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Evaluation of calcium-fortified municipal water as a public health intervention to mitigate lead burdens

Mozhgon Rajaee [a,*], Ernest Dubovitskiy[b] and Victoria C. Brown[a]

[a] Department of Public and Environmental Wellness, School of Health Sciences, Oakland University, 433 Meadow Brook Rd, Rochester, MI 48309, USA
[b] Department of Interdisciplinary Health Sciences, School of Health Sciences, Oakland University, 433 Meadow Brook Rd, Rochester, MI 48309, USA
*Corresponding author. E-mail: rajaee@oakland.edu

MR, 0000-0002-1368-8225

ABSTRACT

Lead has adverse effects on health, society, and the economy. Lead exposure results in increased blood lead levels and storage in bones. Calcium and lead are competitively absorbed and as such calcium can be used to mitigate the body lead burden. Twenty-eight quantitative research studies were reviewed that examined lead exposure (in blood, bone, or breastmilk) and calcium intake or serum calcium to evaluate the efficacy and safety of fortifying potable water supplies with calcium to mitigate lead absorption or resorption. Eighteen of the studies reported a significant inverse relationship between biomarker lead levels and calcium intake or serum calcium. The relationship was most evident with high calcium intake, suggesting a dose-dependent relationship. An intervention with calcium-fortified water could offer an accessible source of supplemental calcium to help meet the recommended dietary allowance (RDA) and mitigate lead absorption. A concentration of 60 mg-Ca/L can supply 22.0 and 16.3% of a 1,000 mg-Ca RDA for men and women, respectively, at the recommended daily water intake.

Key words: calcium, fortified water, intervention, lead, RDA

HIGHLIGHTS

- Population-level interventions such as calcium water fortification aid in meeting the Recommended Dietary Allowance (RDA) of calcium.
- Adequate calcium intake reduces blood and bone lead.
- Increased calcium intake through calcium-fortified water can reduce lead absorption and resorption.
- Calcium-fortified water offers an accessible calcium source to vulnerable populations at risk for high lead and low calcium intakes.

INTRODUCTION

Lead is a well-known neurotoxicant responsible for detrimental social, economic, and health impacts. Despite the regulation or banning of many lead sources, prior exposure to lead, such as lead paint and dust, can cause lifelong health effects (Lanphear 1998; Abelsohn & Sanborn 2010). In children, lead causes neurobehavioral issues and cognitive deficiencies, while in adults it can cause cardiovascular diseases such as hypertension, especially in postmenopausal women (Nash *et al.* 2003; Lanphear *et al.* 2005; Obeng-Gyasi *et al.* 2018). Lead holds a heavy burden not only biologically on an individual scale, but also a multibillion-dollar burden on the economy and society (Gould 2009) that impacts Black Americans and other people of color disproportionately (Ettinger *et al.* 2020; Yeter *et al.* 2020). Calcium maintains healthy bodily function, supports bone and tooth health, and prevents the development of certain diseases (National Institutes of Health [NIH] 2021). It is also recognized for its ability to reduce bone lead absorption and thereby reduce total lead body burdens and the impacts of lead toxicity, particularly for pregnant women, the developing fetus, and infants (Rabinowitz 1991; Ettinger *et al.* 2006). Ingested lead and calcium are competitively absorbed from the intestines (Rabinowitz *et al.* 1993; Brito *et al.* 2005) and then enter the body's soft tissues and organs to be later deposited in bones (Needleman 2004; Barbosa *et al.* 2005) where it can remain for decades

(Fullmer *et al.* 1985; Rabinowitz *et al.* 1993; Brito *et al.* 2005). Lead, mimicking calcium, is released during physiological processes that typically involve the release of calcium such as resorbing bone, pregnancy, lactation, menopause, and significant weight loss (Gulson *et al.* 1997; Ettinger *et al.* 2006; Riedt *et al.* 2009; Jackson *et al.* 2010). These processes increase bone resorption, which results in increased blood lead levels (BLLs) (Fleming *et al.* 1997; Agency for Toxic Substances and Disease Registry 2017). Lead absorbed by a pregnant mother's bones is also released during the second and third trimesters, exposing the fetus to maternal blood lead delivered via the umbilical cord through the blood-placenta route (Arora *et al.* 2014). Significant exposures will therefore result in lead deposition in bones, resulting in lifelong exposure without the initial source being directly present (Fleming *et al.* 1997). Adequate calcium intake is important to reduce maternal and fetal lead exposures during windows of vulnerability, when there is greater mobilization of bone lead into the bloodstream.

