

# Drinking water contaminants in California and hypertensive disorders in pregnancy

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**Background:** Environmental pollutants have been associated with hypertensive disorders in pregnancy including gestational hypertension, preeclampsia, and eclampsia, though few have focused on drinking water contamination. Water pollution can be an important source of exposures that may contribute to adverse pregnancy outcomes.

**Methods:** We linked water quality data on 13 contaminants and two violations from the California Communities Environmental Health Screening Tool to birth records from vital statistics and hospital discharge records (2007–2012) to examine the relationship between drinking water contamination and hypertensive disorders in pregnancy. We examined contaminants in single- and multipollutant models. Additionally, we examined if the relationship between water contamination and hypertensive disorders in pregnancy differed by neighborhood poverty, individual socioeconomic status, and race/ethnicity.

**Results:** Arsenic, nitrate, trihalomethane, hexavalent chromium, and uranium were detected in a majority of water systems. Increased risk of hypertensive disorders in pregnancy was modestly associated with exposure to cadmium, lead, trihalomethane, and hexavalent chromium in drinking water after adjusting for covariates in single pollutant models with odds ratios ranging from 1.01 to 1.08. In multipollutant models, cadmium was consistent, lead and trihalomethane were stronger, and additional contaminants were associated with hypertensive disorders in pregnancy including trichloroethylene, 1,2-Dibromo-3-chloropropane, nitrate, and tetrachloroethylene. Other contaminants either showed null results or modest inverse associations. The relationship between water contaminants and hypertensive disorders in pregnancy did not differ by neighborhood poverty.

**Conclusions:** We found increased risk of hypertensive disorders in pregnancy associated with exposure to several contaminants in drinking water in California. Results for cadmium, lead, trihalomethane, and hexavalent chromium were robust in multipollutant models.

**Keywords:** Pollution, Water contaminant, Preterm birth, Environmental justice, Health disparities

Hypertensive disorders during pregnancy are a common medical problem, complicating 8–10% of pregnancies. Hypertensive

disorders in pregnancy include chronic hypertension, gestational hypertension, preeclampsia, eclampsia, and preeclampsia superimposed on chronic hypertension.<sup>1</sup> Hypertensive disorders in pregnancy are detrimental to short-term and long-term health of the mother and child.<sup>2</sup>

The causes of hypertensive disorders in pregnancy remain incompletely understood; risk factors include maternal age, pre-pregnancy chronic hypertension, body mass index (BMI), gestational diabetes, multiple pregnancy, anemia, and family history of hypertension.<sup>3</sup> Environmental contaminants have been associated with hypertensive disorders in pregnancy,<sup>3–8</sup> specifically gestational hypertension,<sup>2,9</sup> and preeclampsia.<sup>10,11</sup> The majority of these studies have examined air pollution,<sup>5–7,12–17</sup> though others have examined exposures such as lead,<sup>9</sup> cadmium,<sup>18,19</sup> and pesticides.<sup>20,21</sup> A few studies have found gestational hypertension and preeclampsia associated with several contaminants in drinking water, including salinity in Bangladesh,<sup>22</sup> bacteria in Canada,<sup>23</sup> and perfluoroalkyl substances in Ohio.<sup>24</sup> Additionally, arsenic and fluoride in drinking water have been associated with hypertension among nonpregnant adults in Chile<sup>25</sup> and Iran,<sup>26</sup>

**Editors' note:** Related articles appear on pages XXX and XXX.

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Supported by the National Institute of Environmental Health Sciences (R03ES028368 and R01ES031261) and Superfund Research Program (P42ES004705).

The environmental exposure data are publicly available online (<https://oehha.ca.gov/calenviroscreen/report/calenviroscreen-30>). The health outcome data are not publicly available and were obtained from the Office of Statewide Health Planning and Development in California (<https://oshpd.ca.gov/data-and-reports>). Statistical code for analyses is available upon request.

**SDC** Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article ([www.environmental-epidemiology.com](http://www.environmental-epidemiology.com)).

