

DATA ARTICLE

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A human health risk assessment of lead (Pb) ingestion among adult wine consumers

Kevin M. Towle*, Lindsey C. Garnick and Andrew D. Monnot

Abstract

Background: Recent concerns have been raised regarding heavy metal content in wine and its potential health implications. The goal of this study was to determine if lead (Pb) intake poses a health risk among adult consumers of wine. This was achieved by performing a literature review of studies reporting Pb concentration in United States and international wines, determining adult wine consumption rates in the United States using NHANES dietary survey data, utilizing the U.S. EPA's Adult Lead Methodology (ALM) model to estimate adult blood lead levels (BLLs) from wine consumption under various exposure scenarios, and comparing modeled BLLs to guidance values. Models were stratified by average exposure (mean wine Pb concentration) and high exposure (95th percentile wine Pb concentration) scenarios.

Results: Lead concentration data was abstracted from a total of 31 studies, including wine from 18 countries for a total of 472 wine samples. The mean Pb content of international red and white wines were 33.9 µg/L ($n = 282$) and 35.7 µg/L ($n = 118$), respectively, while the mean Pb content of domestic red wine was 4.4 µg/L ($n = 61$). All modelled BLLs were below the Center for Disease Control (CDC) BLL guidance value of 5 µg/dL. Assuming a mean baseline BLL, an individual was required to drink 10.4 glasses of wine per day (all wine types) under the average exposure scenario and 3.7 glasses of wine per day (all wine types) under the high exposure scenario in order to elevate their BLL to the guidance value of 5 µg/dL. When stratified by region, a minimum of approximately 24 glasses of wine from the United States per day was required to raise adult BLLs to the 5 µg/dL guidance value.

Conclusions: Overall, findings suggest that Pb content in wine does not pose a health risk to adult wine consumers.

Keywords: Lead, Pb, Wine, Risk assessment

Background

The historical use of lead (Pb) in gasoline, paints, pipes, plumbing, and various industrial processes has contributed to the current ubiquitous presence of Pb in various environmental media, including soil, water, and air (ATSDR 2007). Recently, it has been reported that wine samples contain detectable levels of heavy metals, raising concerns of potential contamination issues in food and beverages (Haelle 2015; Wilson 2015). Specifically, a recent study reported that Pb was detected in 58% of United States wine samples, concluding that the risk associated with Pb contamination in some wines may be

significant (Wilson 2015). Due to established Pb toxicity at certain exposure levels, it is important to understand whether Pb contamination in commonly consumed beverages, such as wine, poses a health hazard to humans.

The primary route of exposure to Pb in the general population is ingestion, including contaminated food, water, or alcohol (ATSDR 2012). Specifically, it has been estimated that 70% of Pb intake is due to ingestion of food and drinks, and that wine is the alcoholic beverage with the highest levels of Pb (Pyrzyńska 2004). Lead tissue burdens increase as a result of cumulative exposure, and can result in various health effects at certain exposure levels, including effects on the hematological, nervous, renal, and reproductive systems (Needleman 2004; Patrick 2006). Additionally, Pb competes with calcium in the body,

* Correspondence: kevin.towle@cardno.com
Cardno ChemRisk, 101 2nd St. Suite 700, San Francisco CA 94105, USA

which disrupts neurotransmitter release and bone mineral density (Papanikolaou et al. 2005; Beier et al. 2013).

The presence of Pb in wine is believed to arise from climate, soil composition, industrial emissions, fertilizers, and winery equipment (Moreno et al. 2007; Bora et al. 2015). Previously, researchers have noted that wine is an important source of Pb exposure among individuals that regularly consume wine (Elinder et al. 1988). To address potential health concerns, various regulatory and non-regulatory agencies have reported maximum acceptable limits of Pb in wine. The International Organization of Vine and Wine (OIV), an intergovernmental agency comprised of 45 international member states, has a current maximum acceptable limit of 150 µg/L for Pb in wine (OIV 2015a). Additionally, the Vinters Quality Alliance (VQA) of Ontario suggested a standard of 200 ppb for the permissible limit of Pb in wine (VQA 2016).

Current methods for assessing Pb exposure and potential health risks consist of 1) using toxicokinetic models that predict blood lead levels (BLLs) based on estimates of exposure to Pb in the media of interest, followed by 2) benchmarking of the predicted blood Pb levels vs established guidance values. The toxicokinetics of Pb has been evaluated for decades and has been well characterized (Philip and Gerson 1994; Leggett 1993; O'Flaherty 2000; EPA 2001). Adults absorb approximately 5-15% of ingested Pb, with Pb in water and other beverages absorbed to a greater degree than Pb in food (Klassen 2013). BLL is a biomarker used to measure the body burden and internal dose of Pb, and can be used to determine a dose-response relationship for health effects associated with Pb exposure (Mushak 2003; Monnot et al. 2015). In 2015, the Center of Disease Control (CDC) designated a reference BLL for adults and defined raised BLLs as levels that exceeded the guidance value of 5 µg/dL, which is based on the 97.5th percentile of blood Pb distribution in children (NIOSH 2015).

