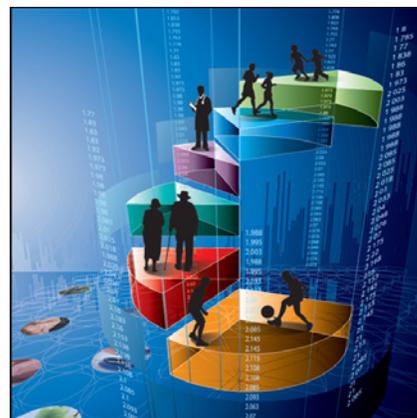


Article

Association between blood lead and blood pressure: Results from the Canadian Health Measures Survey (2007 to 2011)

*by Tracey Bushnik, Patrick Levallois, Monique D'Amour,
Todd J. Anderson and Finlay A. McAlister*

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- . not available for any reference period
- .. not available for a specific reference period
- ... not applicable
- 0 true zero or a value rounded to zero
- 0^s value rounded to 0 (zero) where there is a meaningful distinction between true zero and the value that was rounded
- P preliminary
- r revised
- X suppressed to meet the confidentiality requirements of the *Statistics Act*
- E use with caution
- F too unreliable to be published
- * significantly different from reference category ($p < 0.05$)

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Abstract

Background

Hypertension is the leading risk factor for cardiovascular disease, but its cause is not always known. Interest is increasing in the potential role of environmental chemicals, including lead.

Data and methods

Data are from the first two cycles of the Canadian Health Measures Survey. Lead in whole blood (PbB), and systolic (SBP) and diastolic (DBP) blood pressure were measured and hypertension status was derived for 4,550 respondents aged 40 to 79. Linear regression estimated associations between PbB and SBP and DBP. Logistic regression estimated associations between PbB and hypertension. Adjusted least squares geometric means of PbB were estimated for hypertensive versus non-hypertensive individuals.

Results

Compared with non-hypertensive individuals, those with hypertension had higher average PbB levels, were older, more likely to be male, and more likely to have other hypertension risk factors (diabetes, family history of high blood pressure). In adjusted regression models, a modest association emerged between PbB levels and SBP among 40- to 54-year-olds, and between PbB levels and DBP for the overall population. No association emerged between PbB levels and hypertension prevalence.

Interpretation

A modest association was observed between blood lead levels and blood pressure, but not with hypertension, in Canadian adults aged 40 to 79.

Keywords

Biomonitoring, cardiovascular diseases, environmental exposure, heavy metals

Authors

Tracey Bushnik (tracey.bushnik@statcan.gc.ca) is with the Health Analysis Division at Statistics Canada. Patrick Levallois is with l'Institut national de santé publique du Québec and le Centre de recherche du CHU de Québec. Monique D'Amour is with Health Canada. Todd J. Anderson is with the Libin Cardiovascular Institute. Finlay A. McAlister, Division of General Internal Medicine, University of Alberta, is an Alberta Innovates Health Solutions Senior Health Scholar and the University of Alberta Chair in Cardiovascular Outcomes Research.

Hypertension is recognized as the leading risk factor for cardiovascular disease, accounting for 9.4 million deaths worldwide in 2010.¹ It increases the risk of stroke, myocardial infarction, heart failure and renal failure.² In Canada, hypertension affects at least one in five adults aged 20 or older³ and is the leading modifiable risk factor for stroke.⁴

Hypertension is a heterogeneous disorder, the cause of which is not always known.⁵ Traditional risk factors include age, smoking, obesity, elevated sodium intake, alcohol consumption, lack of exercise, diabetes, kidney disease, and a family history of hypertension.^{6,7} Exposure to environmental chemicals, including lead, is emerging as a potential risk factor.^{8,9}

Lead is a contaminant that is ubiquitous in the environment. Exposure is associated with neurological, immunological, hematological, cardiovascular, renal, and reproductive and developmental effects.^{10,11} People are exposed to low levels of lead through food, drinking water, soil, household dust, air, and some products.¹¹⁻¹³ Although population lead levels have declined significantly over the past 30 years, in 2009/2011, it was detectable in the blood of 100% of the Canadian population aged 3 to 79.¹⁴

The link between lead exposure and hypertension is supported by animal studies.^{10,11} However, the mechanism by which lead may affect blood pressure and cause hypertension is complex, with various potential modes of action including alteration of cellular ion status and oxidative stress.¹⁰ The conclusion of sufficient evidence of a lead-related increase in blood pressure and risk of hypertension has been reported for humans, but results from population studies have varied.^{10,11,15} Some studies have found increased blood pressure and/or an increased risk of hypertension with increasing levels of lead,¹⁵⁻¹⁸ while others have found a weak or no association.¹⁹⁻²¹ The last Canadian study that used national data to examine the association between lead and blood pressure was based on results from the 1978-1979 Canada Health Survey. A weak positive association was found between blood

lead and diastolic blood pressure,²² but at that time, average lead levels in the population were much higher.²³ Little is known about the association between blood pressure and the lower lead levels observed today.

Using data from the first two cycles of the Canadian Health Measures Survey (CHMS), this study examines the association between blood lead (PbB) levels and blood pressure (BP) among adults aged 40 to 79.

Methods

Data source

The data are from the first (2007 to 2009) and second (2009 to 2011) cycles of the CHMS. The CHMS is an ongoing survey designed to provide comprehensive direct health measures at the national level that collects information from the household population. Full-time members of the Canadian Forces and people living on reserves or in other Aboriginal settlements, in institutions and in some remote regions are excluded. The CHMS involves an in-person household interview and a subsequent visit to a mobile examination centre. The household interview gathers general demographic and socio-economic data and detailed health, nutrition and lifestyle information. At the mobile examination centre, direct physical measurements are taken, including collection of blood and urine samples. Information about medication use is obtained during the household interview and also at the mobile examination centre. CHMS participants receive an accelerometer to wear for one week to monitor their activity levels. Detailed information about the CHMS is available elsewhere.^{24,25}

Cycle 1 collected information from people aged 6 to 79, and had an overall response rate of 51.7%—a total of 5,604 respondents. Cycle 2 collected information from people aged 3 to 79; the overall response rate was 55.5%, resulting in 6,395 respondents. Cycle 1 participants were not eligible for cycle 2. The present study combined 40- to 79-year-old participants from each cycle for a total of

4,662 respondents. Only non-pregnant respondents with complete data for all variables of interest were included in this analysis—a study sample of 4,550.