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Environmental Epidemiology (2021) 5:e149

Received: 3 December 2020; Accepted 4 March 2021

Published online 2 April 2021

DOI: 10.1097/EE9.000000000000149

## What this study adds

This is the first study to examine widespread environmental contaminants in drinking water and their impact on hypertensive disorders in pregnancy across California from 2007 to 2012. The few previous have focused on salinity, bacteria, and perfluoroalkyl substances. We found increased risk of hypertensive disorders in pregnancy associated with exposure to several contaminants in drinking water in California, with most robust associations for cadmium, lead, trihalomethane, and hexavalent chromium. These findings add to growing evidence that drinking water contamination remains a potential threat to public health and requires further monitoring and research.

respectively. Our previous work has examined the relationship between drinking water contaminants and preterm birth.<sup>27,28</sup> Water contaminants may affect hypertensive disorders in pregnancy via biological mechanisms such as oxidative stress, epigenetic changes, endocrine disruption, and abnormal placental vascularization.

California has been battling against unsafe drinking water, which has triggered major public health concerns, especially for vulnerable and susceptible populations such as pregnant women. Despite substantial public investment in drinking water infrastructure, roughly 10% of California's public drinking water systems are out of compliance with state water quality standards, and an estimated 6 million Californians are served by systems that have been in violation at some point since 2012.<sup>29,30</sup> In 2012, the Governor of California signed Assembly Bill 685, which recognizes that every human being has the right to safe, clean, affordable, and accessible water, and specifically focuses on disadvantaged communities in rural and urban areas. Unsafe drinking water is an environmental justice concern as poor, mostly rural communities of color are disproportionately exposed to contamination threats in California.<sup>29,31–38</sup>

Challenges to studying health effects of drinking water include inconsistent or lack of testing for many chemicals in drinking water and lack of a central repository of accessible data. Recently, data on existing testing of water contaminants have been incorporated into the California Communities Environmental Health Screening Tool (CalEnviroScreen 3.0) and summarized at the census tract level. To examine the relationship between drinking water contaminants and hypertensive disorders in pregnancy in California, we linked the CalEnviroScreen 3.0 water quality data (over one compliance cycle, 2005–2013) to vital records and hospital discharge records from 2007 to 2012 for hypertensive disorders in pregnancy. Additionally, we examined the role of social vulnerability in relation to water contaminant exposure and hypertensive disorders in pregnancy. To our knowledge, no studies of the relationship between drinking water quality and maternal health outcomes have examined the extent to which social vulnerability factors may amplify observed associations between drinking water contamination and risk of hypertensive disorders in pregnancy. For this study, we hypothesized that associations between drinking water contaminants and hypertensive disorders in pregnancy may be higher in lower socioeconomic areas.

## Methods

### Study population

We used linked data from California birth certificates and maternal and infant hospital discharge records from the Office of Statewide Health Planning and Development (<https://www.oshpd.ca.gov/HID/>) from 2007 to 2012. We restricted our study population to singleton, live births between 2007 and 2012 in California with gestational ages between 22 and 44 weeks, and complete information on key covariates including maternal age, race, education, and payment source of birth costs. Births to those with prepregnancy hypertensive disorders, including preeclampsia/eclampsia superimposed on prepregnancy hypertension, were excluded from the main analysis (Figure 1).

Based on the American College of Obstetricians and Gynecologists' definition of hypertensive disorders in pregnancy,<sup>39</sup> we defined our case group as gestational hypertension (code 642.3), mild preeclampsia (code 642.4), or severe preeclampsia or eclampsia (codes 642.5 and 642.6). We examined cases overall and also severe preeclampsia and eclampsia as a separate, presumably more severely affected case group. To focus on pregnancy-related conditions, we excluded women with preexisting hypertension (codes 401–405, 642.0, 642.1, 642.2, 642.9 or "pregnancy/chronic hypertension" on birth

certificate) and preeclampsia or eclampsia superimposed on preexisting hypertension (code 642.7), though the latter was added to the case groups in a sensitivity analysis.