Calcium is recommended for all persons but the dose depends on age and sex. The recommended dietary allowance (RDA) for calcium ranges from 200 to 1,300 mg in people from birth to 18 years, 1,000 mg for adults aged 19–50 and pregnant or breastfeeding females, 1,000 mg for adult males aged 50–70, and 1,200 mg for adult females aged 50–70 and all adults over 70 years old (NIH 2021). Although calcium is abundant in the US, some 42% of US residents did not meet their estimated average requirements in 2009–2010 (Hoy & Goldman 2014). Calcium intake was also lowest in the most vulnerable groups, including Black Americans and low-income individuals (defined as at 0–130% of the poverty level; Hoy & Goldman 2014).

Calcium intake is traditionally in dietary or supplemental form, and absorption is moderated by 1,25-dihydroxyvitamin D intake (Peacock 2010). In the US, 43% of the population, including 70% of older US females, use calcium supplements to meet their RDA (Bailey *et al.* 2010). Most calcium intake, however, is through dietary sources, although females over 60 years consume close to 50% through supplements (Hoy & Goldman 2014). The amount of calcium in food ranges from 5 mg/100 g of white potatoes, 123 mg/100 g of whole milk, to over 250 mg/100 g of kale (US Department of Agriculture 2021). Supplementary pills – e.g., multivitamins – often contain 200 mg-Ca per pill, which can be 20% of an individual's RDA (Burnett-Hartman *et al.* 2009; NIH 2021). Although RDAs are set at 1,000 mg-Ca/day for non-elder adults, calcium absorption is best when 500 mg or less is consumed at a time – that is, calcium intake should be spread throughout the day (Peacock 2010; NIH 2021). Research on the absorption of dietary and supplemental calcium suggests that only 30% of dietary calcium is absorbed (Peacock 2010), while supplementation increases calcium intake by 56% (Burnett-Hartman *et al.* 2009). Individuals taking calcium supplements have lower bone turnover markers, indicating reduced transfer of maternal lead to the developing fetus (Janakiraman *et al.* 2003).

Calcium can occur naturally or by addition in water. The bioavailability and absorption rate of calcium from a fortified water source is comparable to that of milk and calcium supplements (Greupner *et al.* 2017). A report by the World Health Organization (WHO) proposes adding calcium to water to achieve the RDA (WHO 2009). Given the competitive binding nature of lead and calcium, increasing the calcium available for absorption is one approach to mitigating lead's high binding affinity to calcium transporters while also contributing to the RDA. Notably, the impacts on community infrastructure of an intervention aimed at the general public through water for this purpose are not clear. For this reason, fortification of potable water with calcium must be done carefully to ensure that users and industries utilizing water for non-drinking purposes would not be adversely impacted by higher calcium and other mineral content.

Fortifying municipal water supplies with calcium to mitigate lead absorption is a novel idea, but its efficacy and an effective calcium concentration in water are unknown. To the authors' knowledge, there are no studies on the subject. This paper is a literature review of the interaction and possible dose-dependent relationship of dietary and supplemental calcium intake on lead absorption or resorption. It clarifies the efficacy of supplemental and dietary calcium intake and the intake levels needed to reduce lead absorption or resorption. The objective is to examine the efficacy and safety of a population-level intervention of fortifying potable water supplies with calcium to mitigate lead absorption.

METHODS

Research on the impact of calcium intake on lead levels was reviewed to examine the efficacy and calcium intake amount required to mitigate lead absorption or resorption. Studies were included that:

- ○ measured and reported blood or bone lead levels quantitatively;
- ○ measured or estimated and reported calcium intake levels quantitatively from supplemental and/or dietary sources or serum calcium;
- ○ reported the relationship or interaction between lead levels and calcium intake or serum calcium;
- ○ were empirical in design;
- ○ examined human populations; and,
- ○ were published in English between 1985 and 2020.

Literature was excluded if lead and calcium data were not measured and reported quantitatively, only prior literature was reviewed, only one or a few cases of extreme lead poisoning were examined, or it related to animal toxicity.

