamination from game in the average diet of UK consumers can be ignored, because of the small quantity of game relative to non-game meat eaten when averaged over all consumers, we calculated the average intake of lead per non-game meat meal from the concentration of lead in meat, averaged over all meat types from Table 3a of FSA (2009) and the average adult meat meal mass as 2.733 μg/kg × 0.2 kg = 0.5465 μg. We calculated the average quantity of lead ingested in an adult meal of cooked gamebird meat as 1181 μg/kg × 0.2 kg = 236.20 μg.

We assumed that children eat smaller meat meals than adults. We required estimates of meat meal sizes for children of two ages, 2.5 and 6.9 years (see above). We assumed that the ratio of meat meal size of children, relative to that for adults, was the same as the ratio of Total Energy Expenditure (TEE) of children relative to that of adults. We used equations from Institute of Medicine (2005) that relate the TEE of male and female US children and adults to their body weight, height, activity level and age to calculate expected TEE for 2.5 and 6.9 year old children and 30 year old adults, averaged across both sexes. We assumed that the activity class of both adults and children was midway between classes C2 and C3, which indicate moderate levels of activity. We used age-specific height and weight data for England from Craig et al. (2009). The ratio of TEE for a 2.5 year old child to that of a 30 year old adult was 0.498. The equivalent ratio for a 6.9 year old child was 0.598. Hence, the estimated average mass of a meat meal for a 2.5 year old child is 0.0995 kg and for a 6.9 year old child is 0.1179 kg.

2.5. Calculating the effect on blood lead concentration of dietary lead from gamebird meals

Ingested lead in the diets of people who eat the meat of birds shot with lead ammunition includes fragments of the metal from ammunition used to kill the bird, a small amount of other lead in the birds' tissues and lead from the general diet. The absolute bioavailability of dietary lead derived from ammunition (the proportion of the ingested amount which is absorbed and enters the blood) might be lower than that of lead in the general diet because some of the ingested ammunition lead may remain as metallic fragments after cooking and processing in the alimentary canal. Metallic lead, especially that remaining in large fragments, will not be as soluble nor be absorbed in the intestine as readily as more soluble lead salts and complexes (Barltrop and Meek, 1975; Oomen et al., 2003). The absolute bioavailability in humans of dietary lead from meals of wild game has been estimated from the results of *in vitro* gastrointestinal simulation experiments using cooked meat from partridges *Alectoris rufa* killed with lead shot (Mateo et al., 2011). However, we wished to use an alternative estimate because (1) the reliability of these estimates depends on the uncertain degree to which the *in vitro* experiment mimics human digestion and absorption (Zia et al. 2011), and (2) the cooking methods used recipes with vinegar and wine, which are prevalent in Spain but somewhat different from those most frequently used in the UK. Mateo et al. (2011) showed that the proportion of lead in the cooked gamebird meat that was bioaccessible (soluble and available for absorbtion) in simulated gastrointestinal conditions was considerably greater when a recipe containing vinegar was used than when wine was used, and that much less of the lead in uncooked partridge meat was bioaccessible.

We therefore used observations from two studies of Greenland adults (Bjerregaard et al. 2004; Johansen et al. 2006) to derive an empirical relationship between the mean daily intake of dietary lead from the meat of shot birds and mean B-Pb. Bjerregaard et al. (2004) measured the B-Pb of adults in Greenland and also administered a dietary questionnaire which asked each subject to report their consumption of various foods, including meat from shot wild seabirds (mostly *Uria lomvia*) and ducks (mostly *Somateria mollissima*). They found that B-Pb was positively related to the frequency of consumption of wild bird meals, but multiple regression analysis did not find any significant effects on blood lead of the frequency of consumption of other foods (fish, meat from whales and seals, various imported food items). Bjerregaard et al. (2004) provided mean B-Pbs, adjusted for the effects of age and sex using a regression model, for each of six categories of subjects defined according to their reported intake of wild bird meals. The categories were: rarely, once per month, 2–3 times per month, 1–3 times per week, 4–6 times per week and daily. For each of these categories we calculated a mean daily consumption rate of wild bird meals, using the midpoints of frequencies for those categories defined by a range. For example, we converted the category 2–3 times per month to 0.082 meals per day (2.5/30.44 = 0.082). The category "rarely" was taken to represent zero consumption of wild bird meals. Using data from Johansen et al. (2004),

Bjerregaard et al. (2004) estimated the mean quantity of lead in a meal of cooked wild bird meat as 425 μg. We therefore multiplied the mean number of meals consumed per day by 425 to obtain the mean daily quantity of dietary lead per person from wild bird meat in μg/d. We then performed a weighted ordinary least squares regression of the adjusted mean B-Pb for the six categories of wild bird meal consumption in μg/dL on the mean daily intake rate of lead from this source, with the number of subjects being used as weights.

We performed a similar set of calculations on data from another study by Johansen et al. (2006) who measured the B-Pb of adult men in Greenland and also asked each subject to report his consumption of various foods. They found that B-Pb was positively related to the frequency of consumption of wild bird meals comprising the same species as in the other study. They converted the frequency of consumption data so that lead intake per meal would be that expected if meals were made only from murres (mostly *Uria lomvia*). This conversion takes account of the higher concentration of lead in meals made from *Somateria mollissima.* In this study no adjustment of B-Pb for age was made and no multiple regression analysis of effects of consumption of other foods was reported. Johansen et al. (2006) provided mean B-Pbs, for each of five categories of subjects defined according to their reported monthly intake of murre-equivalent meals. The categories were: none, 0.1–5.0, 5.1–15, 15.1–30 and >30. For each category we calculated a mean daily consumption rate of murre equivalent meals, using the midpoints of frequencies for those categories defined by a range. For the >30 category, we assumed that one murre equivalent meals was eaten per day. Johansen et al. (2004) estimated the mean quantity of lead in a murre equivalent meal as 146 μg. We therefore multiplied the mean number of meals consumed per day by 146 to obtain the mean daily quantity of dietary lead per person from wild bird meat in μg/d. We then performed a weighted ordinary least squares regression of the adjusted mean B-Pb for the five categories of wild bird meal consumption in μg/dL on the mean daily intake rate of lead from this source, with the number of subjects being used as weights.