Protocols for the study were approved by the Committee for the Protection of Human Subjects within the Health and Human Services Agency of the State of California, Stanford University, and the University of California, San Francisco.

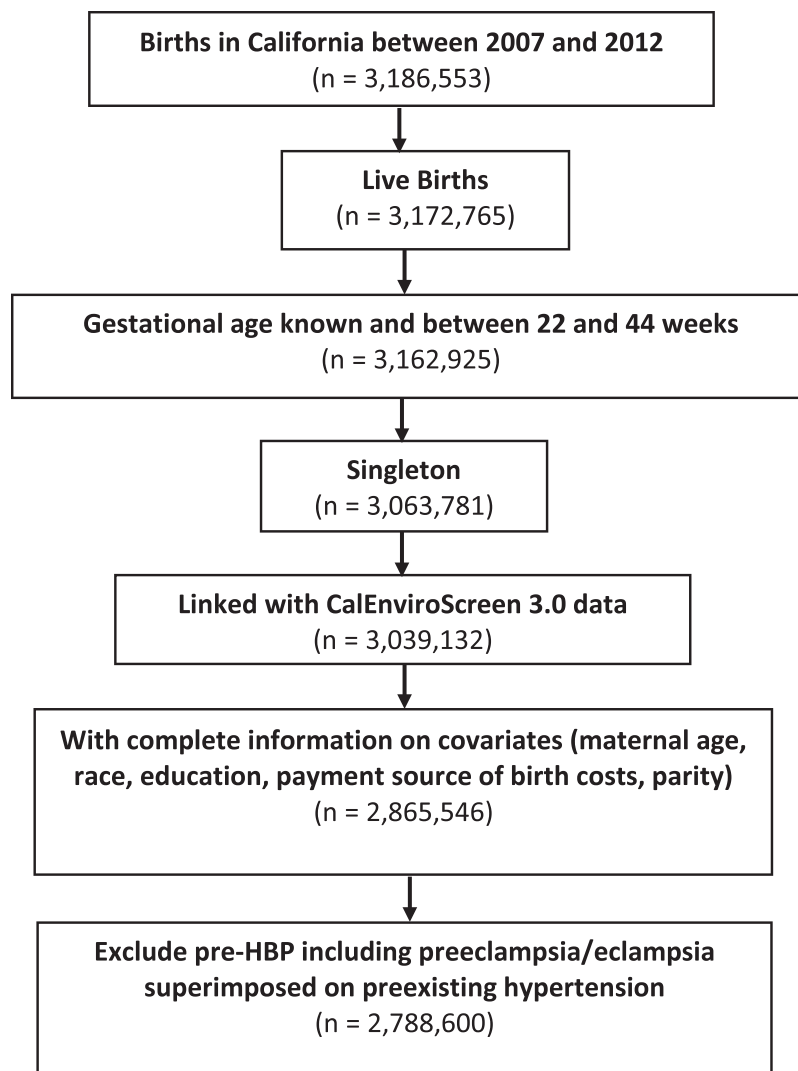
### Exposure assessment

We merged the data with the CalEnviroScreen 3.0 water quality data,<sup>40</sup> at the census tract level based on the maternal residence at birth as recorded on the birth certificate. The CalEnviroScreen was developed by CA's Environmental Protection Agency's Office of Environmental Health Hazard Assessment to evaluate the cumulative existence of multiple pollutants and stressors in communities.<sup>40,41</sup> CalEnviroScreen is used to identify communities disproportionately burdened by cumulative exposures to multiple environmental hazards and to identify disadvantaged communities for allocation of cap and trade funds generated under the Global Warming Solutions Act of 2006. The CalEnviroScreen identifies drinking water systems using the Water Boundary Tool (<http://cehtp.org/water/>) for 2443 water systems that serve 94% of the California population. An additional 471 water systems were either approximated or were estimated with a 6 × 6 mile grid to summarize groundwater concentrations ([https://nationalmap.gov/small\\_scale/a\\_plss.html](https://nationalmap.gov/small_scale/a_plss.html)). Data on groundwater, where available, were used for the remaining 5% of the California population and less than 1% were without any data on water quality. The CalEnviroScreen indicator on drinking water includes 13 contaminants and two violations (Table 1). Drinking water contaminant concentration and violation data were associated with each water system for a select group of contaminants and violations. The average concentration of each contaminant and violations by system were population-weighted to the census tract scale. Drinking water contaminant scores were assigned to each census tract by summing the percentile scores of the tract for all contaminants and violations. Further details are described elsewhere.<sup>28,42</sup>