MEDLINE and CINAHL were searched in 2018 and 2021 for potentially relevant studies, using terms including: lead poisoning, lead exposure, calcium, calcium supplementation, calcium supplement, calcium intake, calcium (dietary/administration and dosage), and bone and bones/chemistry. Studies were also identified from the reference lists of included studies. The authors extracted information about the type of study, objective, populations and subpopulations, methods, participant characteristics, reported lead levels and calcium dosages or intakes, results, conclusions, and limitations.

RESULTS

Calcium and lead interactions

The effects of dietary and supplemental calcium on elevated lead levels from 28 studies (nine with children, 12 with pregnant and/or lactating women, and seven with other adults) are outlined in Table 1. Much of the literature focused on pregnant and lactating women, but the calcium intake and lead level trends observed were largely shared across populations. Studies included participants from different locations with BLLs above and below the 5 μg/dL level defined as elevated (Centers for Disease Control [CDC] 2021a, 2021b). Eighteen studies (64%) reported a significant ($p < .05$) inverse relationship between blood, bone, and/or breastmilk lead levels and calcium intake or serum calcium; no significant inverse relationship was observed in ten studies (36%).

Children

High levels of dietary calcium intake, calcium supplementation, and serum calcium were inversely associated with BLLs in five studies of children under 11 years (Mahaffey *et al.* 1986; Lacasaña *et al.* 2000; Jin *et al.* 2011; Turgeon O'Brien *et al.* 2014; Talpur *et al.* 2018). Approximately 19% of children with lead poisoning (≥10 μg/dL) receiving an intervention of 1,250 mg calcium carbonate had their BLLs decrease below 10 μg/dL (Jin *et al.* 2011). When this was combined with a chelating agent, 68% of participating children had their BLLs decrease below 10 μg/dL (Jin *et al.* 2011). Calcium intake was lower in two of the studies that did not observe an inverse relationship (Laraque *et al.* 1990; Gallicchio *et al.* 2002). Laraque *et al.* (1990) found no interaction between BLLs and calcium intake in children aged 1.5–4 years; this was attributable to participants' average calcium intakes (573.1–681.3 mg-Ca/day) falling below the calcium RDA (700–1,000 mg-Ca/day) for those age groups (NIH 2021). Markowitz *et al.* (2004), on the other hand, enrolled participants with high dietary calcium intake, which may explain why additional supplemental calcium reduced lead absorption no further. Only 20% of participants fell below the calcium RDA in the Turgeon O'Brien *et al.* (2014) study, which showed an inverse calcium intake/BLLs relationship. In general, these results suggest an inverse relationship between BLLs and calcium intake, and that the efficacy of calcium supplementation in mitigating the lead burden is dose dependent.

Pregnant or lactating women

Among lactating and pregnant women, calcium supplementation satisfying the 1,200 mg-Ca/day RDA was effective in lowering BLLs (Hertz-Picciotto *et al.* 2000; Pires *et al.* 2002; Hernandez-Avila *et al.* 2003; Ettinger *et al.* 2006, 2009). Observational studies also found elevated dietary and serum calcium to be associated with lower blood and bone lead levels (Téllez-Rojo *et al.* 2004; Zentner *et al.* 2008; Ikechukwu *et al.* 2012; Hong *et al.* 2014). Adequate calcium intake was crucial in reducing lead burdens. Ettinger *et al.* (2009) found that BLLs fell more than 24% in women who took more than 75% of their prescribed dose. Hernandez-Avila *et al.* (2003) and Ettinger *et al.* (2006) measured 16.4% and 5–10% reductions in BLLs, respectively, among lactating

Table 1 | Relationship of calcium (Ca) intake (dietary, supplemental) and serum calcium on lead (Pb) levels in blood (BLL), bone, plasma, or breast milk, in studies that examined and reported on them quantitatively