Specimen collection and laboratory analysis

Blood specimens were collected, processed and aliquotted at the mobile examination centre. Biospecimens were stored temporarily at -20°C, and once a week, shipped on dry ice to the reference laboratory for analyses. Analysis of lead was performed at the Centre de Toxicologie du Québec, Institut national de santé publique du Québec, Quebec City. Whole blood samples were diluted in a basic solution containing octylphenol ethoxylate and ammonia and analyzed for lead by inductively coupled plasma mass spectrometry (Perkin Elmer Sciex, Elan DRC II). The limit of detection (LOD) of PbB was 0.02 µg/dL in cycle 1 and 0.1 µg/dL in cycle 2. Further information about the laboratory analysis of lead and quality control procedures can be found elsewhere.^{12,26,27}

Measures

Blood lead. All respondents aged 40 to 79 had PbB values above the *highest* LOD²⁸ of the two cycles (0.1 µg/dL); therefore, no PbB values were imputed. PbB concentrations were converted from Système International units (µmol/L) to conventional units (µg/dL) for this study. The resulting values were rounded to two significant digits as per the recommendations for combining cycle 1 and cycle 2 environmental contaminants data.²⁹

Blood pressure. Blood pressure was measured with the BpTRU™ BP-300 device (BpTRU Medical Devices Ltd., Coquitlam, British Columbia) at the mobile examination centre. The BpTRU™ is an automated electronic monitor that has been validated and is recommended for use by the Canadian Hypertension Education Program.^{30,31} Six BpTRU readings were taken for each participant, with the last five averaged to determine the systolic (SBP) and diastolic (DBP) blood pressure reading.³² During the home interview, 39 respondents who

could not visit the mobile examination centre had their blood pressure measured with the BpTRU™ BP-100 device.

Antihypertensive medication use. During data processing, audited medications in current use by respondents were assigned codes from the Anatomical Therapeutic Chemical (ATC) Classification System. The following categories of antihypertensive medications were specified: beta blockers (ATC codes C07, excluding C07AA07, C07AA12 and C07AG02); agents acting on the renin-angiotensin system (ATC codes C09); thiazide diuretics (ATC codes C03, excluding C03BA08 and C03CA01); calcium channel antagonists (ATC codes C08); and miscellaneous antihypertensives (ATC codes C02, excluding C02KX01). Respondents were categorized as using antihypertensive medication if an ATC code corresponded to the above list and/or they self-reported the use of blood-pressure-lowering medication.

Hypertension. Respondents were categorized as hypertensive if they had an average SBP ≥ 140 mmHg and/or an average DBP ≥ 90 mmHg and/or were using antihypertensive medication and/or reported a health care provider diagnosis of hypertension.

Covariates

In addition to age, sex, highest level of education, smoking, average daily alcohol consumption, family history of high blood pressure and antihypertensive medication use, the following covariates were analyzed: average minutes per week of moderate-to-vigorous physical activity, body mass index (BMI), non-fasting non-HDL cholesterol, and indicators of diabetes and chronic kidney disease.

Weekly physical activity was calculated for participants with at least four valid days of accelerometry data, and was categorized as less than 30 minutes per week of moderate-to-vigorous physical activity versus 30 or more minutes per week. Those with less than four valid days of data were categorized as missing. BMI was calculated as measured weight in kilograms divided by measured height

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in metres squared (kg/m^2). Non-fasting non-HDL cholesterol was calculated by subtracting participants' blood measure of high-density lipoprotein cholesterol from their blood measure of total cholesterol and was categorized as below 4.3 mmol/L versus at or above 4.3 mmol/L.³³ Respondents were categorized as having diabetes if the measured percent of glycated hemoglobin A1c in their blood was equal to or greater than 6.5% and/or they had an audited use of glucose-lowering medication and/or they reported a health care provider diagnosis of diabetes.

Chronic kidney disease was defined as an estimated glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 . Estimated GFR = $175 \times (\text{serum creatinine in mg/dL})^{-1.154} \times (\text{age})^{-203} \times (0.742 \text{ if female}) \times (1.212 \text{ if cultural or racial background is black})$.³⁴

Statistical analysis

Analyses were weighted using the CHMS cycle 1/cycle 2 combined survey weights generated by Statistics Canada.²⁹ The data were analyzed with SAS 9.2 and SUDAAN 11.0, using DDF=24 in the

SUDAAN procedure statements. Ten PbB groupings were estimated from the weighted distribution of PbB levels in the population, using cutpoints set at the 5th, 15th, 25th, 35th, 50th, 65th, 75th, 85th, and 95th percentiles. Proportions, means and geometric means were calculated. Variance estimation (95% confidence intervals) and significance testing were done using the replicate weights to account for the survey's complex sampling design. T-tests were used to compare point estimates, and Satterthwaite-adjusted F-tests were used to test significance of regression coefficients. Significance was set at $p \leq 0.05$.