Although numerous studies have reported Pb concentrations in various wines produced from around the world, there are no published quantitative analyses of potential Pb exposures and health risks associated with wine consumption. The purpose of this study was to assess plausible Pb-related health risks associated with wine consumption under a variety of scenarios, using the most current techniques for quantifying and benchmarking Pb exposures. Specifically, in this analysis, we compiled published data concerning Pb levels in United States and international wines of various varieties and regions, determined adult wine consumption rates in the United States using National Health and Nutrition Examination (NHANES) dietary survey data, utilized a biokinetic model to assess potential adult BLLs associated with various wine consumption exposure scenarios,

and determined whether wine consumption is likely to pose a Pb-related health risk. We also evaluated the daily volume of wine that would need to be consumed to reach BLL benchmark values.

Methods

Approach

In this analysis, the impact of Pb ingestion from wine on adult BLLs was assessed. This was achieved by 1) performing a literature review of studies analyzing the Pb concentration in United States and international wines, 2) determining adult wine consumption rates in the United States using NHANES dietary survey data, 3) utilizing the U.S. EPA's Adult Lead Methodology (ALM) model to estimate adult BLLs from wine consumption under various exposure scenarios, and 4) comparing modeled BLLs to guidance values.

Pb content in wine

A literature review was performed to determine the concentration of Pb in commercially available United States and international wines. To reduce confounding by time from historically higher concentrations of Pb in environmental media, results were restricted to studies that analyzed wine samples within the past ten years. Studies were identified by electronic-database searching of PubMed, using the search terms ("lead" or "Pb") and ("wine"). Findings were supplemented with references manually obtained from the search results. The latest search was conducted in November of 2016.

Data were collected for each article, including the country of origin, wine vintage, grape variety, Pb concentration, number of samples, and analytical technique used. When results from different analytical techniques were reported within the same study, preference was given to digested ICP-MS results. When reported Pb concentrations were below the limit of detection (LOD), a value of one-half the LOD was utilized for data analysis. Studies that did not report a LOD in the methodology were excluded from the analyses. Study-specific information was abstracted and assessed for quality control by independent reviewers. A weighted average of the sample means and 95th percentile of reported Pb concentrations were calculated for all data combined, as well as by wine type (red wine and white wine) and geographic location (country of origin).

Wine consumption data

Wine consumption data was extracted from the day one and day two results from the NHANES dietary food interviews. To match the time period of wine Pb concentration analyses, dietary consumption information was restricted to the 2005–2014 NHANES datasets. Wine consumption rates were limited to adult wine consumers, with a

minimum age of 21. Consumption data was calculated for all wine, red wine, and white wine, according to the USDA food codes. Due to the presence of right-skewed consumption data, wine-specific median consumption rates were used as the inputs for the BLL models. All statistical analyses were performed using R software, version 3.1.1.

BLL modelling

The EPA ALM model was selected to estimate adult BLLs in this analysis, as the EPA recommended this model for assessments of non-residential Pb exposures that result in BLLs <25 µg/L, based on the review of multiple biokinetic Pb models for adults (including the O'Flaherty and Leggett models) (EPA 2001). Stratified BLL models were completed by wine type (all wine, red wine, and white wine) and geographic location (United States wines and international wines). Each model was further stratified by different exposure scenarios: average exposure (mean wine Pb concentration) and high exposure (95th percentile wine Pb concentration). A baseline adult BLL of 1.27 µg/dL was used, which was the calculated weighted geometric mean of BLLs in adults aged 20 years or older during the 2005 to 2012 NHANES survey years (CDC 2015). Gastrointestinal absorption of Pb was conservatively assumed to be 20%

in adults (ATSDR 2007; Monnot et al. 2015). We assumed that individuals ingested wine at the median NHANES consumption rate each day, for a total of 365 days per year. The change in BLL from baseline was calculated for each exposure scenario to determine the relative contribution of wine consumption on increased BLLs.

Comparison to guidance values

The BLL guidance value of 5 µg/dL from the Center for Disease Control (CDC) was utilized as the benchmark in this analysis. The amount of ingested wine (g/day and glasses/day) necessary to elevate adult BLLs to guidance values was determined, assuming mean and 95th percentile all wine Pb concentrations for the average and high exposure scenario models, respectively. For these calculations, one glass of wine was assumed to contain 5 oz. BLLs associated with agency-specific maximum acceptable limits of Pb in wine were determined assuming a mean baseline BLL and median NHANES wine consumption rate for all wine types. Additionally, the maximum Pb concentration required to increase adult BLLs to guidance values was calculated using median NHANES all wine consumption data.

Table 1 Wine Pb concentration by country

Country	N (%)	Mean Pb (µg/L)	References
Argentina	20 (4%)	72.5	(Lara et al. 2005)
Australia	28 (6%)	5.0	(Hague et al. 2008; Kristensen et al. 2016)
Brazil	13 (3%)	75.4	(Dessuy et al. 2008; Dessuy et al. 2011; Schiavo et al. 2008)
Bulgaria	2 (<1%)	21.0	(Karadjova et al. 2007)
Chile	6 (1%)	42.4	(Dessuy et al. 2008; Schiavo et al. 2008)
China	3 (1%)	22.4	(Wu et al. 2007)
Croatia	8 (2%)	32.6	(Tariba et al. 2011)
France	1 (<1%)	8.0	(Ajtony et al. 2008)
Germany	2 (<1%)	20.4	(Ajtony et al. 2008)
Hungary	35 (7%)	35.0	(Ajtony et al. 2008)
Italy	68 (14%)	47.2	(Elçi et al. 2009; Illuminati et al. 2014; Karadjova et al. 2007; La Pera et al. 2008)
Macedonia	2 (<1%)	22.3	(Karadjova et al. 2007)
Portugal	43 (9%)	51.6	(Catarino et al. 2006; Catarino et al. 2007; da Costa et al. 2014; Santos et al. 2013; Yamasaki et al. 2012)
Romania	63 (13%)	40.5	(Bora et al. 2015; Geana et al. 2013)
Spain	86 (18%)	15.7	(Ajtony et al. 2008; Dessuy et al. 2008; Gonzalez et al. 2008; Grindlay et al. 2009; Grindlay et al. 2008; Iglesias et al. 2007; Moreno et al. 2007)
Turkey	23 (5%)	0.1	(Aydin et al. 2010; Yildiz et al. 2011)
Ukraine	8 (2%)	0.5	(Vystavna et al. 2014)
United States	61 (13%)	4.4	(Elçi et al. 2009; Wilson 2015)
Total	472 (100%)	30.4	