Given the skewed distribution of most contaminants, our first approach was to dichotomize each of them, comparing the lowest three quartiles of exposure with the highest quartile (referred to for simplicity as "high" vs. "low" exposure). For contaminants with concentrations less than the maximum detection limit and violations (maximum contaminant level [MCL] and total coliform rule [TCR]) with values of zero for more than 25% of the individuals (cadmium, 1,2-Dibromo-3-chloropropane, hexavalent chromium, lead, perchlorate, tetrachloroethylene, radium 226 and radium 228, trichloroethylene, 1,2,3-trichloropropane, and MCL and TCR violations), we considered those with any versus no exposure as high and low. Five contaminants had sufficiently normal distributions to examine as continuous variables (arsenic, hexavalent chromium, nitrate, trihalomethane, and uranium).

### Statistical analyses

We used logistic regression models to evaluate associations between drinking water contaminants and hypertensive disorders in pregnancy using SAS 9.4 (SAS Institute, Inc). We considered both single pollutant (i.e., contaminant or violation) models with each one separately and multipollutant models with all contaminants in a single model (without violations, as it was considered potentially redundant). For contaminants with sufficient distributions, we performed linear regression with exposures specified as continuous including a quadratic form to detect nonlinearity. Estimates were calculated for a SD in the exposure.



**Figure 1.** Study population flow diagram for hypertensive disorders during pregnancy in California.

Outcomes were examined as all hypertensive disorders in pregnancy (including gestational hypertension, mild preeclampsia, severe preeclampsia, and eclampsia) and severe pre-eclampsia/eclampsia separately. Adjusted models included the following covariates derived from birth certificates and hospital discharge records: maternal age (years), race/ethnicity, payment source of birth costs, education, smoking during pregnancy, parity, pre-existing diabetes, and census tract poverty from CalEnviroScreen 3.0 (percent of the population living below two times the federal poverty level based on the 5-year estimate, 2011–2015), based on their potential association with exposure to environmental contaminants and hypertensive disorders in pregnancy.

We examined census tract poverty rate as a potential modifier of the relationship between each contaminant with any hypertensive disorders in pregnancy and severe preeclampsia/eclampsia. The population was dichotomized at the 15th percentile of neighborhood poverty. We performed two additional post hoc analyses to examine payer status for birth costs (private vs. public insurance) and race/ethnicity (white non-Hispanic, US-born Hispanic, and foreign-born Hispanic) as potential effect modifiers. *P* values of interaction terms were examined for statistical significance.

We conducted two sensitivity analyses: (1) we included preeclampsia/eclampsia superimposed on preexisting hypertension (code 642.7) in the case group of hypertensive disorders in pregnancy; and (2) we adjusted for prepregnancy BMI (calculated

from maternal weight divided by height-squared); because an additional 7% of women had missing BMI data, we did not include it in the primary analysis.

## Results

Of the 2.7 million births in our study, 5.3% were to women with hypertensive disorders in pregnancy (Table 2). This ethnically diverse California population was majority Hispanic (52%, with 46% of whom were US-born), 28% non-Hispanic White, 13% Asian or Pacific Islander, 5% Black, and less than 1% “other” (Table 2). Black and US-born Hispanics were over-represented among those with hypertensive disorders in pregnancy (7.6% and 6.0%, respectively, compared to overall 5.3%). Close to 80% of the population were between 18 and 34 years old at delivery and almost half had more than 12 years of education. Approximately 42% were overweight or obese and almost half had private health insurance. Reported cigarette smoking during pregnancy was rare (2%).