Table 1
Selected characteristics of household population aged 40 to 79, by hypertension status, Canada, 2007 to 2011

	Total				Non-hypertensive				Hypertensive			
	Sample size	Mean or %	95% confidence interval		Sample size	Mean or %	95% confidence interval		Sample size	Mean or %	95% confidence interval	
			from	to			from	to			from	to
Geometric mean of blood lead ($\mu\text{g}/\text{dL}$)	4,550	1.64	1.58	1.71	2,708	1.59	1.51	1.66	1,842	1.74*	1.65	1.83
Mean age (years)	4,550	55.4	55.1	55.8	2,708	52.4	51.9	52.8	1,842	60.7*	59.9	61.5
Sex (%)												
Men	2,214	49.5	49.2	49.9	1,254	45.8	43.7	48.0	960	55.9*	52.7	59.0
Women	2,336	50.5	50.1	50.8	1,454	54.2	52.0	56.3	882	44.1*	41.0	47.3
Highest level of education (%)												
Less than secondary school graduation	758	15.4	13.7	17.3	315	11.5	9.7	13.7	443	22.1*	19.5	24.9
Secondary school graduation or higher	3,739	82.2	80.2	84.1	2,366	86.7	84.4	88.7	1,373	74.6*	71.4	77.4
Missing	53	2.4 ^E	1.6	3.4	27	1.8 ^E	1.1	3.0	26	3.4 ^E	1.9	5.9
Current smoking behaviour (%)												
Non-smoker	3,753	80.6	78.9	82.1	2,189	79.1	77.0	81.1	1,564	83.0*	80.2	85.5
Daily or occasional smoker	797	19.4	17.9	21.1	519	20.9	18.9	23.0	278	17.0*	14.5	19.8
Average daily alcohol consumption in past week (%)												
0 or 1 drink	3,939	86.0	83.7	88.0	2,336	86.6	84.6	88.4	1,603	84.9	80.7	88.4
2 or more drinks	568	13.2	11.2	15.5	348	12.8	11.0	14.8	220	14.0	10.6	18.3
Missing	43	0.8 ^E	0.5	1.2	24	0.6 ^E	0.3	1.1	19	1.1 ^E	0.6	1.8
Moderate-to-vigorous physical activity (%)												
At least 30 minutes per week	1,541	33.0	30.0	36.2	1,070	38.1	34.7	41.6	471	24.4*	21.1	28.1
Less than 30 minutes per week	2,179	47.8	43.7	51.8	1,218	45.4	41.1	49.9	961	51.8*	47.1	56.4
Missing	830	19.2	16.8	21.9	420	16.5	13.9	19.5	410	23.8*	20.1	28.0
Mean BMI (kg/m^2)	4,550	28.0	27.7	28.4	2,708	26.9	26.5	27.3	1,842	30.0*	29.5	30.4
Non-HDL cholesterol (%)												
Less than 4.3 mmol/L	3,133	68.7	65.5	71.7	1,801	67.9	64.0	71.6	1,332	70.0	66.2	73.5
4.3 mmol/L or more	1,417	31.3	28.3	34.5	907	32.1	28.4	36.0	510	30.0	26.5	33.8
Diabetes (%)	610	12.8	10.9	15.0	151	5.5	4.0	7.5	459	25.3*	22.1	28.9
Chronic kidney disease (%)	421	7.2	6.1	8.4	101	3.1	2.3	4.2	320	14.1*	12.0	16.5
Family history of high blood pressure (%)												
Yes	2,191	51.2	48.9	53.5	1,153	45.8	42.5	49.0	1,038	60.5*	56.8	64.0
No	2,002	41.4	39.0	43.8	1,383	47.7	44.6	50.9	619	30.5*	26.9	34.4
Don't know	357	7.4	6.2	8.9	172	6.5	5.1	8.3	185	9.0	7.0	11.4
Antihypertensive medication use (%)	1,469	28.9	26.7	31.2	1,469	78.4 [†]	74.2	82.0

* significantly different from non-hypertensive ($p < 0.05$)

[†] testing not applicable

^E use with caution

...not applicable

Notes: All percentage and mean estimates are weighted using combined cycle 1/cycle 2 survey weights. All confidence intervals are based on variance estimates produced using combined cycle 1/cycle 2 bootstrap weights.

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

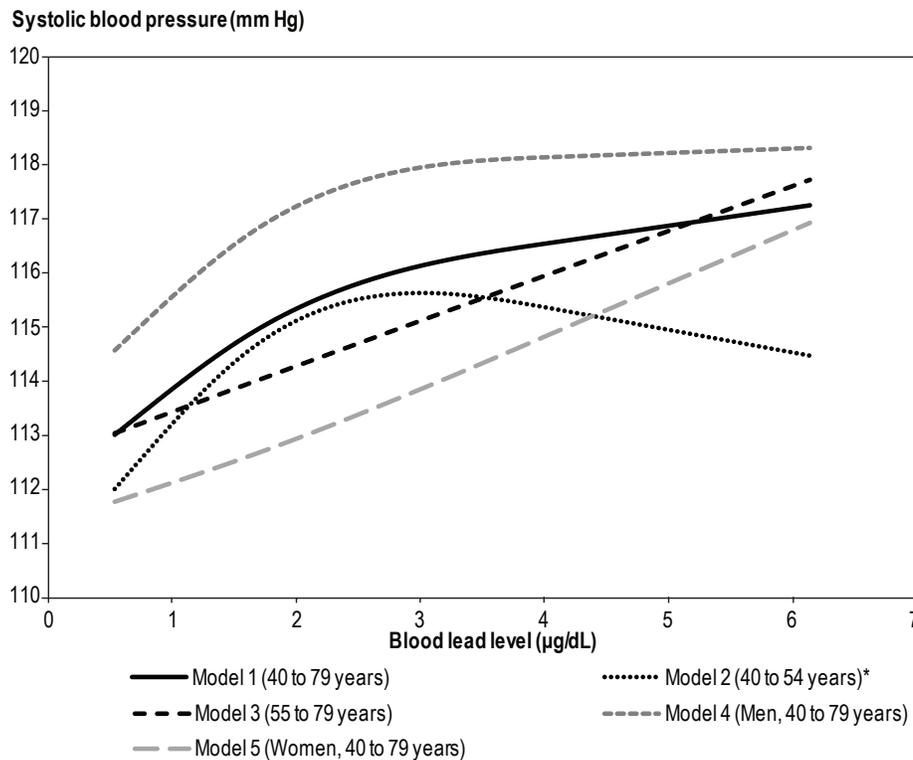
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Table 2
Average systolic and diastolic blood pressure and hypertension prevalence, by blood lead percentile, household population aged 40 to 79, Canada, 2007 to 2011