Results

Pb content in wine

Lead concentration data was abstracted from a total of 31 studies, including wine from 18 countries for a total of 472 wine samples (Table 1). There was geographic variance in the Pb concentrations, with highest mean wine Pb concentrations among wine samples from Brazil (75.4 µg/L), Argentina (72.5 µg/L), and Portugal (51.6 µg/L), and lowest among wine samples from Turkey (0.1 µg/L), Ukraine (0.5 µg/L), and the United States (4.4 µg/L). The mean Pb concentration among all wine samples was 30.4 µg/L. It should be noted that a probabilistic exposure model paired with the distribution of samples by country of origin resulted in a Pb concentration of 29.6 µg/L for all wine samples. The more conservative mean value was used in the following analyses. White wine samples (35.7 µg/L) had a higher Pb concentration than red wine samples (28.7 µg/L). When stratified by origin of wine, Pb concentrations in United States wines were lower than international wines: 4.4 µg/L and 34.3 µg/L, respectively. Table 2 includes wine Pb concentrations by wine type and geographic location.

Wine consumption data

According to wine consumption data from the 2005–2014 NHANES dietary data survey (Table 3), adult (age 21+) wine drinkers consumed a median 195 g/day of wine per day. This equated to approximately 6.59 fluid ounces of wine, or approximately one-and-a-half glasses of wine per day. Consumption data was further analyzed by wine type, with adults having a higher consumption of white wine (205.8 g/day) than red wine (180 g/day).

BLL modelling

Table 4 reports the modelled adult BLLs associated with various wine consumption exposure scenarios. All estimated BLLs were below the CDC guidance value. When stratified by wine type, consumption of white wine was associated with larger increases in BLLs than red wine. Consumption of United States red wine was associated with the smallest change in BLL from baseline for both the average and high exposure scenarios (+0.06 µg/dL

and +0.19 µg/dL, respectively), while consumption of international white wine was associated with the largest change in BLL (+0.59 µg/dL for the average exposure model and +2.15 µg/dL for the high exposure model).

Comparison to guidance values

The required number of glasses of wine per day necessary to raise an adult's BLL to the CDC guidance value is reported in Table 5. Assuming a mean baseline BLL, an individual was required to drink 10.4 glasses of wine per day (all wine types) under the average exposure scenario and 3.7 glasses of wine per day (all wine types) under the high exposure scenario in order to elevate their BLL to the guidance value of 5 µg/dL. Consumption of 2.4 glasses of white wine per day under the high exposure model was associated with a BLL of 5 µg/dL. When stratified by region, a minimum of approximately 24 glasses of wine from the United States was required to raise adult BLLs to the 5 µg/dL guidance value.

Table 6 reports various agency maximum acceptable limits of wine Pb concentrations and associated BLLs. The OIV limit of 150 µg/L was associated with a BLL of 3.61 (+2.34) µg/dL while the VQA limit of 200 µg/L was associated with a BLL of 4.39 (+3.12) µg/dL. Assuming a mean baseline BLL and median NHANES wine consumption rate for all wine types, a wine Pb concentration of 239 µg/L was required to elevate adult BLLs to the guidance value of 5 µg/dL (Table 7).

Discussion

Concerns have been raised regarding the heavy metal content of wine and its potential health implications. Recently, studies have reported heavy metal concentrations, including Pb, in various wine samples from around the world (Kristensen et al. 2016; Monnot et al. 2016; Wilson 2015). The presence of Pb in wine can arise from environmental sources (region, climate, and soil composition) and anthropogenic sources (metal-based pesticides, fertilizers, chemical sprays, industrial emissions, and winery equipment) (Bora et al. 2015). Since pollutants are able to disperse via air, surface water, and groundwater, heavy metal contamination has become a growing problem in viticultural regions (Bora et al. 2015).