Arsenic, nitrate, trihalomethane, hexavalent chromium, and uranium were detected in drinking water for a majority of individuals (Table 3). The remainder of the contaminants had a majority of values below the maximum detection limit (Table 3). The water contaminants were not strongly correlated with each other (Table S1; <http://links.lww.com/EE/A133>). Few contaminants had

**Table 1.**  
Description of the drinking water contaminants in CES 3.0 database.

	Population weighted averages (units)
Arsenic	Arsenic ( $\mu\text{g/L}$ )
Cadmium	Cadmium ( $\mu\text{g/L}$ )
DBCP	1,2-Dibromo-3-chloropropane ( $\mu\text{g/L}$ )
Hex Chrom	Hexavalent Chromium ( $\mu\text{g/L}$ )
Lead	Lead ( $\mu\text{g/L}$ )
Nitrate	Nitrate (as $\text{NO}_3$ ) ( $\mu\text{g/L}$ )
Perchlorate	Perchlorate ( $\mu\text{g/L}$ )
PCE	Tetrachloroethylene ( $\mu\text{g/L}$ )
Radium	Combined Radium 226 and Radium 228 (pCi/l)
TCE	Trichloroethylene ( $\mu\text{g/L}$ )
TCP	1,2,3-trichloropropane ( $\mu\text{g/L}$ )
THM	Trihalomethane ( $\mu\text{g/L}$ )
Uranium	Uranium (pCi/l)
Violations	
MCL-V	MCL—number of times a system had an unacceptably high level of a specific contaminant
TCR-V	TCR—number of times a system had a positive test in more than 5% of samples

moderate (Pearson coefficient  $>0.4$ ) correlations including tetrachloroethylene and trichloroethylene (0.45), arsenic and TCR violations (0.43), and MCL and TCR violations (0.58).

We found increased risk of hypertensive disorders in pregnancy associated with exposure to cadmium, lead, trihalomethane, and hexavalent chromium in drinking water after adjusting for covariates, based on 95% confidence intervals (CIs) that excluded 1.0 (Table 4). For cadmium, results were consistent in multipollutant models and among the group of women with severe preeclampsia or eclampsia, with odds ratios (ORs) ranging from 1.011 to 1.15 for high versus low contaminant levels. For lead, associations were stronger in multipollutant models both for hypertensive disorders in pregnancy (OR = 1.16, 95% CI = 1.13, 1.19) and severe preeclampsia or eclampsia (OR = 1.20, 95% CI = 1.16, 1.24). In the multipollutant models, additional contaminants (trichloroethylene, 1,2-Dibromo-3-chloropropane, nitrate, and tetrachloroethylene) were associated with hypertensive disorders in pregnancy and/or preeclampsia or eclampsia.

Other contaminants either showed null results or modest inverse associations (perchlorate, tetrachloroethylene, uranium, and MCL and TCR violations). The unadjusted results (Table S2; <http://links.lww.com/EE/A133>) showed generally similar results with more of the CIs excluding 1.0 (including arsenic and severe preeclampsia or eclampsia in a single pollutant model). Results of the continuous models with quadratic forms of the exposure (for contaminants that had sufficient distributions: arsenic, hexavalent chromium, nitrate, trihalomethane, and uranium) revealed similar results. A SD change in hexavalent chromium (19.73  $\mu\text{g/L}$ ) was associated with an increased odds of hypertensive disorders in pregnancy (OR = 1.24, 95% CI = 1.20, 1.28) and severe preeclampsia/eclampsia (OR = 1.28, 95% CI = 1.23, 1.34) after adjustment for maternal age (years), race/ethnicity, payment source of birth costs, education, smoking during pregnancy, parity, preexisting diabetes, and census tract poverty. Results of nitrate were null and arsenic, trihalomethane, and uranium showed small, but inverse associations with ORs ranging from 0.95 to 0.97.