Blood lead percentile	Systolic blood pressure (mmHg)			Diastolic blood pressure (mmHg)			Prevalence of hypertension		
	Mean	95% confidence interval		Mean	95% confidence interval		%	95% confidence interval	
		from	to		from	to		from	to
Total	117.4	116.3	118.6	73.7	73.0	74.4	36.8	34.4	39.3
≤5th (mean 0.54 µg/dL)	111.9	108.8	114.9	72.1	69.9	74.3	32.8	22.9	44.6
5th to ≤15th (mean 0.81 µg/dL)	113.2	111.1	115.3	72.3	71.0	73.6	30.7	24.7	37.5
15th to ≤25th (mean 1.05 µg/dL)	114.8	111.6	118.0	72.4	70.4	74.5	30.1	22.0	39.5
25th to ≤35th (mean 1.25 µg/dL)	117.2	112.9	121.6	73.8	70.6	77.0	35.5	27.0	45.0
35th to ≤50th (mean 1.49 µg/dL)	117.1	114.8	119.5	73.7	72.6	74.8	33.5	27.4	40.2
50th to ≤65th (mean 1.82 µg/dL)	118.2	116.7	119.8	73.8	72.7	74.9	42.3	35.8	49.0
65th to ≤75th (mean 2.21 µg/dL)	117.8	115.5	120.0	74.3	73.1	75.6	36.4	29.9	43.4
75th to ≤85th (mean 2.66 µg/dL)	119.8	117.2	122.3	74.4	72.7	76.0	38.7	31.0	47.0
85th to ≤95th (mean 3.45 µg/dL)	121.3	118.3	124.3	74.8	73.4	76.3	45.5	39.0	52.2
> 95th (mean 6.14 µg/dL)	122.8	119.1	126.4	75.4	73.2	77.5	44.8	35.3	54.7

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

Figure 1
Model-adjusted systolic blood pressure across blood lead levels, household population aged 40 to 79, Canada, 2007 to 2011



* significant association between blood lead level and systolic blood pressure ($p < 0.05$)

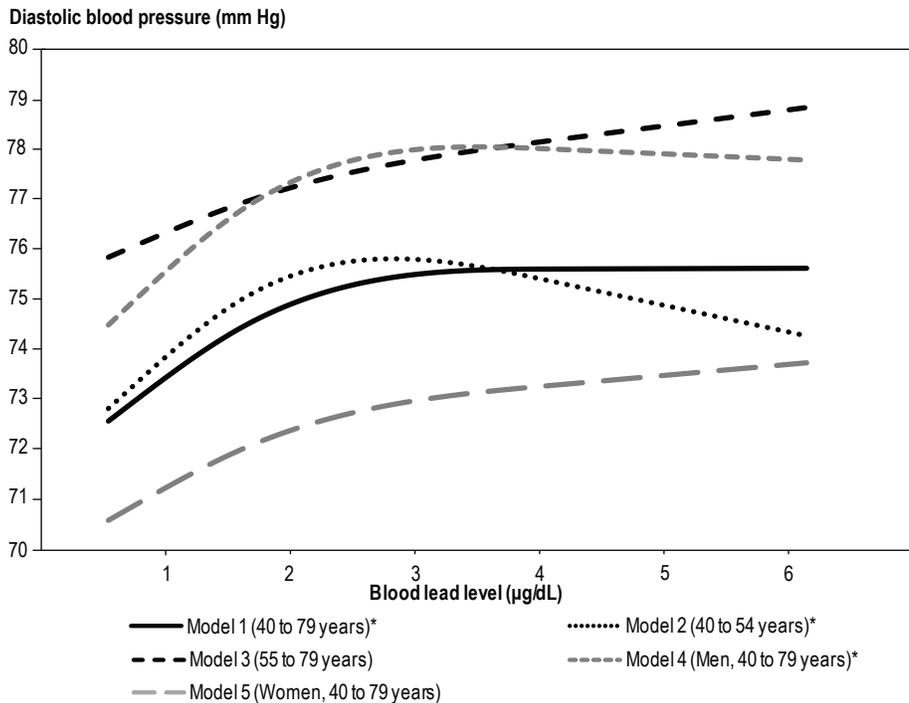
Note: Models 1, 2 and 3 adjusted for age, sex, education, smoking, alcohol, physical activity, BMI, non-HDL cholesterol, diabetes, chronic kidney disease, family history of high blood pressure, and antihypertensive medication use; Model 4 and 5 adjusted for same covariates except sex.

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

Linear regression was used to estimate the association between PbB and SBP and DBP. Logistic regression was used to estimate the association between PbB and hypertension. The unadjusted model included only PbB; the adjusted model added all other covariates. To model the functional relationship between PbB and each outcome, separate models were tested with PbB as a linear, quadratic, and cubic term, and additional models were run with five different spline functions for PbB: linear, quadratic, cubic, restricted quadratic, and restricted cubic.³⁵ Knot selection for the spline functions was based on the weighted percentile distribution of PbB, and three sets of knots—(5th, 50th, 95th), (5th, 25th, 75th, 95th), and (5th, 25th, 50th, 75th, 95th)—were tested with each spline function.³⁶ An F-test of differences in R² was used to compare linear models.³⁷ The log-likelihood-based chi-square test was used to compare nested logistic regression models.³⁸ Significance was set at $p \leq 0.05$. Test results indicated that the three-knot restricted cubic spline function for PbB maximized the explained variance in the linear models of SBP and DBP, while the three-knot linear spline function for PbB produced the best model fit for hypertension. The three knots were set at the 5th (0.65 µg/dL), 50th (1.6 µg/dL) and 95th (4.1 µg/dL) percentile cutpoints.