Pb content by wine type

Reported wine Pb concentrations varied by wine type (Table 2). During the wine making process, red wine is fermented with the grape skins, while white wine is pressed to remove the grape skins prior to fermentation, a process that may impact heavy metal content in wine (Almeida and Vasconcelos 2003). Once stratified by wine type, white wine had a higher concentration of Pb than red wine. It has been suggested that yeast present in

Table 2 Wine Pb concentration data used to model adult BLL

Wine Origin	Wine Type	n	Mean Pb (µg/L)	95th Percentile Pb (µg/L)
All wine	All Wine	472	30.4	85
	Red Wine	343	28.7	84.9
	White Wine	118	35.7	130.6
International wine	All Wine	411	34.3	100.9
	Red Wine	282	33.9	97.9
	White Wine	118	35.7	130.6
United States wine	Red Wine	61	4.4	13.1

Table 3 NHANES wine consumption data

Dataset	Consumption (g/day) ^a														
	All Wine					Red Wine					White Wine				
	n	Min	Median	Mean	Max	n	Min	Median	Mean	Max	n	Min	Median	Mean	Max
2005–2006	514	1.23	191.1	228.8	1440	254	1.23	188.5	218.6	1102	210	2.45	205.8	230.7	1029
2007–2008	596	9.8	176.4	224.5	1521	314	9.8	176.4	203.2	1029	221	14.7	205.8	226.4	852.6
2009–2010	734	1.23	176.4	230.3	1522	352	2.45	161.7	214.9	1352	304	4.9	176.4	237	1491
2011–2012	624	0.82	205.8	245.2	2117	357	0.82	205.8	233.6	994.2	226	4.9	205.8	246.3	2117
2013–2014	650	1.25	202.5	240.5	2028	348	1.25	180	219.9	1050	231	5	210	228.5	1050
2005–2014	3118	0.82	195	234.1	2117	1625	0.82	180	218.4	1352	1192	2.45	205.8	234	2117

^a Among adult wine consumers aged 21–85

grape skins binds heavy metals and may remove these elements from the aqueous solution (Aguilar et al. 1987). This may explain the observed reduction of Pb content in red wine, due to its extended length of contact with grape skins during the fermentation process. Alternative explanations could include differences in accumulation of metals by grape varieties, as well as variances in geographic regions and soil compositions for red and white grapes; however, this is an area of research that requires further investigation (Greenough et al. 1997; Yang et al. 2010; Bertoldi et al. 2011).

Reported wine Pb concentrations also varied by country of origin (Table 1). A variety of factors might explain this regional variability, including differences in climate, grape varieties, soil type, historical and current Pb emissions into the environment, and wine-making processes. The observed variance could be influenced by sample size, as some countries had a limited number of wine samples and analyses performed. In the present analysis, red wine samples from the United States consistently had lower Pb concentrations than red wines from top producing European countries, including France, Italy, and Spain (Elçi et al. 2009; OIV 2015b; Wilson 2015). It should be noted that while 61 wine samples were analyzed from the United States, all samples were from red wine varieties (Wilson 2015; Elçi et al. 2009). Once stratified by region, mean Pb concentrations were

comparable between international red and white wine samples (difference of ~2 µg/L). Given this finding, one would expect the mean United States white wine Pb concentrations to not be materially different from mean United States red wine Pb concentrations.

Risk associated with Pb in wine

While numerous studies have assessed the heavy metal content of wine, quantitative risk analyses have not been performed to assess the potential health effects from Pb exposure due to wine consumption. To date, our study is the only analysis to model BLLs resulting from wine consumption among adults. BLL modeling is a metric used to characterize human health risks, and has previously been employed to evaluate the risk of Pb exposure from juice and consumer products (Tvermoes et al. 2014; Monnot et al. 2015).

All modelled adult BLLs under various wine consumption exposure scenarios were below the CDC guidance value. This includes an exposure scenario in which it was assumed that an individual consumed approximately one-and-a-half glasses of wine containing the maximum 95th percentile of Pb (130.6 µg/L) every day. These results suggest that wine consumption is unlikely to be associated with a Pb-related health risk. White wine consumption was associated with a higher BLL than red wine consumption, due to both a higher concentration

Table 4 Modelled adult BLL by exposure scenario

Wine Origin	Wine Type	Average Exposure Scenario ^a		High Exposure Scenario ^b	
		Geometric mean BLL (µg/dL)	ΔBLL from baseline	Geometric mean BLL (µg/dL)	ΔBLL from baseline
All wine	All Wine	1.74	+0.47	2.60	+1.33
	Red Wine	1.68	+0.41	2.49	+1.22
	White Wine	1.86	+0.59	3.42	+2.15
International wine	All Wine	1.81	+0.54	2.84	+1.57
	Red Wine	1.76	+0.49	2.68	+1.41
	White Wine	1.86	+0.59	3.42	+2.15
United States wine	Red Wine	1.33	+0.06	1.46	+0.19

^a Mean wine-specific Pb concentration, median wine-specific consumption data, and baseline BLL of 1.27 µg/dL

^b 95th percentile wine-specific Pb concentration, median wine-specific consumption data, and baseline BLL of 1.27 µg/dL

Table 5 Wine consumption required to elevate adult BLLs to guidance values

Guidance Value Agency	Geometric Mean BLL ($\mu\text{g}/\text{dL}$)	Wine Type	Average Exposure Scenario ^a		High Exposure Scenario ^b	
			g/day	glasses/day ^c	g/day	glasses/day ^c
CDC	5.0	All Wine	1532	10.4	548	3.7
		Red Wine	1623	11.0	549	3.7
		White Wine	1301	8.8	357	2.4
		United States Wine	10488	70.9	3558	24.1

^a Assuming mean wine-specific Pb concentration and baseline BLL of 1.27 $\mu\text{g}/\text{dL}$

^b Assuming 95th percentile wine-specific Pb concentration and baseline BLL of 1.27 $\mu\text{g}/\text{dL}$