									Inverse relationship observed between:		
Study	**Study type[a]**	**Population**	**Total sample size (n)**	**Lead medium[b]**	**Mean BLL (μg/dL)**	**Mean dietary Ca (mg/day)**	**Mean supplemental Ca (mg/day)[c]**	**Mean serum Ca (mg/dL)**	**Pb levels and Ca intake**	**Pb resorption and Ca intake**	**BLLs and serum Ca levels**
Mahaffey *et al.* (1986)	O	Children, 1976–1980, USA (1–11 yrs)	2,926	Blood	15.7	851	–	–	Yes*	–	–
Laraque *et al.* (1990)	O	Black urban children, PA, USA (1.5–4 yrs)	64	Blood	35.0	Controls: 573–681[d]; Cases: 593–697[d]	–	Controls: 45.7; Cases: 45.4	No[e]	–	No[e]
Lacasaña *et al.* (2000)	O	Children, Mexico City, Mexico (<5 yrs)	200	Blood	9.9	516	–	–	Yes*	–	–
Gallicchio *et al.* (2002)	O	Children in old urban housing, Baltimore, USA (1 yr)	205	Blood	4.0[f]	562	–	–	No[e]	–	–
Lanphear *et al.* (2002)	O	Children, Rochester, NY, USA (0.5–2 yrs)	249	Blood	2.9[g]	679[f]	–	–	No[e]	–	–
Markowitz *et al.* (2004)	E	Inner-city children with elevated BLLs, NY, USA (1–6 yrs)	88	Blood	20.7[g]	973	1,800	9.6	No	–	–
Jin *et al.* (2011)	E	Preschool children with elevated Pb, Anshan, China (4–6 yrs)	72	Blood	14.3–14.6[g]	–	1,250[h]	–	Yes*	–	–
Turgeon O'Brien *et al.* (2014)	O	Inuit preschool children, 2006–2010, Nunavik, Canada (1–4 yrs)	245	Blood	2.1	896	–	–	Yes*	–	–
Talpur *et al.* (2018)	O	Malnourished and well-nourished children, Sindh, Pakistan (1–10 yrs)	310	Blood	Malnourished: 15.4–19.6[i]; Well-nourished: 6.7–9.8[i]	–	–	Malnourished: 79.6–92.7[i]; Well-nourished: 128.2–149.2[i]	–	–	Yes*
Hertz-Picciotto *et al.* (2000)	O	Healthy pregnant women, 1992–1995, Pittsburgh, USA (<20 to >30 yrs)	369	Blood	< 5.0	–	≤600 to >2,000	–	Yes[j]	–	–

(*Continued.*)

Table 1 | Continued

									Inverse relationship observed between:		
Study	**Study type[a]**	**Population**	**Total sample size (n)**	**Lead medium[b]**	**Mean BLL (µg/dL)**	**Mean dietary Ca (mg/day)**	**Mean supplemental Ca (mg/day)[c]**	**Mean serum Ca (mg/dL)**	**Pb levels and Ca intake**	**Pb resorption and Ca intake**	**BLLs and serum Ca levels**
Téllez-Rojo *et al.* (2004)	O	Pregnant women, 1997–1999, Mexico City, Mexico (15–43 yrs)	327	Blood, plasma and bone	7.1[k]	989.2[f]	–	–	Yes, plasma*, bone* and blood	–	–
Gulson *et al.* (2004)	E	Immigrants that conceived after entering Australia (19–32 yrs)	12	Blood	2.4	–	920–1,200	–	No	–	–
Zentner *et al.* (2008)	O	Women admitted to hospital for delivery, 2002, Santo Amaro City, Brazil (20–34 yrs)	55	Blood	<5–≥10	420	–	–	Yes*	–	–
Ettinger *et al.* (2009)	E	Pregnant women in their first trimester, 2001–2003, Mexico City, Mexico (25.9[l]–26.9[l])	670	Blood	3.8	900	1,200	–	Yes*	–	–
Ikechukwu *et al.* (2012)	O	Pregnant women, 2006–2008; Nigeria (20–35 yrs)	311	Blood	Pregnant: 35.7; Non-pregnant: 13.1	–	–	Pregnant: 33.3; Non-pregnant: 41.9	–	–	Yes*
Hong *et al.* (2014)	O	Pregnant women, 2006–2010; Seoul, Chonan, and Ulsan, South Korea (30.2[l] yrs)	1,150	Blood	1.3	541	–	–	Yes, in early* and late pregnancy	–	–
Pires *et al.* (2002)	E	Pregnant women in their third trimester and during lactation, São Gonçalo, Brazil (15–39 yrs)	47	Blood	< 5	643	500	–	Yes*, during lactation but not pregnancy	–	–
Hernandez-Avila *et al.* (2003)	E	Breastfeeding women, 1994–1995, Mexico City, Mexico (24.5 yrs[l])	617	Blood and bone	9.2–9.4	1,160	1,200	–	Yes, blood*, limited in bone*	–	–
Ettinger *et al.* (2006)	E	Lactating women, 1994–1995, Mexico City, Mexico (<20 to >30 yrs[m])	367	Blood and breast milk	8.6[g]	–	1,200	–	Yes, in breast milk* and blood over the course of lactation[m]	–	–