We took the weighted mean of the estimates of the regression coefficients from the two studies to represent the mean increase in B-Pb for each additional μg/d of dietary lead derived from wild bird meat. The total number of subjects contributing data to each of the two studies were used as weights in this calculation. We were unable to find other published studies in which dietary lead intake rates from wild gamebirds shot with lead ammunition and B-Pb had both been measured. In particular, we were unable to find an equivalent study of children. The bioavailability of lead in the ordinary diet is considerably higher in children than in adults (Mushak 1998), so we need an additional step to be able to calculate the effect on the B-Pb of children of dietary lead derived from wild gamebird meat.

The regression coefficient b from our analysis of the data from Greenland adults is directly comparable to the coefficient used in the method of Carlisle and Wade (1992) to calculate the effect of the mean daily quantity of dietary lead in the ordinary diet on the B-Pb of adults. When intake rate is in μg/d and B-Pb is in μg/dL the value of the coefficient recommended by Carlisle and Wade is 0.04. Our regression coefficient and the coefficient in the calculation of Carlisle and Wade are not the same as absolute bioavailability and, to draw attention to this, we refer to them henceforth in this paper as bioavailability coefficients. However, we assume that the ratio of our estimate of b to the value 0.04 for Carlisle and Wade's bioavailability coefficient can be taken to represent the expected ratio of the absolute bioavailability of dietary lead from cooked wild bird meat to that for lead from the ordinary diet in both adults and children. We therefore estimated the absolute bioavailability of dietary lead from cooked wild bird meat for children by multiplying a widely used value for the absolute bioavailability of dietary lead from lead from the ordinary diet (0.5, from Mushak 1998) by the quantity $b/0.04$. Hence, we estimated the absolute bioavailability for children of dietary lead from cooked wild bird meat as $0.5b/0.04$.

2.6. Calculating blood lead concentration for UK adults and children for a given gamebird meat consumption scenario

We estimated the likely effects on B-Pb of a specified level of exposure to lead, including dietary exposure determined as described above, by using previously published models. Following EFSA CONTAM (2010), we used different models for children and adults because Carlisle and Wade's (1992) method has been successfully applied to adults, but is less suitable for children (Lakind, 1998). To estimate expected B-Pb in children we used the Integrated Exposure Uptake Biokinetic (IEUBK) Model (IEUBKwin version 1.1; EPA (2007)), a widely validated exposure assessment model applicable to children of up to 7 years old. We assumed that exposure to lead from soil and dust involved lead concentrations in soil and dust at the median level for European studies cited in EFSA CONTAM (2010) (23 mg/kg) and that ingestion rates for soil and dust were at the age-specific default values used in IEUBKwin1.1. We also used the age-specific default values in IEUBKwin1.1 for exposure to lead from air and water. We calculated the dietary intake of lead for 2.5 and 6.9 year old children as described above. In applying the dietary intake module of IEUBKwin1.1, we took the absolute bioavailability of dietary lead for children to be either (a) 0.5, which is the value for dietary lead in the ordinary diet given by Mushak (1998) and is also the default value used by IEUBKwin1.1, or (b) the weighted mean of 0.5 and the bioavailability of lead in wild bird meals, calculated from the Greenland data according to the method described in Section 2.5. We used the proportions of dietary lead derived from non-gamebird and gamebird sources in each scenario as the weights in this calculation.

For adults, we followed EFSA CONTAM (2010) in ignoring non-dietary exposure as this is considered to be negligible. We calculated daily dietary intake of lead by adults in μg/d as described above and calculated the increment in B-Pb in μg/dL from this by either (a) multiplying it by 0.04, which is the value used by Carlisle and Wade (1992) for dietary lead in the ordinary diet, or (b) the weighted mean of 0.04 and the bioavailability coefficient b from our regression analysis of the data from Greenland adults described in Section 2.5. We used the proportions of total dietary lead derived from non-gamebird and gamebird sources in each scenario as the weights in this calculation.

3. Results

3.1. The effect of lead from meals of cooked wild bird meat on blood lead concentration

There was a strong relationship in the data from both Greenland studies between mean B-Pb and the estimated mean rate of intake of dietary lead from meals of cooked wild bird meat across the categories of adults defined according to their wild bird meat intake ($r = 0.951$ and $r = 0.901$ for the studies of Bjerregaard et al. (2004) and Johansen et al. (2006) respectively; Fig. 1). The value of the fitted regression coefficient b from the first of these studies was 0.01938 ± 0.00450 (±1 SE) and it was 02978 ± 0.01208 for the second study. The weighted mean of these two estimates of b is 0.02448. Hence, when using method (b) from Section 2.6 of the Methods for adults, we calculated the expected increment in mean B-Pb in μg/dL from a given intake rate of dietary lead in μg/d by multiplying the intake rate by the weighted mean of 0.04 and

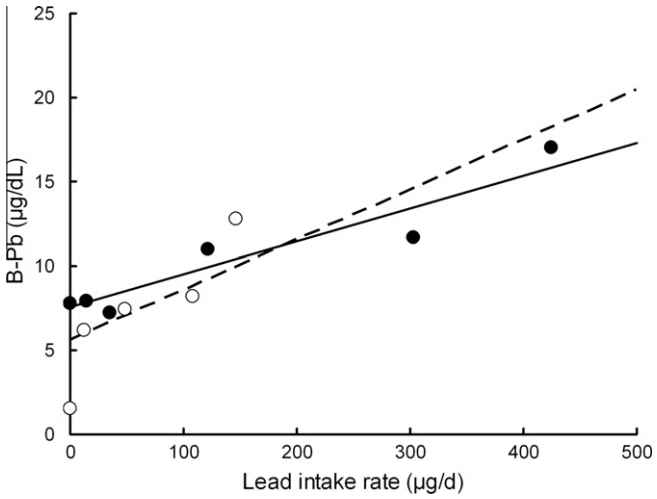

Fig. 1. Relationship between mean blood lead concentration (B-Pb) and mean daily dietary intake of lead from the cooked meat of wild seabirds and ducks in groups of Greenland adults. Each point represents a value for one of these groups, which were defined according to their frequency of consumption of wild bird meals. Filled circles show data from Bjerregaard et al. (2004). The solid line is the weighted regression model fitted to them: B-Pb = 7.595 + 0.01938*intake. Open circles show data from Johansen et al. (2006). The dashed line is the weighted regression model fitted to them: B-Pb = 5.609 + 0.02978*intake.