Cycle-to-cycle differences in SBP and DBP and the log odds of hypertension were not statistically significant at $p \leq 0.05$ (Satterthwaite-adjusted F-test), and therefore, a cycle indicator was removed from the final models. Because diabetes, chronic kidney disease and family history of hypertension might be intermediate variables in the association between PbB and the outcomes, the models were re-run excluding these variables; the association between PbB and the outcomes did not change, so these risk factors were retained in the models. Because interactions between PbB and sex, and PbB and age (40 to 54 versus 55 to 79) were statistically significant, the models were sex- and age-stratified. Adjusted least squares geometric means (LSGM) of PbB were estimated for hypertensive

Figure 2
Model-adjusted diastolic blood pressure across blood lead levels, household population aged 40 to 79, Canada, 2007 to 2011

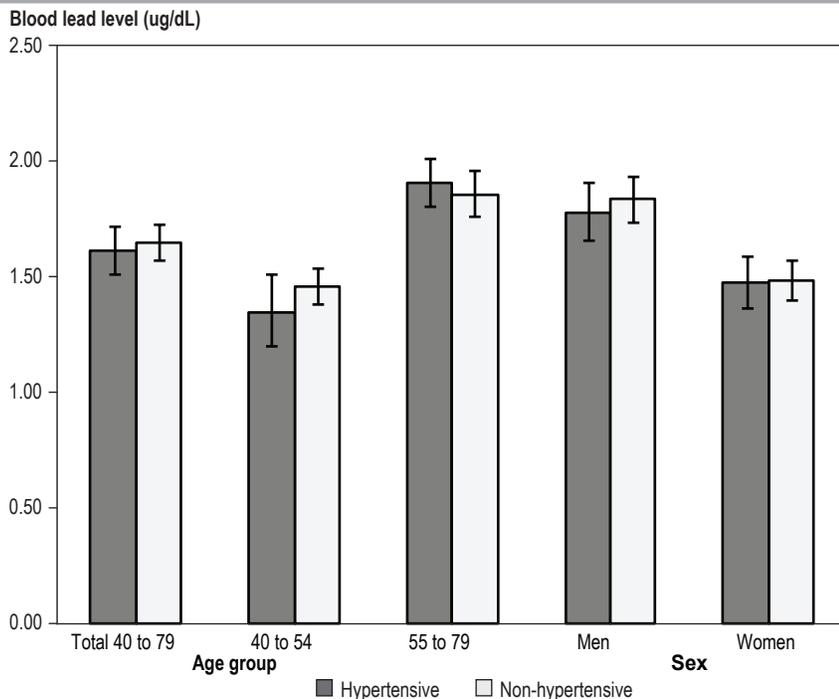


* significant association between blood lead level and diastolic blood pressure ($p < 0.05$)

Note: Models 1, 2 and 3 adjusted for age, sex, education, smoking, alcohol, physical activity, BMI, non-HDL cholesterol, diabetes, chronic kidney disease, family history of high blood pressure, and antihypertensive medication use; Model 4 and 5 adjusted for same covariates except sex.

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

Figure 3
Model-adjusted geometric mean blood lead level, by hypertension status, age group and sex, household population aged 40 to 79, Canada, 2007 to 2011



I = 95% confidence interval

Note: Overall and age-stratified models adjusted for age, sex, education, smoking, alcohol, physical activity, BMI, non-HDL cholesterol, diabetes, chronic kidney disease, and family history of high blood pressure; sex-stratified models adjusted for all covariates except sex.

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

versus non-hypertensive individuals, controlling for all other covariates. As part of a sensitivity analysis, the logistic regression model for hypertension was tested with PbB as a log-transformed term and PbB categorized into quartiles. For ease of comparison with other studies, the adjusted models for SBP and DBP were also run excluding those who reported being treated for hypertension, and all adjusted models were run for the non-Hispanic white population only.

Results

Based on the combined results of the 2007 to 2009 and 2009 to 2011 CHMS, the average PbB level for adults aged 40 to 79 was 1.64 µg/dL, and approximately 37% of people in this age range met the definition of hypertension. Hypertensive individuals had higher average PbB levels than did non-hypertensive individuals, and were older, more likely to be male, and more likely to have not completed secondary school (Table 1). Those with hypertension were less likely to be current smokers, less likely to be physically active, had a higher average BMI, and were more likely to have diabetes, chronic kidney disease, and a family history of high blood pressure; 78% reported taking antihypertensive medication.

Average SBP was higher at higher levels of PbB (Table 2). For people whose PbB was in the bottom 5th percentile of the distribution, average SBP was 111.9 mmHg, compared with 122.8 mmHg for those in the 95th percentile. A similar gradient was observed for DBP. The association with hypertension was less clear. The prevalence of hypertension was 32.8% among those in the bottom 5th percentile of PbB, 33.5% among those in the 35th to the 50th percentile, and 44.8% among those in the 95th percentile. The variability in the prevalence estimates, as indicated by relatively wide confidence intervals, adds uncertainty to the nature of this association.