^c Assuming 5 oz per glass of wine

of Pb in white wine, as well as a higher median consumption of white wine among wine consumers. Under the average exposure scenario (consumption of approximately one-and-a-half glasses of wine per day at the mean Pb concentration), consumption of all wine types was associated with a maximum BLL increase of 0.59 $\mu\text{g}/\text{dL}$, which is below the mean adult baseline BLL of 1.27 $\mu\text{g}/\text{dL}$. Similarly, under the high exposure scenario (consumption of approximately one-and-a-half glasses of wine per day at the 95th percentile Pb concentration), consumption of United States red wine was associated with a maximum BLL increase of 0.19 $\mu\text{g}/\text{dL}$. These findings suggest that background Pb exposure (mainly from dietary sources) is the main contributor to adult BLL in the typical wine consumer. In contrast, consumption of all wine types under the high exposure scenario increased the modelled BLL by 2.15 $\mu\text{g}/\text{dL}$, which exceeded background BLL (Table 4). This finding agrees with previous research which suggests that wine consumption could be an important source of Pb exposure among certain wine consumers (Elinder et al. 1988; Birgisdottir et al. 2013; Tagne-Fotso et al. 2016).

Potential increased risk is driven by both wine type and consumption rate. Specifically, under the average exposure scenario, an adult would have to drink approximately 11 glasses of red wine or 8.8 glasses of white wine per day in order to increase their BLLs to the CDC guidance value of 5 $\mu\text{g}/\text{dL}$ (Table 5). In contrast, under the high exposure scenario, an adult would have to drink approximately 3.7 glasses of red wine or 2.4 glasses of white wine per day in order to increase their BLLs to the same extent. However, this analysis also suggests that it is unlikely that an individual could reach the CDC BLL guidance value as a

result of consumption of wines from the United States. Specifically, an adult consuming red wine from the United States would have to drink approximately 71 or 24 glasses of wine per day under the average and high exposure scenarios, respectively.

Out of the 472 wine samples, 13 samples resulted in reported Pb concentration averages that were in excess of the OIV 150 $\mu\text{g}/\text{L}$ maximum acceptable limit for Pb in wine, ten of which were Italian wines and three of which were Brazilian wines. None of the samples were above the Canada VQA standards of 200 $\mu\text{g}/\text{L}$. Modelled BLLs based on these guidance values (assuming median wine consumption rate) did not exceed 5 $\mu\text{g}/\text{dL}$, suggesting that these current limits are protective of health under the examined average exposure scenario (Table 6). At the median consumption rate, a BLL of 5 $\mu\text{g}/\text{dL}$ would only be achieved if the wine contained 239 $\mu\text{g}/\text{L}$. All of the United States red wine samples were far below this value, again suggesting that United States wines do not pose a Pb-related health risk.

While some wines were reported to contain Pb concentrations above the current EPA drinking water standard for Pb (15 $\mu\text{g}/\text{L}$), it is critical to note that the EPA's drinking water consumption rate is considerably higher than the typical daily intake rate of wine. The recommended maximum intake for wine is one to two 5-oz glasses per day, whereas the recommended daily intake for water is 2.7 to 3.7 L (91 to 125 oz) per day, and the EPA estimated consumption rate for adults is 2.4 L (81 oz) per day (ACE 2008; DHHS 2005; EPA 2011, 2015). Furthermore, the maximum contaminant level (MCL) takes into account "analytical methodology, treatment technology and costs, economic impact, and regulatory impact" (EPA 1992). Taken together, wine exceeding the MCL for Pb on a sporadic basis does not

Table 6 Maximum acceptable limits of Pb in wine and associated modelled BLLs

Agency	Wine Maximum Acceptable Limit ($\mu\text{g}/\text{L}$)	Reference	BLL ^a ($\mu\text{g}/\text{dL}$) [A _{baseline}]
OIV	150	OIV 2015	3.61 [+2.34]
Canada VQA	200	VQA 2016	4.39 [+3.12]

^a Estimated using ALM model, assuming median NHANES consumption rate for all wine types and baseline BLL of 1.27 $\mu\text{g}/\text{dL}$

Table 7 Wine Pb concentration required to elevate adult BLLs to guidance values

Guidance Value Agency	Geometric Mean BLL ($\mu\text{g}/\text{dL}$)	Wine Pb Concentration (ppm) ^a
CDC	5.0	0.239

^a Assuming median NHANES wine consumption rate for all wine types and baseline BLL of 1.27 $\mu\text{g}/\text{dL}$

necessarily indicate an increased health risk due to Pb exposure.

Strengths and limitations

Modeling Pb exposure scenarios is inherently limited by the complexity of Pb toxicity, including inter-individual variances. Factors that influence the toxicokinetics of ingested Pb include age, genetics, fasting state, and nutritional status (McCabe 1979; Mahaffey 1990; Onalaja and Claudio 2000). To address this, we chose the ALM model, which uses a general, population-based consideration of these toxicokinetic parameters. The model was further limited by the robustness of underlying wine Pb concentration data. By matching the time period of analysis and consumption data, we excluded prior analyses that may have included increased sample sizes for countries with high production of wine (i.e., white wine samples from the United States). However, the restriction of this historical data improved the model by limiting the wine to samples that were able to be consumed during the dietary survey time period, as well as removing potential confounding from historically increased environmental levels of Pb.