0.02448, with the proportions of total dietary lead derived from non-gamebird and gamebird sources in each gamebird meal scenario being used as the weights in this calculation.

We also used our estimate of *b* to calculate a value for the absolute bioavailability of dietary lead in cooked meat of wild birds in children for use in IEUBKwin1.1. Using the procedure described in Section 2.5, we calculated the absolute bioavailability in children of dietary lead derived from the cooked meat of wild birds as $0.5 \times 0.024488/0.04 = 0.3060$.

The results of our calculations of the dietary intake of lead of UK adults under our eight gamebird meal consumption scenarios and the expected mean B-Pb resulting from them are shown in Table 2. Equivalent results for UK children are shown in Tables 4 and 5.

3.2. Potential cardiovascular effects in adults associated with consumption of meat from UK gamebirds

We used equations relating systolic blood pressure (SBP) to B-Pb taken from the four studies used by EFSA CONTAM (2010) to calculate SBP for each of the eight gamebird meat consumption scenarios. The studies used were carried out on adults in the USA (Glenn et al., 2003; Vupputuri et al., 2003; Nash et al., 2003) and in South Korea (Glenn et al., 2006). When the value 0.04 was used as the bioavailability coefficient, these calculations indicated that consuming one gamebird meal per week would elevate SBP by 0.1 to 0.6 mm Hg above the value for those consuming no game meat, depending on the health effect study used (Table 3). The mean effect of one gamebird meal per week across all four studies was 0.4 mm Hg (Table 3). EFSA CONTAM (2010) defined the Benchmark Response of the effect of lead on systolic blood pressure as 1.2 mm Hg, so consumption of 3.2 gamebird meals per week, using the average across the four studies, would be needed to elevate SBP by the Benchmark Response. When we used the weighted mean of 0.04 and the value derived from the Greenland studies as the bioavailability coefficient, we found that consuming one gamebird meal per week would elevate SBP by 0.1 to 0.4 mm Hg above the value for those consuming no game meat, depending on the study used. The mean effect of one gamebird meal per week across all four studies was 0.2 mm Hg (Table 3) and the consumption of 5.2 gamebird meals per week, using the average across the four studies, would be needed to elevate SBP by the Benchmark Response.

3.3. Potential effects on the prevalence of chronic kidney disease in adults associated with consumption of meat from UK gamebirds

We used two statistical models fitted to the data of Navas-Acien et al. (2009) to describe the relationship between B-Pb and the proportion of adult US subjects with chronic kidney disease (CKD), defined as an estimated glomerular filtration rate of <60 mL/min/1.73 m^2. The first model was the log-probit model fitted to the unadjusted data on the prevalence of CKD, following Appendix C of EFSA CONTAM (2010). The second model was Model 3 of Navas-Acien et al. (2009) in which adjustment was made for the effects of survey year, age, sex, race/ethnicity, body mass index, education, smoking, serum creatinine, alcohol, hypertension, diabetes mellitus, menopausal status and blood cadmium level. We used these models to calculate the expected prevalence of CKD under the eight gamebird consumption scenarios described above.

When the value 0.04 was used as the bioavailability coefficient, these calculations indicated that consuming one gamebird meal per week would elevate the prevalence of CKD by 5.1–8.6% above the value for those consuming no game meat, depending on which health effect model was used (Table 3). EFSA CONTAM (2010) defined the Benchmark Response of the effect of lead on CKD as 10% increase in prevalence, so consumption of 1.2 gamebird meals per week, using the unadjusted model, or of 4.0 gamebird meals per week, using the adjusted model, would be required to increase the risk of CKD by the Benchmark Response. When we used the weighted mean of 0.04 and the value derived from the Greenland studies as the bioavailability coefficient, we found that consuming one gamebird meal per week would elevate the prevalence of CKD by 3.8% or 5.6% above the value for those consuming no game

Table 6
Sensitivity of estimates of the number of gamebird meals per week required to give specified changes in health effects to assumptions about exposure to dietary lead from components of the diet other than gamebirds. The table shows the number of gamebird meals per week required to produce an effect if mean daily exposure to dietary lead intake from foods other than gamebirds was half (Low) or twice (High) that which we assumed in our main calculations. Effect sizes given as Benchmark Responses by EFSA CONTAM (2010) are marked with asterisks. Results are shown for the default (Method a) and weighted mean (Method b) values of bioavailability.

Age group	Health effect	B-Pb - effect model	Effect size criterion	Bioavailability a		Bioavailability b	
				Low	High	Low	High
Adults	Systolic blood pressure	Mean	SBP increase of 1.2 mm Hg*	3.2	3.2	5.2	5.2
Adults	Chronic kidney disease	EFSA Contam (2010)	CKD prevalence increase of 10%*	1.2	1.3	1.9	2.1
Adults	Chronic kidney disease	Navas-Acien et al. (2009)	CKD prevalence increase of 10%*	3.1	5.3	5.1	8.4
Adults	Spontaneous abortion	Borja-Aburto et al. (1999)	Abortion increase of 1%	2.8	2.8	4.6	4.5
6.9 year-old children	Decrease in IQ	Lanphear et al. (2006)	IQ decrease of 1 IQ point*	0.4	0.5	0.5	0.7
2.5 year-old children	Decrease in SATs score	Chandramouli et al. (2009)	KS1 score decrease of 0.2	1.4	1.2	2.3	2.0

meat, depending on the model used (Table 3). The consumption of 1.9 (unadjusted model) or 6.5 (adjusted model) gamebird meals per week would be needed to elevate the prevalence of CKD by the Benchmark Response.

3.4. Potential effects on the prevalence of spontaneous abortion in pregnant women associated with consumption of meat from UK gamebirds

We used a statistical model fitted by Borja-Aburto et al. (1999) to describe the relationship between B-Pb and the proportion of pregnant women in Mexico City who incurred spontaneous abortion. The model adjusted for the effect of a previous history of spontaneous abortion. We used this model to calculate the expected proportion of subjects incurring spontaneous abortion under the eight gamebird consumption scenarios described above.