In stratified analyses, we found that the relationship between water contaminants and hypertensive disorders in pregnancy was elevated among women living in neighborhoods with  $<15\%$  of the population living below two times the federal poverty level (Table 5). This pattern was apparent for cadmium, 1,2-Dibromo-3-chloropropane, hexavalent chromium, lead, and MCL and TCR violations. When stratified by payer status for delivery costs, risk of HDP was higher among those with private insurance, particularly for cadmium, 1,2-Dibromo-3-chloropropane, and MCL and TCR violations (Table S3; <http://links.lww.com/EE/A133>).

**Table 2.**  
Study population characteristics, 2007–2012 (N = 2,788,600).

Characteristics	Total study population	Hypertensive disorders in pregnancy <sup>a</sup>
	2,788,600	147,146 (5.28%)
Race/ethnicity		
Non-Hispanic White	787,148 (28.23)	42,366 (28.79)
Non-Hispanic Black	152,862 (5.48)	11,570 (7.86)
Asian/Pacific Islander	375,617 (13.47)	14,847 (10.09)
Hispanic (US-born)	671,857 (24.09)	40,556 (27.56)
Hispanic (Foreign-born)	786,924 (28.22)	36,866 (25.05)
Other	14,192 (0.51)	941 (0.64)
Maternal age at delivery (years)		
$<18$	79,126 (2.84)	5898 (4.01)
18–34	2,228,850 (79.93)	114,677 (77.93)
$>34$	480,624 (17.24)	26,571 (18.06)
Prepregnancy BMI		
$<18.5$ (underweight)	107,962 (3.87)	3298 (2.24)
18.5–25 (normal)	1,309,183 (46.95)	50,346 (34.22)
25–30 (overweight)	670,325 (24.04)	38,372 (26.08)
$\geq 30$ (obese)	513,017 (18.40)	44,662 (30.35)
Missing	188,113 (6.75)	10,468 (7.11)
Maternal education (years)		
$<$ High school	681,936 (24.45)	34,599 (23.51)
Completed high school	736,516 (26.41)	41,571 (28.25)
$>$ High school	1,370,148 (49.13)	70,976 (48.24)
Payer for delivery costs		
Private insurance	1,294,280 (46.41)	68,658 (46.66)
Public insurance	1,494,320 (53.59)	78,488 (53.34)
Cigarette use during pregnancy		
Yes	62,794 (2.25)	3421 (2.32)
No	2,725,806 (97.75)	143,725 (97.68)
Prepregnancy diabetes		
Yes	31,200 (1.12)	4,624 (3.14)
No	2,757,400 (98.88)	142,522 (96.86)
Parity		
Nulliparous	1,106,982 (39.70)	84,527 (57.44)
Parous (1+)	1,681,618 (60.30)	62,619 (42.56)

<sup>a</sup>Those with preexisting hypertension were excluded.

Differences were more apparent for hypertensive disorders in pregnancy than severe preeclampsia/eclampsia. Similar results were observed when stratified by race/ethnicity (Table S4; <http://links.lww.com/EE/A133>). Stronger associations were observed among White, non-Hispanic mothers between cadmium, 1,2-Dibromo-3-chloropropane, lead, and nitrate. One pollutant, trihalomethane, was associated with hypertensive disorders in pregnancy among Hispanic mothers, but not White mothers.

Sensitivity analyses including those with preeclampsia or eclampsia superimposed on preexisting hypertension (code 642.7) resulted in an additional 9921 cases, though the results did not change substantially (Table S5; <http://links.lww.com/EE/A133>). Additionally, when adjusting for BMI, which excluded an extra 6.7% of the sample, results were similar (Table S6; <http://links.lww.com/EE/A133>).