The NHANES dataset is a large sample size national health survey with high standards for data collection. However, since dietary data is self-reported, there is potential for exposure misclassification that may misestimate wine consumption among adult users. Additionally, since the NHANES data pertains to United States wine consumers, it should be noted that the mean Pb content for all wine samples may overestimate BLLs among consumers that are more likely to drink wine produced in the United States. Another limitation of the ALM model is that it does not allow for the estimation of BLLs after acute exposures to Pb. Renal effects among workers have been observed at acute high-dose exposures (i.e., BLL in excess of 60 µg/dL). However, an individual would experience symptoms from acute alcohol poisoning prior to consuming the required number of glasses of wine to elevate their BLL to this acute exposure threshold.

Areas for future research

Future quantitative risk analyses would benefit from additional studies and more robust wine-specific information on Pb content related to geographic origin, vintage, and grape varietal (e.g., white wine in the United States). Subsequent studies should also evaluate the potential health risks from multiple metals in wine, as previous analyses have focused on individual metals such as arsenic (Monnot et al. 2016). Previous studies have noted that the metal content (specifically arsenic) is correlated with the price of the wine, with more expensive wines having a lower arsenic concentration than less-expensive wines (Paustenbach et al. 2016). It would be

useful to evaluate if this observation holds true for other metals as well. Additional studies evaluating BLLs in populations of wine drinkers relative to non-wine drinkers may also be insightful in determining the accuracy of our findings, as well as the best way to model Pb exposures.

Conclusions

This analysis used a biokinetic model to perform a risk assessment of Pb exposure from wine consumption among adults. Overall, findings suggest that Pb content in United States and international wine does not pose a health risk to adult wine consumers under both average and high exposure scenarios. Consumption of United States wines was associated with maximum BLL increases that were below background adult BLLs. This evaluation also demonstrates that the safety of beverages should be assessed not only by determining the presence and amounts of hazardous contents, but also by examining the hazard in context of relevant background exposures and through comparison to guidance values.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All of the authors of this work participated in the concept and design of the study, as well as data analysis, interpretation, and manuscript generation. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Received: 20 February 2017 Accepted: 5 April 2017

Published online: 18 April 2017

References

- ACE. Fit facts: healthy hydration. In: American Council on Exercise. 2008.
- Aguilar MV, Martinez MC, Masoud TA. Arsenic content in some Spanish wines. Influence of the wine-making technique on arsenic content in musts and wines. *Z Lebensm Unters Forsch*. 1987;185:185–7.
- Ajtóny Z, Szoboszlay N, Suskó EK, Mezei P, György K, Bencs L. Direct sample introduction of wines in graphite furnace atomic absorption spectrometry for the simultaneous determination of arsenic, cadmium, copper and lead content. *Talanta*. 2008;76:627–34.
- Almeida CMR, Vasconcelos MTS. Multielement composition of wines and their precursors including provenance soil and their potentialities as fingerprints of wine origin. *J Agric Food Chem*. 2003;51:4788–98.
- ATSDR. Toxicological profile for lead. In: U.S. Department of Health and Human Services: agency for toxic substances and disease registry. 2007.
- ATSDR. Agency for toxic substances and disease registry case studies in environmental medicine (CSEM) lead toxicity. 2012.
- Aydin I, Yuksel U, Guzel R, Ziyadanogullari B, Aydin F. Determination of trace elements in Turkish wines by ICP-OES and HG-ICP-OES. *At Spectrosc*. 2010;31:67.
- Beier EE, Maher JR, Sheu T-J, Cory-Slechta DA, Berger AJ, Zuscik MJ, Puzas JE. Heavy metal lead exposure, osteoporotic-like phenotype in an animal model, and depression of Wnt signaling. *Environ Health Perspect (Online)*. 2013; 121:97.