(*Continued.*)

Table 1 | Continued

									Inverse relationship observed between:		
Study	**Study type^{a}**	**Population**	**Total sample size (n)**	**Lead medium^{b}**	**Mean BLL (μg/dL)**	**Mean dietary Ca (mg/day)**	**Mean supplemental Ca (mg/day)^{c}**	**Mean serum Ca (mg/dL)**	**Pb levels and Ca intake**	**Pb resorption and Ca intake**	**BLLs and serum Ca levels**
Lagerkvist *et al.* (1996)	O	Pregnant women and infants 1989–1991, Sweden (17–43 yrs)	484	Blood	Pregnant women: 2.5–2.8^{g}; Infants: 2.3–2.9	–	–	Pregnant women: 42.0^{g}; Infants: 48.5–48.9	–	–	No
Gulson *et al.* (2006)	O & E^{n}	Pregnant and non-pregnant adult migrants and non-migrants, children, 1993–2002, Australia (6–11 & 19–38 yrs)	55	Blood	2.3–3.0	314–651	–	–	No^{e}	–	–
Muldoon *et al.* (1994)	O	Older White women, 1990–1991, Monongahela Valley and Baltimore, USA (65–87 yrs)	530	Blood	5.3	1,191–1,262	–	–	Yes, blood*	–	–
Riedt *et al.* (2009)	E	Women recruited for weight loss and maintenance studies, 2002–2005, USA (24–75 yrs)	73	Blood	1.4–1.9^{g}	1,080–1,200^{g}	200–1,500	–	Yes, in blood* at baseline, but not after severe weight loss	No	–
Jackson *et al.* (2010)	O	Pre- and postmenopausal women, 1999–2002, USA (20–85 yrs)	2,671	Blood	1.4^{o}	1,000–≥ 1,200	–	–	Yes*, in post-menopausal women	Yes*, in post-menopausal women	–
Proctor *et al.* (1996)	O	Older men, Normative Aging Study, 1991–1993, Greater Boston, USA (43–93 yrs)	798	Blood	6.5	819	–	–	Yes, blood	–	–
Kristal-Boneh *et al.* (1998)	O	Men working in Pb exposed and unexposed industries, 1995–1996, Israel (25–64 yrs)	146	Blood	Unexposed: 4.5; Exposed: 42.6	775–858	–	–	No^{e}	–	–
Elmarsafawy *et al.* (2006)	O	Older men, Normative Aging Study, 1991, Greater Boston area, USA (21–80 yrs)	471	Bone (and blood)	6.6	660.2–1,062.5	–	–	Yes, in tibia and patella*	–	–

(*Continued.*)

Table 1 | Continued

									Inverse relationship observed between:		
Study	**Study type[a]**	**Population**	**Total sample size (n)**	**Lead medium[b]**	**Mean BLL (μg/dL)**	**Mean dietary Ca (mg/day)**	**Mean supplemental Ca (mg/day)[c]**	**Mean serum Ca (mg/dL)**	**Pb levels and Ca intake**	**Pb resorption and Ca intake**	**BLLs and serum Ca levels**
Theppeang *et al.* (2008)	O	Urban adults, 2001–2005, Baltimore, USA (50–70 yrs)	1,140	Blood and bone	3.5	580–730	–	–	Yes, in tibia*; no in blood[e]	–	–

*Statistically significant relationship ($p < .05$).

[a] O = observational, E = experimental study design.

[b] Only media for which the relationship between Ca intake and Pb levels were reported are included.

[c] Only the supplemental group is reported.

[d] Ca intake is presented as a range from the mean of the 4-day record to the 24-hour dietary recall.

[e] No indication of either a positive or negative (statistically insignificant) association.

[f] 95% confidence interval reported.

[g] Levels at baseline.

[h] Ca supplementation (Jin *et al.* 2011) was done in a group with only Ca supplement and another group with Ca supplementation and succimer treatment.

[i] Lowest to highest values for the 95% confidence intervals for 1–5 and 6–10 year old children.

[j] No indication of the significance of the observed inverse relationship between BLLs and Ca intake.

[k] Median.

[l] Mean age.

[m] Age of study participants not included, but they were compared to a reference group of 19–50 years old for Ca DRI. It was noted that with supplementation during lactation, BLLs decreased; however, this association was not directly tested in the study.