The results of the linear regression models for SBP and DBP are shown in Appendix Table A; only the coefficients for PbB are presented. Most unadjusted

models show a significant association between SBP and PbB, but this does not hold when other risk factors are taken into account. The adjusted model suggests that a significant association exists between SBP and PbB for 40- to 54-year-olds (Model 2), but not for 55- to 79-year-olds (Model 3), thus confirming the modifying effect of age. Although only borderline significant—likely due to lack of power because of reduced sample size—the model coefficients were similar when the sample was restricted to 40- to 54-year-olds not treated for hypertension (Model 2a). The model for men aged 40 to 79 (Model 4) approached statistical

significance, but the model for women aged 40 to 79 (Model 5) did not. The curves in Figure 1 show model-adjusted predicted values of SBP across PbB values ranging from 0.54 (average of the 5th percentile of PbB) to 6.14 $\mu\text{g}/\text{dL}$ (average of the 95th percentile of PbB) with all other covariates held constant at the study population's overall averages (Table 1). The statistically significant results for 40- to 54-year-olds suggest that a 1- $\mu\text{g}/\text{dL}$ increase in PbB from 0.54 to 3 $\mu\text{g}/\text{dL}$ would have a corresponding increase of approximately 2 mmHg in SBP. Conversely, a 1 $\mu\text{g}/\text{dL}$ increase in PbB from 3 to 4 $\mu\text{g}/\text{dL}$ would result in a decrease in SBP of somewhat less than 1 mmHg. In other words, the association suggests that an average person aged 40 to 54 with lower levels of PbB would experience a 1- to 2-mmHg increase in SBP for every 1- $\mu\text{g}/\text{dL}$ increase in PbB up to approximately 3 $\mu\text{g}/\text{dL}$ of PbB, beyond which, a slight decrease in SBP would occur.

The adjusted models for DBP (Appendix Table A) show a statistically significant association with PbB (Model 1), which appears to be driven by 40- to 54-year-olds (Model 2) and men (Model 4). These results hold when the analysis is limited to those not treated for hypertension (Models 1a, 2a, and 4a). The curves in Figure 2 show the model-adjusted predicted values of DBP across PbB values ranging from 0.54 to 6.14 $\mu\text{g}/\text{dL}$, with all other covariates held constant at the study population's overall averages (Table 1). The statistically significant results suggest that an increase of a 1- $\mu\text{g}/\text{dL}$ in PbB from 0.54 to 3 $\mu\text{g}/\text{dL}$ would have a corresponding increase of 2 to 3 mmHg in DBP for those in the younger age group (Model 2) and for men (Model 4). At higher PbB levels, a 1- $\mu\text{g}/\text{dL}$ increase in PbB would result in a less-than-1-mmHg decrease in DBP.

The results of the logistic regression models for hypertension appear in Appendix Table B. In the adjusted models for those aged 40 to 79 and 40 to 54, the PbB linear term and spline knot 1 for PbB were statistically significant. These results suggest a decrease in risk of hypertension for PbB levels

from 0 to 0.65 $\mu\text{g}/\text{dL}$, and a slight increase in risk at PbB levels from 0.65 to 1.6 $\mu\text{g}/\text{dL}$. However, alternative specifications of PbB in the models, namely, log-transformed and categorized into quartiles, found no statistically significant association between PbB and hypertension (data not shown). Furthermore, the LSGM values of PbB for hypertensive versus non-hypertensive individuals across age and sex strata suggest that there is no significant association between PbB and hypertension (Figure 3).

Discussion

Using data for 2007 to 2011 from the CHMS, the present study examined associations between blood lead levels and blood pressure among Canadians aged 40 to 79. People in this age range had an average PbB level of 1.64 $\mu\text{g}/\text{dL}$, and 37% were hypertensive. Although average PbB levels were higher among those who were hypertensive, these people also tended to have other hypertension risk factors (diabetes, family history of high blood pressure).

Statistically significant associations between PbB levels and SBP and DBP emerged for specific populations when other risk factors were taken into account. A significant curvilinear association was observed between PbB and SBP for 40- to 54-year-olds, where those with lower levels of PbB would experience a 1- to 2-mmHg increase in SBP for every 1- $\mu\text{g}/\text{dL}$ increase in PbB up to a level of 3 $\mu\text{g}/\text{dL}$, after which a slight decrease in SBP would occur. A similar curvilinear association was observed between PbB and DBP for 40- to 54-year-olds and for men. These findings held when the analysis was restricted to those not treated for hypertension.

Although statistically significant, the effects of increasing levels of PbB on SBP and DBP are modest compared with the effects of changes in other risk factors. For example, earlier studies have shown that lifestyle modifications such as reduced sodium and alcohol consumption, smoking cessation, and weight loss can decrease blood pressure levels.³⁹⁻⁴³

What is already known on this subject?

- Hypertension is recognized as the leading risk factor for cardiovascular disease, but its cause is not always known.
- There is increasing interest in the potential role of exposure to environmental chemicals, including lead, in cardiovascular effects.
- The link between lead exposure and hypertension is supported by animal studies, but results from human studies vary.

What does this study add?

- The Canadian Health Measures Survey is the first national population-based survey to allow for the examination of the association between blood lead (PbB) and hypertension in Canada since the 1978-1979 Canada Health Survey.
- The association between PbB and blood pressure varies by sex and age group.
- PbB levels have a modest association with blood pressure and no association with hypertension prevalence among Canadian adults aged 40 to 79.

In this study, BMI and daily alcohol consumption were significantly associated with SBP and DBP when other covariates including PbB were taken into account (data not shown).

The findings for hypertension are slightly different. The spline model results suggest a decline in hypertension risk if PbB levels increase within the lowest 5th percentile, with a slight increase in risk as PbB levels rise from the 5th to the 50th percentile. Beyond that, there is no change in risk. Whether this indicates a true association between PbB and hypertension is unclear. It may simply reflect the heterogeneity of the population with very low levels of PbB. Furthermore, when all covariates were taken into account, the LSGMs of PbB for hypertensive and non-hypertensive individuals did not differ, even when stratified by age group and by sex.