When the value 0.04 was used as the bioavailability coefficient, these calculations indicated that consuming one gamebird meal per week would elevate the prevalence of abortion by 0.3% above the value for those consuming no game meat (Table 3). Consumption of 2.8 gamebird meals per week would be required to increase the prevalence of abortion to 1% above that if no game meat was consumed. When we used the weighted mean of 0.04 and the value derived from the Greenland studies as the bioavailability coefficient, we found that consuming one gamebird meal per week would elevate the prevalence of abortion by 0.2% above the value for those consuming no game meat (Table 3). Consumption of 4.6 gamebird meals per week would be required to increase the prevalence of abortion to 1% above that if no game meat was consumed. EFSA CONTAM (2010) did not cite this study in their opinion and did not identify a Benchmark Response. However, JECFA (in WHO, 2011) cited the study and considered this to be well-designed.

3.5. Potential neurodevelopmental effects on children associated with the consumption of meat from UK gamebirds

We used the log-linear regression model of Lanphear et al. (2005) of IQ in relation to concurrent blood lead concentration, adjusted for effects of site, maternal IQ, HOME Inventory, birth weight, and maternal education. The model was based upon pooled data from seven studies of children in the USA, Mexico, Australia and Yugoslavia. We used the model to estimate the expected IQ values of children from the blood lead levels derived from the gamebird meat consumption scenarios.

When the value 0.5 was used as the bioavailability of dietary lead, these calculations indicated that consuming 0.4 gamebird meals per week would reduce IQ by one point beyond any IQ reduction caused by the base-diet containing no game meat (Table 4). When we used the weighted mean of 0.5 and the value derived from the Greenland studies as the bioavailability, we found that consuming 0.6 gamebird meals per week would reduce IQ by one point beyond any IQ reduction caused by the base-diet with no game meat (Table 4). EFSA CONTAM (2010) defined the Benchmark Response of the effect of lead on IQ as one IQ point, so the effects reported above and in Table 4 in IQ points are equivalent to responses in Benchmark Response units.

3.6. Potential effects on the academic performance of UK schoolchildren associated with consumption in early childhood of meat from UK gamebirds

Chandramouli et al. (2009) reported a negative association of academic test results of UK schoolchildren at Key Stage 1 (SATs tests) with B-Pb measured at 30 months of age. We used the relationship between the mean outcome of the SATs writing test and blood lead shown in Figure 3 of their paper and in their Table 2. This effect may be non-linear, because Chandramouli et al. (2009) did not detect a significant difference from zero in the effect of B-Pb on SATs score for the B-Pb bins 0–2 and 2–5 μg/dL. We therefore set the effect of B-Pb on SATs score for these bins at zero. We assumed that the effect of B-Pb on SATs score for the B-Pb bins 5–10 μg/dL and >10 μg/dL were those shown in Figure 3 of Chandramouli et al. (2009) and that the mean B-Pb associated with these effects was the mean value for the children studied in each of these bins. We then used linear interpolation between these values to estimate SATs score differences for the expected B-Pb values obtained from our gamebird meat consumption scenarios and expressed these as a difference from the expected value with no game consumption (Table 5). When the value 0.5 was used as the bioavailability, these calculations indicated that a reduction of 0.2 SATs writing test points at Key Stage 1, relative to the performance expected if no gamebird meat had been consumed, would result from consumption of 1.4 gamebird meals per week. When three gamebird meals are consumed per week the expected reduction in SATs score was 0.43. When we used the weighted mean of 0.5 and the value derived from the Greenland studies as the bioavailability, we found that a reduction of 0.2 SATs writing test points would result from consumption of 2.2 gamebird meals per week. When three gamebird meals are consumed per week the expected reduction in SATs score was 0.34. Given that the SATs writing test is scored from 1 to 4, with 2 being the approximate average, these are small but non-trivial effects. This study had not been published when the EFSA opinion was written and we therefore cannot express the results in terms of a Benchmark Response.

3.7. Sensitivity of results to assumptions about dietary exposure to lead from sources other than gamebird meat

Our calculations of the potential effects of dietary lead from gamebirds on human health involve many assumptions and approximations. We have examined the effects of one of these already by comparing results that assume two different values for the bioavailability of lead in gamebird meals. However, many of our assumptions concern the mean daily dietary intake of lead from sources other than gamebirds. To examine the sensitivity of our results to these assumptions, we repeated our calculations after either halving or doubling the daily dietary intake rate of lead from sources other than gamebirds. We call these two modifications "Low" and "High" baseline diet lead intake rates. We recalculated the number of gamebird meals per week required to produce a set of specified effects on human health under the Low and High baseline dietary exposure scenarios. For most of the health effects, the differences in the required number of gamebird meals caused by baseline dietary lead exposure were small (Table 6). The largest difference was for the Navas-Acien et al. (2009) model of chronic kidney disease.

4. Discussion

Our estimates for adults of the bioavailability of lead in cooked meals made from shot wild birds indicate that it is lower than for lead in the general diet, as expected given that some of the lead in the cooked meat is likely to be in the form of metallic fragments. Our analyses of data derived from studies of B-Pb and dietary lead intake in Greenland adults found that the ratio of the bioavailability coefficient for dietary lead from cooked meals made from shot wild birds to the bioavailability coefficient for lead in the ordinary diet was 0.02448/0.04 = 0.612. That is, about 40% less of the dietary lead in gamebird meals was absorbed compared with lead from

other parts of the diet. We assumed that the ratio of bioavailability coefficients that we determined for adults could be used to estimate the absolute bioavailability for children of dietary lead from gamebird meals. This assumption leads to an estimate of absolute bioavailability of gamebird lead in children of 0.306, which compares with estimates of 0.157 and 0.236 from *in vitro* gastrointestinal simulation experiments with partridge meat cooked using two recipes (Mateo et al. 2011). In our assessments of the potential health effects of gamebird consumption, we have presented results calculated using our new estimates of the bioavailability of gamebird lead, but we also include, for comparison, equivalent calculations using bioavailability values that have been widely applied in other studies of the impacts of dietary lead on human health (bioavailability coefficient = 0.04 for adults and absolute bioavailability = 0.5 for children).