- Bertoldi D, Larcher R, Bertamini M, Otto S, Concheri G, Nicolini G. Accumulation and distribution pattern of macro-and microelements and trace elements in *Vitis vinifera* L. cv. Chardonnay berries. *J Agric Food Chem*. 2011;59:7224–36.
- Birgisdottir B, Knutsen H, Haugen M, Gjelstad I, Jenssen M, Ellingsen D, Thomassen Y, Alexander J, Meltzer H, Brantsæter A. Essential and toxic element concentrations in blood and urine and their associations with diet: results from a Norwegian population study including high-consumers of seafood and game. *Sci Total Environ*. 2013;463:836–44.
- Bora F-D, Bunea C-I, Rusu T, Pop N. Vertical distribution and analysis of micro-, macroelements and heavy metals in the system soil-grapevine-wine in vineyard from North-West Romania. *Chem Cent J*. 2015;9:1.
- Catarino S, Curvelo-Garcia A, de Sousa RB. Measurements of contaminant elements of wines by inductively coupled plasma-mass spectrometry: a comparison of two calibration approaches. *Talanta*. 2006;70:1073–80.
- Catarino S, Madeira M, Monteiro F, Rocha F, Curvelo-Garcia A, De Sousa RB. Effect of bentonite characteristics on the elemental composition of wine. *J Agric Food Chem*. 2007;56:158–65.
- CDC. Fourth national report on human exposure to environmental chemicals, updated tables. In: National Center for Environmental Health Division of Laboratory Sciences. 2015.
- da Costa AS, Delgado I, Rudnitskaya A. Detection of copper, lead, cadmium and iron in wine using electronic tongue sensor system. *Talanta*. 2014;129:63–71.
- Dessuy MB, Vale MGR, Souza AS, Ferreira SL, Welz B, Katskov DA. Method development for the determination of lead in wine using electrothermal atomic absorption spectrometry comparing platform and filter furnace atomizers and different chemical modifiers. *Talanta*. 2008;74:1321–9.
- Dessuy MB, Vale MGR, Welz B, Borges AR, Silva MM, Martelli PB. Determination of cadmium and lead in beverages after leaching from pewter cups using graphite furnace atomic absorption spectrometry. *Talanta*. 2011;85:681–6.
- DHHS. Dietary guidelines for Americans 2005. In: U.S. Department of Health and Human Services - U.S. Department of Agriculture. 2005. www.healthier.us.gov/dietaryguidelines.
- Elçi L, Arslan Z, Tyson JF. Determination of lead in wine and rum samples by flow injection-hydrate generation-atomic absorption spectrometry. *J Hazard Mater*. 2009;162:880–5.
- Elinder C, Lind B, Nilsson B, Oskarsson A. Wine—an important source of lead exposure. *Food Addit Contam*. 1988;5:641–4.
- EPA. Guidelines for exposure assessment: EPA/600/Z-92/001. In: Federal Register 57 (104). 1992.
- EPA. Review of adult lead models evaluation of models for assessing human health risks associated with lead exposures at non-residential areas of superfund and other hazardous waste sites. In: U.S. environmental protection agency: office of solid waste and emergency response. 2001.
- EPA. Exposure factors handbook: 2011 edition. In: EPA/600/R-090/052F U.S. environmental protection agency: office of research and development. 2011.
- EPA. EPA response to scientific views from the public on draft updated national recommended water quality criteria for the protection of human health. Docket ID No. EPA-HQ-OW-2014-0135. In: EPA 822-R-15-001 Office of Water and Office of Science and Technology. 2015.
- Geana I, Iordache A, Ionete R, Marinescu A, Ranca A, Culea M. Geographical origin identification of Romanian wines by ICP-MS elemental analysis. *Food Chem*. 2013;138:1125–34.
- Gonzalez A, Armenta S, Pastor A, De La Guardia M. Searching the most appropriate sample pretreatment for the elemental analysis of wines by inductively coupled plasma-based techniques. *J Agric Food Chem*. 2008;56:4943–54.
- Greenough J, Longrich H, Jackson S. Element fingerprinting of Okanagan Valley wines using ICP-MS: relationships between wine composition, vineyard and wine colour. *Aust J Grape Wine Res*. 1997;3:75–83.
- Grindlay G, Mora J, Maestre S, Gras L. Application of a microwave-based desolvation system for multi-elemental analysis of wine by inductively coupled plasma based techniques. *Anal Chim Acta*. 2008;629:24–37.
- Grindlay G, Mora J, Gras L, de Loos-Vollebregt MT. Ultratrace determination of Pb, Se and As in wine samples by electrothermal vaporization inductively coupled plasma mass spectrometry. *Anal Chim Acta*. 2009;652:154–60.
- Haelle T. Arsenic and California wine: do you need to worry? *Forbes*; 2015. <https://www.forbes.com/sites/tarahaelle/2015/03/23/arsenic-and-california-wine-do-you-need-to-worry/#44d079107f3e>.
- Hague T, Petroczi A, Andrews PL, Barker J, Naughton DP. Determination of metal ion content of beverages and estimation of target hazard quotients: a comparative study. *Chem Cent J*. 2008;2:1–9.
- Iglesias M, Besalú E, Anticó E. Internal standardization-atomic spectrometry and geographical pattern recognition techniques for the multielement analysis and classification of Catalonian red wines. *J Agric Food Chem*. 2007;55:219–25.
- Illuminati S, Annibaldi A, Truzzi C, Scarponi G. Recent temporal variations of trace metal content in an Italian white wine. *Food Chem*. 2014;159:493–7.
- Karadjova IB, Lampugnani L, D'Ulivo A, Onor M, Tsalev D. Determination of lead in wine by hydride generation atomic fluorescence spectrometry in the presence of hexacyanoferrate (III). *Anal Bioanal Chem*. 2007;388:801–7.
- Klassen C. Casarett & Doull's Toxicology: the basic science of poisons, eighth edition. New York: McGraw-Hill Education; 2013.
- Kristensen LJ, Taylor MP, Evans AJ. Tracing changes in atmospheric sources of lead contamination using lead isotopic compositions in Australian red wine. *Chemosphere*. 2016;154:40–7.
- La Pera L, Dugo G, Rando R, Di Bella G, Maisano R, Salvo F. Statistical study of the influence of fungicide treatments (mancozeb, zoxamide and copper oxychloride) on heavy metal concentrations in Sicilian red wine. *Food Addit Contam*. 2008;25:302–13.
- Lara R, Cerutti S, Salonia J, Olsina R, Martinez L. Trace element determination of Argentine wines using ETAAS and USN-ICP-OES. *Food Chem Toxicol*. 2005;43:293–7.
- Leggett RW. An age-specific kinetic model of lead metabolism in humans. *Environ Health Perspect*. 1993;101:598.
- Mahaffey KR. Environmental lead toxicity: nutrition as a component of intervention. *Environ Health Perspect*. 1990;89:75.
- McCabe EB. Age and sensitivity to lead toxicity: a review. *Environ Health Perspect*. 1979;29:29.
- Monnot AD, Christian WV, Abramson MM, Follansbee MH. An exposure and health risk assessment of lead (Pb) in lipstick. *Food Chem Toxicol*. 2015;80:253–60.
- Monnot AD, Tvermoes BE, Gerads R, Gürleyük H, Paustenbach D. Risks associated with arsenic exposure resulting from the consumption of California wines sold in the United States. *Food Chem*. 2016;211:107–13.
- Moreno IM, González-Weller D, Gutierrez V, Marino M, Cameán AM, González AG, Hardisson A. Differentiation of two Canary DO red wines according to their metal content from inductively coupled plasma optical emission spectrometry and graphite furnace atomic absorption spectrometry by using probabilistic neural networks. *Talanta*. 2007;72:263–8.
- Mushak P. Lead remediation and changes in human lead exposure: some physiological and biokinetic dimensions. *Sci Total Environ*. 2003;303:35–50.
- Needleman H. Lead poisoning. *Annu Rev Med*. 2004;55:209–22.
- NIOSH. Adult blood lead epidemiology and surveillance (ABLES). Center for Disease Control and Prevention; 2015. <https://www.cdc.gov/niosh/topics/ables/description.html>.
- O'Flaherty EJ. Modeling normal aging bone loss, with consideration of bone loss in osteoporosis. *Toxicol Sci*. 2000;55:171–88.
- OIV. Annex: maximum acceptable limits. In: International code of oenological practices: OIV code sheet - issue 2015/01. 2015a.
- OIV. Global economic vitiviniculture data: press release. 2015b.
- Onalaja AO, Claudio L. Genetic susceptibility to lead poisoning. *Environ Health Perspect*. 2000;108:23.
- Papanikolaou NC, Hatzidaki EG, Belivanis S, Tzanakakis GN, Tsatsakis AM. Lead toxicity update. A brief review. *Med Sci Monit*. 2005;11:RA329–36.
- Patrick L. Lead toxicity, a review of the literature. part I: exposure, evaluation, and treatment. *Altern Med Rev*. 2006;11:2–23.
- Paustenbach DJ, Insley AL, Maskrey JR, Bare JL, Unice KM, Conrad VB, Iordanidis L, Reynolds DW, DiNatale KS, Monnot AD. Analysis of total arsenic content in California wines and comparison to various health risk criteria. *Am J Enol Vitic*. 2016;2015:15041.
- Permissible limits for chemical analysis: VQA Ontario - regulations - standards. 2016. Available from <http://www.vqaontario.ca/Regulations/Standards>. Accessed 4 Oct 2016.
- Philip AT, Gerson B. Lead poisoning—part I. Incidence, etiology, and toxicokinetics. *Clin Lab Med*. 1994;14:423–44.
- Pyrzyńska K. Analytical methods for the determination of trace metals in wine. *Crit Rev Anal Chem*. 2004;34:69–83.
- Santos S, Lapa N, Alves A, Morais J, Mendes B. Analytical methods and validation for determining trace elements in red wines. *J Environ Sci Health B*. 2013;48:364–75.
- Schiavo D, Neira JY, Nóbrega JA. Direct determination of Cd, Cu and Pb in wines and grape juices by thermospray flame furnace atomic absorption spectrometry. *Talanta*. 2008;76:1113–8.