[n] Included participants recruited from prior studies. Experimental design used for one group of pregnant women; all other participants followed an observational study design.

[o] Geometric mean.

women taking 1,200 mg-Ca/day. Supplementation of 1,200 mg-Ca/day during pregnancy was also associated with reduced bone resorption, which provides an effective method of minimizing the lead mobilization that contributes to maternal-fetal lead exposure (Janakiraman *et al.* 2003; Téllez-Rojo *et al.* 2004). In alignment with the supplementation effects, higher dietary calcium levels (600–2,000 mg-Ca/day) during pregnancy were inversely associated with BLLs (Hertz-Picciotto *et al.* 2000). Among lactating women with low dietary calcium intake (average 603 mg-Ca/day) and low lead exposure (BLLs < 5 μg/dL), however, 500 mg-Ca/day of supplement acted to reduce the amount of free lead in blood (Pires *et al.* 2002).

Calcium supplementation in pregnancy showed a reduction in BLLs dependent on the period of gestation (Ettinger *et al.* 2009; Hong *et al.* 2014). Reductions were most pronounced when supplementation occurred in earlier months (Ettinger *et al.* 2009; Hong *et al.* 2014). In pregnant women, 1,200 mg-Ca/day was sufficient to slow the rate of increase in BLLs during pregnancy by 14 and 8% in the second and third trimesters, respectively (Ettinger *et al.* 2009). Hong *et al.* (2014) reported similar findings, with the greatest calcium intake effects associated with early pregnancy. Observational studies with no calcium supplementation found that serum calcium levels decreased while BLLs increased as pregnancy progressed (Lagerkvist *et al.* 1996; Ikechukwu *et al.* 2012). When serum levels are low, bone remodeling to achieve homeostatic calcium levels can result in lead mobilization from bones to blood (Khan *et al.* 2021). Collectively, these results support the hypothesis that calcium supplementation and high dietary calcium intake during pregnancy can reduce the fetal lead burden by reducing bone remodeling and confining the umbilical-cord transfer of lead in late pregnancy, thus limiting fetal lead exposure.

Non-pregnant adults

Among adults who are neither pregnant nor lactating, an inverse relationship was found between BLLs and calcium intake, dependent on bone lead levels and bone turnover (Muldoon *et al.* 1994; Proctor *et al.* 1996; Elmarsafawy *et al.* 2006; Theppeang *et al.* 2008; Jackson *et al.* 2010). Postmenopausal women with dietary calcium intakes above the RDA and low levels of bone turnover markers (bone alkaline phosphatase and N-terminal telopeptide) were found to have 12–18% lower mean BLLs than women below the RDA (Jackson *et al.* 2010). In a study assessing the ability of dietary and supplemental calcium intake to mitigate the lead burden during weight loss among moderate and severely obese women, an inverse association between calcium intake and BLLs at the baseline was lost after weight loss and subsequent bone turnover had occurred (Riedt *et al.* 2009). This suggests that during times of high bone turnover such as significant weight loss, calcium intake (dietary and supplemental) effects on lowering BLLs may be limited. This aligns with the limited protective effect observed in late pregnancy where rates of bone turnover are also high. Greater age, never breastfeeding, and the years since menopause in women were also associated with elevated blood and tibia lead levels (Muldoon *et al.* 1994; Kristal-Boneh *et al.* 1998; Theppeang *et al.* 2008), likely related to lead accumulation and bone resorption.

DISCUSSION

Evaluation of calcium-fortified water

Adding calcium to water to mitigate the lead burden needs careful consideration. A clinically significant calcium dose that can both contribute to individual RDA and promote a sustainable water pH should be determined. Calcium concentrations in US municipal water supplies range from 2 to 85 mg/L, with median national concentrations of 48 mg/L in groundwater and 36 mg/L in surface water (Azoulay *et al.* 2001). The concentrations of calcium and other minerals in water influence its pH, and can have adverse implications for health, the environment, and the sustainability of water distribution systems and homes (WHO 2009). Typically, lead ingested through water occurs with soft waters, which are characteristically acidic and leach lead from soldered pipes (Santucci & Scully 2020). Conversely, hard water promotes scaling, which provides protection against heavy metal leaching, but can affect the lifespan of water distribution systems (WHO 2009). Over half of all US homes were built before 1980 (US Census Bureau 2021) and are more likely to contain lead service lines, lead pipes, and/or lead soldering (US Environmental Protection Agency [USEPA] 2021).