Another source of uncertainty in our calculations involves the mean daily dietary intake rate of lead from sources other than gamebirds. We have used the midpoint between zero and the LOQ to estimate lead concentrations in food types with mean concentrations <LOQ, but have also examined the sensitivity of our results to altering assumptions about non-game dietary exposure. We did this by repeating our calculations after either halving or doubling the daily dietary intake rate of lead from sources other than gamebirds. It should be noted that FSA (2009) reported, from total diet studies, a twenty-fold reduction in dietary exposure to lead of the general UK population between 1980 and 2006, with exposures decreasing from 0.12 mg [120 μg] per day to 0.006 mg [6 μg] per day. However, the FSA (2009) UK total dietary exposure values are lower than the Great Britain (GB) values used in the EFSA (2010) study and lower than those found in many other European countries. The FSA (2009) total mean dietary exposure to lead for adults (mean consumers) in the UK was estimated to be 0.090–0.10 μg/kg bw/day, depending upon whether zero or LOQ values were used to represent samples <LOQ (FSA 2009; Table 4b) whereas EFSA CONTAM (2010) used mean GB figures of 0.47–0.96 μg/kg bw/day (EFSA CONTAM 2010; Table 22); some five or more times higher. While we see no reason to doubt the results presented by FSA, it is important that these uncertainties are taken into account in the interpretation of our results. However, our sensitivity analyses indicate a the small impact of halving and doubling dietary exposure from sources other than gamebirds.

Our analyses indicate that, in the UK context:

- consumption of 0.4–0.7 gamebird meals per week may be associated with a 1 point decrease in the IQ of children, the Benchmark Response identified by EFSA CONTAM (2010),
- consumption of three gamebird meals per week may be associated with reductions in children's SATs writing tests scores of 0.34–0.43 points,
- consumption of 2.8–4.6 gamebird meals per week may be associated with a 1% increase in the prevalence of spontaneous abortion in pregnant women
- consumption of 1.2–1.9 or 4.0–6.5 gamebird meals per week (depending upon the statistical model used) may be associated with a 10% increased prevalence of chronic kidney disease in adults, the Benchmark Response identified by EFSA CONTAM (2010)
- consumption of 3.2–5.2 gamebird meals per week may be associated with a 1% increase in systolic blood pressure in adults, the Benchmark Response identified by EFSA CONTAM (2010).

In each case we have given the results for the higher assumed value of bioavailability first, followed by that for the lower value.

The Benchmark Responses for IQ, SBP and CKD were selected by EFSA because such changes could have significant consequences for human health on a population basis. Studies in the US have related a 1 point reduction in IQ to a 4.5% increased risk of failure to graduate from high school and a 2% decrease in productivity in later life (Schwartz, 1994; Grosse et al., 2002). Studies have associated the BMR for cardiovascular effects (an increase of SBP of 1.2 mm Hg) with an increase in the percentage of the population treated for hypertension by 3.1%, and a 2.6 % or 2.4% increase in expected annual mortality from cerebral stroke or myocardial infarction, respectively (Selmer et al., 2000). While these levels of game consumption do not occur in the population at large, they may be of concern for those consuming large quantities of game, whether from choice, such as sports hunting groups, and those making an ethical choice to eat the meat of wild rather than captive-reared animals, or from necessity, such as those who are economically constrained in their food choices. In addition, the lead concentrations in game presented by Pain et al. (2010) are for marketed game, and it is possible that exposure may be higher in groups that consume game that is not commercially sold. An unpublished survey conducted in 2004 by the Countryside Alliance, the British Association for Shooting and Conservation and the National Gamekeepers' Association (Compass, 2004) indicated that 20% of the game shot in Britain was given away, presumably mostly to guns, pickers-up and other shoot helpers. Assuming that most of this meat is consumed by this relatively small group and their close associates, this implies high levels of per capita consumption. Exposure to lead could be increased in this group if the game animals given or sold informally to game management employees and helpers were those of low market value because they have been visibly damaged by shot, as the bodies of such animals may contain more lead shot than those sent to market. If this is the case then average lead concentrations in game consumed by this putative high-exposure group may also be higher than the average indicated by our analyses of meat from marketed game.

Many of the assumptions and approximations involved in our calculations affect the level of dietary exposure to lead from components of the diet other than gamebird meals. These uncertainties include the true lead concentrations in foods for which the reported concentration was below the LOQ, the degree to which the diet composition of individuals and age, sex and social groups differ from that of the average diet upon which our calculations are based and the applicability to the situation in the UK of the ratio of the lead intake for children and adults in Germany. Our sensitivity analysis of the effects of halving or doubling the calculated level of this background dietary exposure showed that it had minor effects for most health effects, with their direction and size depending upon the form of the model that related the health effect to B-Pb. The doubling and halving of background dietary exposure in our sensitivity test is probably greater or of a similar order to the uncertainties in the calculations. For example, dietary exposure from non-meat diet components would have been 1.6× the value we used if concentrations for all foods with concentrations less than the LOQ had been set at the LOQ and 0.4× the value we used if concentrations for all of these foods had been set at zero. We conclude that our results are generally robust against failures in our assumptions and approximations in calculating dietary lead exposure from foods other than gamebird meat.

We are unable to estimate the proportion of people in the UK exposed to sufficient dietary lead from game meat consumption to cause responses exceeding the BMR because we have little information on game consumption levels in the UK. However, we consider that the range of 0–7 meals of game per week is likely to cover the amounts consumed by many hunting communities in the UK and possibly elsewhere across the EU. For example, Haldimann et al. (2002) recruited 31 active hunters or family members in the same household from a local hunting society for a study evaluating the risk from ingesting lead from game. In this group, the range of meals of game shot with lead ammunition consumed

per week during the hunting season was 0.3–6 (mean of 2.2) giving an average daily intake of approximately 50 g of game meat. Game sales in the UK have increased rapidly in recent years. A consumer survey by Mintel in 2006 (Mintel 2007) estimated annual retail game sales at £57 million in the UK, with large forecast increases, and found that >40% of people ate some game, with an additional 12% of people keen to try game. Game has been actively promoted on television by celebrity chefs and in campaigns that promote game consumption, partly on the basis of being a healthy alternative to many other red meats (e.g. http://www.gametoeat.co.uk/article/nutritional-facts accessed 18 February 2012). Increasing game consumption trends as people select foods that are perceived to be healthier could result in a higher proportion of the population consuming levels of game that may be associated with the effects described in this paper.