Differences in study design, populations of interest, parameter specifications and analytical methodology make comparisons with other studies challenging. However, the modest association between PbB and SBP and DBP in this study has been reported elsewhere. According to *The National Toxicology Program Monograph on Health Effects of Low-Level Lead*,¹¹ 29 cross-sectional analyses support a small increase in SBP or DBP with increases in PbB; 17 analyses did not support a relationship. Using National Health and Nutrition Examination Survey (NHANES) data, Scinicariello et al. found associations between PbB levels and DBP for untreated non-Hispanic white men and women aged 20 or older, but not between PbB and SBP.⁴⁴ Furthermore, the National Toxicology Program reported increased prevalence of hypertension with increases in PbB among certain populations but not in others. Using different years of NHANES data, Scinicariello et al. and Muntner et al. reported significant associations between PbB and hypertension for non-Hispanic black men and Mexican Americans, but no significant association for non-Hispanic whites aged 20 or older of either sex.^{44,45} Given the race/ethnicity composition of the CHMS respondents in the present study (83% reported non-Hispanic white; 2%,

non-Hispanic black; and the remaining 15%, other races/ethnicities), it was not possible to stratify analyses by race/ethnicity. However, restricting the analytical population to non-Hispanic white left the null association between PbB and hypertension unchanged (data not shown).

The present analysis has several strengths. It is population-based, with a large sample size. SBP and DBP were assessed objectively using an automated device with high quality control. The trace metal analyses were done independently and blinded to the BP results. The methodology ensured that PbB was well specified in the models. To isolate the association with lead exposure, several important risk factors for hypertension were considered in the statistical analysis. The study pertained only to adults aged 40 to 79 in order to target people with a higher risk of hypertension and higher levels of past exposure to lead.

This analysis also has a number of limitations. The CHMS is a cross-sectional survey; thus, the study examined the association between a single measure of PbB and of blood pressure at a single point in time. Whether the PbB measure represents recent exposure or movement of PbB from bone into blood from previous exposures is unknown, as are the timing, frequency and duration of exposure that may have contributed to the observed associations. In other studies,¹¹ bone lead levels have been more consistently associated with BP levels, but the CHMS did not measure bone lead. Information about medications and past medical diagnoses was gathered by questionnaire and not verified in medical records. This may have led to some misclassification of conditions such as diabetes. The combined cycle 1/cycle 2 response rate was 53.5%,²⁹ and although applying the survey weights ensured that the sample was representative of the target population, bias might exist if non-respondents differed systematically from respondents.

Conclusion

Taking into account a number of risk factors for hypertension, this population-based study found a modest association between blood lead levels and blood pressure, and no association between blood lead levels and hypertension prevalence among Canadian adults aged 40 to 79.

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Appendix

Table A
Association between blood lead and systolic and diastolic blood pressure, by age group and sex, household population aged 40 to 79, Canada, 2007 to 2011

Model, age group and sex	Systolic blood pressure								Diastolic blood pressure							
	Unadjusted				Adjusted [†]				Unadjusted				Adjusted [†]			
	95% confidence interval				95% confidence interval				95% confidence interval				95% confidence interval			
	Beta	from	to	p-value	Beta	from	to	p-value	Beta	from	to	p-value	Beta	from	to	p-value
Model 1. Aged 40 to 79																
Blood lead linear (µg/dL)	5.17*	2.89	7.45	0.000	1.85	-0.20	3.90	0.075	1.83*	0.60	3.07	0.005	1.91*	0.75	3.08	0.002
Blood lead restricted cubic spline	-0.49*	-0.78	-0.19	0.003	-0.15	-0.40	0.09	0.208	-0.18*	-0.32	-0.05	0.011	-0.19*	-0.33	-0.06	0.006
Model 1a. Untreated for hypertension[‡]																
Blood lead linear (µg/dL)	5.22*	2.82	7.63	0.000	1.50	-1.00	4.00	0.227	2.69*	1.17	4.22	0.001	1.99*	0.42	3.56	0.015
Blood lead restricted cubic spline	-0.53*	-0.82	-0.24	0.001	-0.16	-0.44	0.13	0.266	-0.28*	-0.46	-0.10	0.004	-0.21*	-0.39	-0.02	0.031
Model 2. Aged 40 to 54																
Blood lead linear (µg/dL)	3.75*	1.43	6.07	0.003	2.63*	-0.03	5.29	0.052	3.15*	1.33	4.97	0.002	2.28*	0.31	4.26	0.025
Blood lead restricted cubic spline	-0.42*	-0.74	-0.10	0.012	-0.31*	-0.62	0.00	0.053	-0.37*	-0.61	-0.13	0.004	-0.29*	-0.54	-0.03	0.029
Model 2a. Untreated for hypertension[‡]																
Blood lead linear (µg/dL)	4.45*	1.95	6.95	0.001	2.80	-0.40	6.00	0.084	3.80*	2.02	5.59	0.000	2.83*	0.59	5.08	0.016
Blood lead restricted cubic spline	-0.51*	-0.84	-0.17	0.005	-0.33	-0.69	0.04	0.076	-0.44*	-0.67	-0.21	0.001	-0.33*	-0.61	-0.06	0.019
Model 3. Aged 55 to 79																
Blood lead linear (µg/dL)	1.51	-1.76	4.77	0.350	0.86	-2.41	4.12	0.593	1.41	-0.54	3.37	0.149	1.07	-0.73	2.87	0.230
Blood lead restricted cubic spline	-0.07	-0.47	0.34	0.736	-0.00	-0.39	0.39	0.991	-0.11	-0.34	0.11	0.308	-0.08	-0.28	0.12	0.441
Model 3a. Untreated for hypertension[‡]																
Blood lead linear (µg/dL)	0.50	-2.90	3.91	0.763	0.04	-3.43	3.50	0.983	0.93	-1.77	3.63	0.484	0.35	-2.05	2.75	0.766
Blood lead restricted cubic spline	0.00	-0.41	0.41	0.994	0.04	-0.37	0.45	0.835	-0.06	-0.37	0.25	0.700	0.00	-0.28	0.28	0.991
Model 4. Men aged 40 to 79																
Blood lead linear (µg/dL)	4.02*	1.54	6.50	0.003	2.17	-0.08	4.42	0.058	0.88	-0.53	2.30	0.210	2.36*	0.94	3.79	0.002
Blood lead restricted cubic spline	-0.39*	-0.68	-0.10	0.010	-0.21	-0.46	0.04	0.090	-0.10	-0.25	0.05	0.191	-0.25*	-0.40	-0.10	0.002
Model 4a. Untreated for hypertension[‡]																
Blood lead linear (µg/dL)	2.94	-0.27	6.16	0.071	0.85	-1.86	3.56	0.522	1.75*	0.20	3.30	0.029	2.46*	0.95	3.98	0.003
Blood lead restricted cubic spline	-0.29	-0.69	0.10	0.138	-0.07	-0.40	0.26	0.654	-0.20*	-0.37	-0.02	0.034	-0.25*	-0.44	-0.07	0.010
Model 5. Women aged 40 to 79																
Blood lead linear (µg/dL)	5.25*	1.48	9.03	0.008	0.76	-2.72	4.24	0.656	0.98	-1.00	2.95	0.319	1.43	-0.51	3.38	0.142
Blood lead restricted cubic spline	-0.42	-1.05	0.20	0.176	0.02	-0.55	0.59	0.935	-0.08	-0.34	0.18	0.528	-0.12	-0.37	0.12	0.313
Model 5a. Untreated for hypertension[‡]																
Blood lead linear (µg/dL)	5.53*	2.01	9.04	0.003	1.88	-1.89	5.65	0.314	1.39	-1.07	3.85	0.253	1.66	-0.97	4.29	0.205
Blood lead restricted cubic spline	-0.56*	-1.11	-0.01	0.046	-0.22	-0.76	0.32	0.403	-0.14	-0.50	0.22	0.427	-0.17	-0.52	0.18	0.336