Consumption of hard water is generally considered safe, with some concern noted for those prone to milk alkali syndrome and hypercalcemia (WHO 2009). Research on potential cardiovascular health implications of calcium-fortified water has remained inconsistent and unsuccessful in demonstrating a definitive relationship between calcium intake and cardiovascular disease (Bucher *et al.* 1996; van Mierlo *et al.* 2006; WHO 2009;

Ross *et al.* 2011; Prentice *et al.* 2013). Excessive calcium intake above its tolerable upper intake level (UL), the highest average daily intake level without likely adverse health risks, can interfere with nutrient absorption and cause vascular and soft tissue calcification, kidney stones, and constipation (Institute of Medicine [IOM] 2011). Tightly regulated intestinal absorption of calcium mediated by vitamin D and elimination of excess calcium via the kidneys provide protection against excessive calcium intake (WHO 2009). While calcium ingestion can reduce iron absorption, long-term studies examining the impact of calcium supplementation have not shown adverse impacts on iron or zinc absorption (Sandström 2001).

Several health benefits have been associated with consuming calcium-fortified water. Crawford & Clayton (1973) showed a decreased amount of lead was stored in rib bones of residents living in towns with hard water compared to soft water. However, this assessment did not account for differences in lead exposure. Among women, consumption of calcium-fortified water has been associated with improved bone mineral density (especially in postmenopausal women), decreased bone resorption, and limited age-related bone loss (Aptel *et al.* 1999; Meunier *et al.* 2005). Calcium water concentrations of 5.39 mg/L (supplying 9.1% of RDA) were associated with a 15% reduction of hip fractures in men (Dahl *et al.* 2015). Consumption of calcium via water at various concentrations has been found to positively impact indicators of cardiovascular health including a reduction in low density lipoproteins, serum cholesterol, blood pressure, and risk of myocardial infarction (Nerbrand *et al.* 2003; Rylander & Arnaud 2004; Yang *et al.* 2006). Calcium water intakes have a protective effect of lowering the rate of very low birth weights, possibly due to reductions in blood pressure in pregnant mothers (Yang *et al.* 2002). Additionally, researchers assessing the association of cancer prevalence in hard and soft water areas found that those with hard water had significantly reduced prevalence of breast and prostate cancers (Yang & Chiu 1998).

Calcium-fortified municipal water would increase calcium intake for individuals at risk of lower calcium intake and of higher lead exposures. Lactose maldigestion and intolerance are more prevalent among Black and Mexican Americans than White Americans, which might limit consumption of common dietary calcium sources such as dairy products (Bailey *et al.* 2013). Calcium-fortified water would thus provide a more comfortable, accessible source of calcium. There might be additional, indirect health benefits of increasing calcium intake and mitigating lead absorption, too. Elmarsafawy *et al.* (2006) observed an inverse relationship between high bone and blood lead levels and low calcium intake (<800 mg-Ca/day) associated with an increased risk of hypertension among adult males. Proctor *et al.* (1996) also noted an inverse association of dietary calcium and diastolic blood pressure, but only with BLLs below 15 μg/dL. These results suggest that dietary calcium intake can help to reduce the risks that the cumulative lead burden imposes on blood pressure (Elmarsafawy *et al.* 2006).

Population-level intervention for mitigating lead burdens

Given the collective observations in the studies reviewed, calcium supplementation offers a potential intervention to mitigate lead burdens. A population-based intervention utilizing calcium-fortified water could offer a highly absorbable source of supplemental calcium (Heaney 2006) that is readily accessible and cost-effective. Furthermore, the WHO has recommended fortifying drinking water with calcium and magnesium in order to meet the RDA and decrease the morbidity associated with inadequate intake (WHO 2009). Vulnerable individuals with low calcium intake and elevated lead exposures are at greatest risk of health complications and would benefit most from calcium-fortified water.

As observed in this review, the protective effects of calcium against lead were absent or less prevalent when intake levels were below the RDA. For calcium-fortified water to be effective, a clinically significant dose adequate to help meet RDA should be determined. Table 2 comprises a range of calcium concentrations with the corresponding amount of calcium and proportion of 1,000 mg-Ca/day (RDA) for the US mean daily personal water consumption (0.71 L/day; USEPA 2019) and the recommended water intakes for women and men, 2.72 and 3.67 L, respectively (Mayo Clinic 2020). Women and men consuming their recommended daily water intake with 60 mg-Ca/L could achieve 16.3% (163 mg) and 22.0% (220 mg) of their RDA, respectively. This concentration would also ensure that those already meeting their RDA through diet and/or supplementation would remain below their ULs (2,000–3,000 mg-Ca/day for children over one year, non-pregnant adults, and pregnant or lactating adults; IOM 2011), since it would only provide an additional 241 mg-Ca for someone consuming ~4 litres of water.