A limitation of our analysis is that we have no information on the extent to which game consumption is confined to certain times of year and how this varies regionally and by social group. Our calculations assume a constant rate of game consumption. Shooting seasons for different game species span the whole year. For example, gamebird seasons vary with species, in England spanning 12th August-20th February, and deer shooting seasons span the whole year, according to species and sex; woodpigeon can be shot year round for defined purposes (such as crop damage) under the terms and conditions of a general licence, and rabbits and hares can be shot year round (though is subject to a close season on moorland and unenclosed land (see http://www.basc.org.uk//en/departments/game-and-gamekeeping/game-shooting/shooting-seasons.cfm.). In addition, game meat may be frozen or otherwise preserved and consumed out of season.

It is important to note that our modelling analyses give an indication of the best estimate of the *expected* result, i.e. what the data suggest would be the most likely health outcome associated with given levels of game consumption. Analyses of risk, such as those conducted by EFSA, are based not upon the exposure level or BMD (associated with a pre-specified BMR), but upon the lower one-sided 95% confidence bound of the BMD, denoted BMDL. Note that we have not performed calculations to determine the level of consumption of gamebird meat required to produce the BMDL. BMDL calculations attempt to allow for uncertainty in the relationship between exposure and response and are precautionary in that regard. Had we calculated the number of gamebird meals required to produce the BMDL, the numbers of meals per week required would have been lower than those given above. We did not calculate the BMDL because we were unable to incorporate, in a sufficiently robust way, the uncertainties in all the steps in our calculations, including the estimation of bioavailability and of lead exposure from the baseline diet and other sources. Had we done so, the number of gamebird meals per week required to produce the BMDL would have been lower than those required to give the Benchmark Response.

It is also important to note that the effects presented in our analysis are *additional*, i.e. the expected changes in IQ, SAT tests, CKD and SBP are over and above any changes that would be expected to occur from exposure to lead by just consuming the base diet, in the absence of gamebird consumption. This is particularly important with respect to children, the most vulnerable group. EFSA CONTAM (2010) concluded that for some infants, children and pregnant women there is already potential concern about effects on neurodevelopment at current levels of exposure to lead, without regular consumption of game meat. In infants and children, the consumption of less than one game meal per week would be predicted to further decrease IQ by 1 point.

The European Commission takes into account EFSA Scientific Opinions. Game meat is not currently included as a foodstuff for which Maximum Levels are set under Regulation (EC) No 1881/2006 (EC, 2006), and a high proportion of game samples across the EU exceed the Maximum Levels set for other meats, sometimes by several orders of magnitude (Pain et al. 2010). While this is of less concern for those who eat game infrequently, it is important to also consider potential health risks associated with groups that are vulnerable because of higher than average exposure to lead, such as communities that consume game frequently, or because of increased effects of lead at given levels of exposure, such as in children and pregnant women. National institutions responsible for public health have also responded to EFSA's scientific opinion. Both the Federal Institute for Risk Assessment in Germany (BfR, 2011) and the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN, 2012) have recently evaluated risks from the consumption of game shot with lead ammunition and recommended that pregnant women, women wishing to become pregnant and children (under 6 or 7, respectively) should avoid eating meat from game shot with lead ammunition, and that its consumption should be limited in other groups (BfR 2011; AESAN 2012).

While our results are calculated for a hypothetical range of dietary consumption levels for gamebirds, and subject to a number of assumptions and uncertainties, they use the most current available data, and they give an indication of the approximate numbers of meals of game a week that may be associated with critical health endpoints. We hope that the analyses presented in our study will help further inform the development of appropriate responses to the risks from ingesting lead from ammunition in game in the UK, EU and elsewhere.

Conflict of Interest

The authors declare that there is no conflict of interest.

Acknowledgments

We thank Professor Len Levy for his guidance and advice during the preparation of this paper, Rafael Mateo for advice on bioavailability calculations and two anonymous referees for their constructive comments.

References

ACCLPP, 2012. Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention. Report of the Advisory Committee on Childhood Lead Poisoning Prevention of the Centers for Disease Control and Prevention pp. 57 <www.cdc.gov/nceh/lead/ACCLPP/Final_Document_010412.pdf.>

AESAN, 2012. Informe del Comité Científico de la Agencia Española de Seguridad Alimentaria y Nutrición (AESAN) sobre el riesgo asociado a la presencia de plomo en carne de caza silvestre en España Número de referencia: AESAN-2012-002 Documento aprobado por el Comité Científico en su sesión plenaria de 22 de febrero de 2012 www.aesan.msc.es/AESAN/docs/docs/.../LEAD_GAME.pdf. Also available in English: AESAN 2012. Report of the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) in relation to the risk associated with the presence of lead in wild game meat in Spain. Reference Number: AESAN-2012-002 Report approved by the Scientific Committee on plenary session February 22th, 2012.

Barltrop, D., Khoo, H.E., 1975. The influence of nutritional factors on lead absorption. Postgrad. Medical J. 51, 795–800.

Barltrop, D., Meek, F., 1975. Absorption of different lead compounds. Postgrad. Medical J. 51, 805–809.

Barry, P.S.I., 1975. A comparison of concentrations of lead in human tissues. Br. J. Ind. Med. 32, 119–139.

BfR., 2011. BfR (The Federal Institute for Risk Assessment, Germany) Lead fragments in game meat can be an added health risk for certain consumer groups 32/2011, 19.09.2011 <http://www.bfr.bund.de/en/press_information/2011/32/lead_fragments_in_game_meat_can_be_an_added_health_risk_for_certain_consumer_groups-127610.html.>

Bjerregaard, P., Johansen, P., Mulvad, G., Pedersen, H.S., Hansen, J.C., 2004. Lead sources in human diet in greenland source. Environ. Health Perspect 112, 1496–1498.