* significant (p < 0.05)

[†] adjusted for age, sex, education, smoking, alcohol, physical activity, BMI, non-HDL cholesterol, diabetes, chronic kidney disease, family history of high blood pressure, antihypertension medication use

[‡] excludes those who reported using antihypertensive medication; antihypertensive medication use dropped from adjusted models

Notes: Values of covariates except age held at population means in Table 1; age centered at 50. Age-group-stratified models include age as covariate; sex-stratified models exclude sex as covariate. P-values correspond to Satterthwaite-adjusted F-test results.

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

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Table B
Association between blood lead and hypertension, by age group and sex, household population aged 40 to 79, Canada, 2007 to 2011

Age group and sex	Hypertension							
	Unadjusted				Adjusted [†]			
	Beta	95% confidence interval		p-value	Beta	95% confidence interval		p-value
from		to	from			to		
Aged 40 to 79								
Blood lead linear (µg/dL)	-4.00*	-7.39	-0.62	0.022	-3.87*	-7.46	-0.29	0.035
Blood lead spline knot 1	4.60*	1.09	8.11	0.012	4.00*	0.32	7.67	0.034
Blood lead spline knot 2	-0.48*	-0.91	-0.05	0.031	-0.13	-0.78	0.51	0.671
Blood lead spline knot 3	-0.14	-0.35	0.08	0.197	0.02	-0.25	0.29	0.887
Aged 40 to 54								
Blood lead linear (µg/dL)	-5.80*	-9.07	-2.53	0.001	-4.93*	-8.47	-1.39	0.008
Blood lead spline knot 1	6.19*	2.70	9.69	0.001	5.09*	1.03	9.14	0.016
Blood lead spline knot 2	-0.50	-1.47	0.46	0.295	-0.37	-1.65	0.92	0.562
Blood lead spline knot 3	0.03	-0.71	0.77	0.932	0.23	-0.60	1.05	0.578
Aged 55 to 79								
Blood lead linear (µg/dL)	-3.51	-16.82	9.80	0.591	-4.70	-15.83	6.43	0.392
Blood lead spline knot 1	3.68	-9.99	17.35	0.583	4.82	-6.73	16.37	0.398
Blood lead spline knot 2	-0.13	-0.91	0.64	0.723	-0.02	-0.89	0.84	0.953
Blood lead spline knot 3	-0.02	-0.30	0.26	0.871	-0.09	-0.42	0.25	0.600
Men								
Blood lead linear (µg/dL)	-9.20	-19.01	0.61	0.065	-6.37	-15.02	2.29	0.142
Blood lead spline knot 1	9.38	-0.82	19.58	0.070	6.16	-2.91	15.23	0.174
Blood lead spline knot 2	-0.05	-0.88	0.79	0.911	0.23	-0.92	1.37	0.689
Blood lead spline knot 3	-0.20	-0.55	0.16	0.270	-0.03	-0.48	0.42	0.898
Women								
Blood lead linear (µg/dL)	-4.09*	-8.18	0.01	0.050	-4.18	-8.78	0.42	0.073
Blood lead spline knot 1	4.94*	0.59	9.29	0.028	4.60	-0.26	9.45	0.063
Blood lead spline knot 2	-0.79*	-1.52	-0.05	0.038	-0.47	-1.49	0.55	0.354
Blood lead spline knot 3	-0.01	-0.61	0.58	0.965	0.08	-0.57	0.73	0.799

* significant ($p < 0.05$)

[†] adjusted for age, sex, education, smoking, alcohol, physical activity, BMI, non-HDL cholesterol, diabetes, chronic kidney disease and family history of high blood pressure

Notes: Values of covariates except age held at population means in Table 1; age centered at 50. Age-group-stratified models include age as covariate; sex-stratified models exclude sex as covariate. P-values correspond to Satterthwaite-adjusted F-test results. Respondents with missing value for average daily use of alcohol (n=43) were excluded because small cell size introduced instability into models when stratified by age group. Together, the linear and spline knot components of blood lead are statistically significant at $p < 0.01$ in the unadjusted model for 40- to 79-year-olds.

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.