Contingent on community needs, calcium could be added to municipal water or water could be softened to 60 mg-Ca/L. This concentration is well below the hard water classification and could supply those meeting

Table 2 | Total calcium (mg) consumed and proportion of a 1,000 mg-Ca RDA met for US average water consumption for all ages (0.71 L) and the recommended water consumption for women (2.72 L) and men (3.67 L) at various calcium concentrations in water

	Water consumption (litres)					
	0.711		2.72		3.67	
Calcium concentration (mg/L)	Calcium (mg)	% of RDA	Calcium (mg)	% of RDA	Calcium (mg)	% of RDA
50	35.6	3.6	136.0	13.6	183.4	18.3
60	42.7	4.3	163.2	16.3	220.0	22.0
70	49.8	5.0	190.5	19.0	256.7	25.7
80	56.9	5.7	217.7	21.8	293.4	29.3
90	64.0	6.4	244.9	24.5	330.0	33.0
100	71.1	7.1	272.1	27.2	366.7	36.7

their recommended daily water intakes with a clinically significant calcium dose to help them meet their RDA and receive potential lead protective effects. The calcium in the water supply is meant to fill individual nutrition deficits for those not meeting their Ca-RDA, not replace dietary sources. The recommendation is not an alternative to removing lead from homes and/or water systems, or a replacement for repairs to antiquated infrastructure, which are necessary to eliminate lead risks. However, lead can be leached during partial replacement of lead service lines (Deshommes *et al.* 2018), and consumption of calcium-fortified water could help boost bodily resistance to lead absorption at these times. The WHO (2009) suggest that implementation of calcium into water systems should be considered at the municipal level to enable optimal calcium dosing to meet the intake needs of the recipients while minimizing the potential adverse effects of altered water properties.

Challenges and limitations

Water filters and softeners use presents a significant challenge to the proposed intervention. In 2005, more than 40% of US Americans used some type of residential water treatment (USEPA 2005). Point-of-use and point-of-entry water filters sold in the US to soften water can reduce the calcium content or remove it completely (WHO 2009). The effects of hard water on household appliances and consumer's desire to remove solid particles and toxicants like lead from drinking water drive the US water filter market (USEPA 2005). The intervention proposed could be enhanced by alternative home treatment options that do not remove all calcium.

The increasing consumption of bottled water could limit the impact of this suggested intervention. Annual per capita consumption of bottled water in the US increased from 35 L in 1999 (Ferrier 2001) to 162 L in 2015–2016 (Vieux *et al.* 2020). Despite the growing consumption of bottled water, most US Americans consume more than 60% of their water from taps (Vieux *et al.* 2020). Tap water consumption is lowest for people with low incomes, and Mexican, other Hispanic/Latinx, and Black Americans (Vieux *et al.* 2020), which could inhibit the influence of public water system intervention for populations most at risk to lead exposure. Well-known cases of lead contamination in water systems have driven public distrust and a switch to bottled water, particularly in low-income communities (Pierce & Gonzalez 2017; Javidi & Pierce 2018).

Naturally occurring, moderately hard water does not necessarily coincide with areas with elevated lead exposure risks, such as older and/or urban neighborhoods that are more likely to have lead-based paint, leaded or lead soldered pipes, and/or leaded gasoline deposits near roads. People living in older, urban neighborhoods are at greater risk of lead poisoning, however, as they rely more heavily on public or private water systems than rural populations (97% vs. 56%) (US Census Bureau 2021). A public health intervention to fortify water supplies relies on public or private water distribution systems and the consumption of tap water.

CONCLUSION

Lead is a persistent neurotoxicant that will come to the fore as communities grapple with lead abatement and infrastructure improvement projects in the coming decades. Calcium-fortified water is a means of boosting calcium ingestion and increasing the proportion of residents meeting the Ca-RDA, and thus potentially mitigating lead absorption and resorption during windows of vulnerability or for at-risk populations.

DECLARATIONS

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

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