Borja-Aburto, V.H., Hertz-Picciotto, I., Rojas Lopez, M., Farias, P., Rios, C., Blanco, J., 1999. Blood lead levels measured prospectively and risk of spontaneous abortion. Am. J. Epidemiol. 150, 590–597.

Carlisle, J.C., Wade, M.J., 1992. Predicting blood lead concentrations from environmental concentrations. Regul. Toxicol. Pharmacol. 16, 280–289.
CDC., 1975. Increased lead absorption and lead poisoning in young children: a statement by the Center for Disease Control. Atlanta GA: US Department of Health, Education, and Welfare, CDC, 1975.
CDC., 1985. Preventing lead poisoning in young children: a statement by the Centers for Disease Control. Atlanta GA: US Department of Health and Human Services, CDC, 1985; DHHS publication no. (CDC) 99–2230.
CDC., 1991. Preventing lead poisoning in young children: a statement by the Centers for Disease Control—October 1991. Atlanta GA: US Department of Health and Human Services, Public Health Service, CDC, 1991.
CDC., 2005. Preventing Lead Poisoning in Young Children. CDC, Atlanta, Georgia, USA.
Chandramouli, L., Steer, C.D., Ellis, M., Emond, A.M., 2009. Effects of early childhood lead exposure on academic performance and behaviour of school age children. Arch. Dis. Child. 94, 844–848.
Chisolm, J.J., Harrison, H.E., 1956. The exposure of children to lead. Pediatrics 18, 934–955.
Compass, 2004. Game to Eat Survey: Final Report. Compass Research Analysis Solutions, Porton, UK.
Craig, R., Mindell, J., Hirani, V., 2009. Health Survey for England -2008. 2009 Joint Health Surveys Unit. National Centre for Social Research, University College London, London.
Dewailly, E., Ayotte, P., Bruneau, S., Lebel, G., Levallois, P., Weber, J.P., 2001. Exposure of the inuit population of nunavik (Arctic Quebec) to lead and mercury. Arch. Environ. Health 56, 350–357.
Dobrowolska, A., Melosik, M., 2008. Bullet-derived lead in tissues of the wild boar (*Sus scrofa*) and red deer (*Cervus elaphus*). Europ. J. Wildl. Res. 54, 231–235.
EC ,2006. COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. Official Journal of the European Union 20.12.2006 L364/5-L364/24.
EFSA CONTAM, 2010. European Food Safety Authority Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Lead in Food. EFSA Journal 2010 (8), 1570.
EPA., 2007. User's Guide for the Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK). Syracuse Research Corporation, North Syracuse, USA.
FSA., 2009. Measurement of the concentrations of metals and other elements from the 2006 UK total diet study. pp. 45. food.gov.uk/multimedia/pdfs/fsis0109metals.pdf.
Gilbert, S.G., Weiss, B., 2006. A rationale for lowering the blood lead action level. from 10 to 2 μg/dL. Neurotoxicol. 27, 693–701.
Glenn, B.S., Stewart, W.F., Links, J.M., Todd, A.C., Schwartz, B.S., 2003. The longitudinal association of lead with blood pressure. Epidemiology 14, 30–36.
Glenn, B.S., Bandeen-Roche, K., Lee, B.K., Weaver, V.M., Todd, A.C., Schwartz, B.S., 2006. Changes in systolic blood pressure associated with lead in blood and bone. Epidemiology 17, 538–544.
Grosse, S.D., Matte, T.D., Schwartz, J., Jackson, R.J., 2002. Economic gains resulting from the reduction in children's exposure to lead in the United States. Environ. Health Perspect 110, 563–569.
Gulson, B.L., Mizon, K.J., Korsch, M.J., Palmer, J.M., Donnelly, J.B., 2003. Mobilization of lead from human bone tissue during pregnancy and lactation–a summary of long-term research. Sci. Tot. Environ. 303, 79–104.
Haldimann, M., Baumgartner, A., Zimmerli, B., 2002. Intake of lead from game meat – a risk to consumers' health? Europ. Food Res. Tech. 215, 375–379.
Hunt, W.G., Burnham, W., Parish, C.N., Burnham, K.K., Mutch, B., Oaks, J.L., 2006. Bullet fragments in deer remains: Implications for lead exposure in avian scavengers. Wildl. Soc. Bull. 34, 167–170.
Hunt, W.G., Watson, R.T., Oaks, J.L., Parish, C.N., Burnham, K.K., Tucker, R.L., Belthoff, J.R., Hart, G., 2009. Lead bullet fragments in venison from rifle-killed deer: potential for human dietary exposure. PLoS ONE 4, e5330.
Institute of Medicine., 2005. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients). National Academies Press, Washington, D.C.
Iqbal, S., Blumenthal, W., Kennedy, C., Yip, F.Y., Pickard, S., Flanders, W.D., Loringer, K., Kruger, K., Caldwell, K.L., Jean brown, M., 2009. Hunting with lead: association between blood lead levels and wild game consumption. Environ. Res. 109, 952–959.
JECFA., 2010. JECFA/73/SC. Joint FAO/WHO expert committee on food additives. Seventy-third meeting. Geneva, 8–17 June 2010. Summary and conclusions. Issued 24 June 2010 pp. 17.
Johansen, P., Asmund, G., Riget, F., 2004. High human exposure to lead through consumption of birds hunted with lead shot. Environ. Pollut. 127, 125–129.
Johansen, P., Pedersen, H.S., Asmund, G., Riget, F., 2006. Lead shot from hunting as a source of lead in human blood. Environ. Pollut. 142, 93–97.
Kaufmann, R.B., Staes, C.J., Matte, T.D., 2003. Deaths related to lead poisoning in the United States, 1979–1998. Environ. Res. 91, 78–84.
Knott, J., Gilbert, J., Hoccom, D.G., Green, R.E., 2010. Implications for wildlife and humans of dietary exposure to lead from fragments of lead rifle bullets in deer shot in the UK. Sci. Tot. Environ. 409, 95–99.