- Tagne-Fotso R, Leroyer A, Howsam M, Dehon B, Richeval C, Nisse C. Current sources of lead exposure and their relative contributions to the blood lead levels in the general adult population of Northern France: the IMEPOGE study, 2008–2010. *J Toxic Environ Health A*. 2016;79:245–65.
- Tariba B, Pizent A, Kljaković-Gašpić Z. Determination of lead in Croatian wines by graphite furnace atomic absorption spectrometry. *Arch Ind Hyg Toxicol*. 2011;62:25–31.
- Tvermoes BE, Banducci AM, Devlin KD, Kerger BD, Abramson MM, Bebenek IG, Monnot AD. Screening level health risk assessment of selected metals in apple juice sold in the United States. *Food Chem Toxicol*. 2014;71:42–50.
- Vystavna Y, Rushenko L, Diadin D, Klymenko O, Klymenko M. Trace metals in wine and vineyard environment in southern Ukraine. *Food Chem*. 2014;146:339–44.
- Wilson D. Arsenic content in American wine. *J Environ Health*. 2015;78:16.
- Wu H, Jin Y, Luo M, Bi S. A simple and sensitive flow-injection on-line preconcentration coupled with hydride generation atomic fluorescence spectrometry for the determination of ultra-trace lead in water, wine, and rice. *Anal Sci*. 2007;23:1109–12.
- Yamasaki A, Oliveira JA, Duarte AC, Gomes MTS. An insight into the adsorption and electrochemical processes occurring during the analysis of copper and lead in wines, using an electrochemical quartz crystal nanobalance. *Talanta*. 2012;98:14–8.
- Yang Y, Duan C, Du H, Tian J, Pan Q. Trace element and rare earth element profiles in berry tissues of three grape cultivars. *Am J Enol Vitic*. 2010;61:401–7.
- Yıldız O, Citak D, Tuzen M, Soylak M. Determination of copper, lead and iron in water and food samples after column solid phase extraction using 1-phenylthiosemicarbazide on Dowex Optipore L-493 resin. *Food Chem Toxicol*. 2011;49:458–63.

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