Kosnett, M.J., 2009. Health effects of low dose lead exposure in adults and children, and preventable risk posed by consumption of game meat harvested with lead ammunition. In: R.T. Watson, M. Fuller, M. Pokras and W.G. Hunt (Eds). Ingestion of Lead from Spent Ammunition: Implications for Wildlife and Humans. The Peregrine Fund, Boise, Idaho USA. DOI:10.4080/ilsa.2009.0103. <http://www.peregrinefund.org/lead_conference/2008PbConf_Proceedings.htm.>
Lakind, J.S., 1998. Comparison of three models for predicting blood lead levels in children: episodic exposures to lead. J. Expo. Analy. Environ. Epidem. 8, 399–406.
Landrigan, P.J., 2002. The worldwide problem of lead in petrol. Bull. W.H.O. 80, 10.
Landrigan, P., Nordberg, M., Lucchini, R., Nordberg, G., Grandjean, P., Iregren, A., Lorenzo, A., 2006. The Declaration of Brescia on Prevention of the Neurotoxicity of Metals Brescia, Italia 17–18 June 2006. La Medicina del Lavoro 97, 811–814.
Lanphear, B.P., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D., Canfield, R.L., Dietrich, K.N., Bornschein, R., Greene, T., Rothenberg, S.J., Needleman, H.L., Schnaas, L., Wasserman, G., Graziano, J., Roberts, R., 2005. Low-level lead exposure and children's intellectual function: an international pooled analysis. Environ. Health Perspect. 113, 894–899.
Mateo, R., Baos, A.R., Vidal, D., Camarero, P.R., Martinez-Haro, M., Taggart, M.A., 2011. Bioaccessibility of Pb from ammunition in game meat is affected by cooking treatment. PLoS ONE 6, e15892.
Mintel, 2007. Game and Exotic Meat – UK – February 2007. A report of the Mintel International Group Limited supplied to the British Association for Shooting and Conservation.
Mushak, P., 1998. Uses and limits of empirical data in measuring and modeling human lead exposure. Environ. Health Perspect 106 (Suppl. 6), 1467–1484.
Nash, D., Magder, L., Lustberg, M., Sherwin, R.W., Rubin, R.J., Kaufmann, R.B., Silbergeld, E.K., 2003. Blood lead, blood pressure, and hypertension in perimenopausal and postmenopausal women. JAMA 289, 1523–1532.
Navas-Acien, A., Tellez-Plaza, M., Guallar, E., Muntner, P., Silbergeld, E., Jaar, B., Weaver, V., 2009. Blood cadmium and lead and chronic kidney disease in US adults: a joint analysis. Amer. J. Epidem. 170, 1156–1164.
Oomen, A.G., Tolls, J., Sips, A.J., Groten, J.P., 2003. In vitro intestinal lead uptake and transport in relation to speciation. Arch. Environ. Contam. Toxicol. 44, 116–124.
Pain, D.J., Cromie, R.L., Newth, J., Brown, M.J., Crutcher, E., Hardman, P., Hurst, L., Mateo, R., Meharg, A.A., Moran, A.C., Raab, A., Taggart, M.A., Green, R.E., 2010. Potential hazard to human health from exposure to fragments of lead bullets and shot in the tissues of game animals. PLoS ONE 5, e10315.
Rabinowitz, M.B., Kopple, J.D., Wetherill, G.W., 1980. Effect of food intake on fasting gastrointestinal lead absorption in humans. Am. J. Clin. Nutr. 33, 1784–1788.
Rabinowitz, M.B., 1991. Toxicokinetics of bone lead. Environ. Health. Perspect 91, 33–37.
Rabinowitz, M.B., Wetherill, G.W., Kopple, J.D., 1976. Kinetic analysis of lead metabolism in healthy humans. J. Clin. Invest. 58, 260–270.
Sand, S., Victorin, K., Filipsson, A.F., 2008. The current state of knowledge on the use of the benchmark dose concept in risk assessment. J. Appl. Toxicology 28, 405–421.
SCF, 1994. European Commission's Scientific Committee for Food (SCF) Opinion of 19 June 1992, Thirty second series, 1994, pp. 7, <http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_32.pdf.>
Schwartz, J., 1994. Societal benefits of reducing lead exposure. Environ. Res. 66, 105–124.
SCOOP, 2004. Report on tasks for scientific cooperation (SCOOP). Assessment of the dietary exposure to arsenic, cadmium, lead and mercury of the population of the EU member states. Brussels, Commission of the European Communities, Directorate-General of Health and Consumer Protection, 2004. SCOOP task 3.2.11; <http://ec.europa.eu/food/food/chemicalsafety/contaminants/scoop_3-2-11_heavy_metals_report_en.pdf.>
Selmer, R.M., Kristiansen, I.S., Haglerod, A., Graff-Iversen, S., Larsen, H.K., Meyer, H.E., Bonaa, K.H., Thelle, D.S., 2000. Cost and health consequences of reducing the population intake of salt. J. Epidem. Commun. Health 54, 697–702.
Tsuji, L.J.S., Wainman, B.C., Martin, I.D., Sutherland, C., Weber, J.P., Dumas, P., Nieboer, E., 2008. The identification of lead ammunition as a source of lead exposure in First Nations: the use of lead isotope ratios. Sci. Tot. Environ. 393, 291–298.
Vupputuri, S., He, J., Muntner, P., Bazzano, L.A., Whelton, P.K., Batuman, V., 2003. Blood lead level is associated with elevated blood pressure in blacks. Hypertension 41, 463–468.
WHO, 2007. Exposure of children to chemical hazards in food. European Environment and Health Information System. Fact Sheet No 4.4. Code RPG4_Food_Ex1 <http://www.euro.who.int/Document/EHI/ENHIS_Factsheet_4_4.pdf.>
WHO, 2011. World Health Organisation Food Additives Series: 64. Safety Evaluation of Certain Food Additives and Contaminants. Prepared by the Seventy-third meeting of the joint FAO/WHO Expert Committee on Food Additives (JECFA). World Health Organisation, Geneva.
Zia, M.H., Codling, E.E., Scheckel, K.G., Chaney, R.L., 2011. In vitro and in vivo approaches for the measurement of oral bioavailability of lead (Pb) in contaminated soils; a review. Environ. Pollut. 159, 2320–2327.
Ziegler, E.E., Edwards, B.B., Jensen, R.L., Mahaffey, K.R., Fomon, S.J., 1978. Absorption and retention of lead by infants. Pediatr. Res. 12, 29–34.