## Discussion

We found increased risk of hypertensive disorders in pregnancy associated with exposure to cadmium, lead, trihalomethane, and hexavalent chromium in drinking water in California. Results for cadmium and lead were robust in multipollutant models and stronger associations were found with the more severe types of hypertensive disorders in pregnancy, preeclampsia, and eclampsia. Multipollutant models also suggested additional contaminants should be examined further including trichloroethylene, 1,2-dibromo-3-chloropropane, nitrate, and tetrachloroethylene.

Our results support previous findings of associations between hypertensive disorders in pregnancy and cadmium, lead, and

**Table 3.**  
**Distribution of water contaminants.**

Pollutants	Total study population						Hypertensive disorders in pregnancy						MCL <sup>a</sup>
	N = 2,788,600						N = 147,146 (5.28%)						
	Min	25th	50th	75th	Max	Mean (SD)	Min	25th	50th	75th	Max	Mean (SD)	
Arsenic	<MDL	0.20	0.79	1.66	32.09	1.29 (2.06)	<MDL	0.16	0.79	1.66	32.09	1.27 (2.03)	10
Cadmium	<MDL	<MDL	<MDL	<MDL	4.17	0.01 (0.08)	<MDL	<MDL	<MDL	<MDL	4.17	0.01 (0.08)	5
DBCP	<MDL	<MDL	<MDL	<MDL	1.29	0.02 (0.07)	<MDL	<MDL	<MDL	<MDL	1.29	0.02 (0.08)	0.2
Hex Chrom	<MDL	<MDL	0.49	1.57	362.60	2.77 (19.80)	<MDL	0.75	0.56	1.62	362.60	2.77 (18.35)	NA
Lead	<MDL	<MDL	<MDL	0.02	205.13	0.19 (3.60)	<MDL	<MDL	<MDL	0.03	205.13	0.18 (3.02)	15
Nitrate	1.41	1.75	5.71	10.82	85.48	7.70 (7.29)	1.41	1.75	5.71	10.39	85.48	7.62 (7.20)	10
Perchlorate	<MDL	<MDL	<MDL	<MDL	5.35	0.17 (0.64)	<MDL	<MDL	<MDL	<MDL	5.35	0.16 (0.61)	6
PCE	<MDL	<MDL	<MDL	0.09	16.43	0.16 (0.86)	<MDL	<MDL	<MDL	0.09	16.43	0.16 (0.85)	5
Radium	<MDL	<MDL	<MDL	0.16	10.96	0.15 (0.44)	<MDL	0.75	<MDL	0.13	10.96	0.15 (0.53)	5 pCi/L
TCE	<MDL	<MDL	<MDL	0.07	21.49	0.30 (1.44)	<MDL	<MDL	<MDL	0.08	21.49	0.30 (1.29)	5
TCP	<MDL	<MDL	<MDL	<MDL	1.41	0.00 (0.02)	<MDL	<MDL	<MDL	<MDL	1.41	0.00 (0.02)	0.005
THM	<MDL	7.07	27.91	44.86	96.80	27.35 (19.82)	<MDL	6.15	25.96	45.23	96.80	26.94 (19.87)	80
Uranium	0.71	0.87	1.89	3.10	137.65	2.69 (3.65)	0.71	0.75	1.84	3.02	137.65	2.60 (3.61)	20 pCi/L
MCL-V	<MDL	<MDL	<MDL	<MDL	30.00	0.19 (0.74)	<MDL	<MDL	<MDL	<MDL	30.00	0.18 (0.69)	NA
TCR-V	<MDL	<MDL	<MDL	<MDL	32.52	0.47 (2.41)	<MDL	<MDL	<MDL	<MDL	32.52	0.45 (2.35)	5%

<sup>a</sup>µg/L unless otherwise noted.

DBCP indicates 1,2-Dibromo-3-chloropropane; Hex Chrom, hexavalent chromium; MDL, maximum detection limit; NA, not applicable; PCE, tetrachloroethylene; TCE, Trichloroethylene; TCP, 1,2,3-trichloropropane; THM, trihalomethane.

**Table 4.**  
**Adjusted ORs and 95% CIs of single and multipollutant models for HPD and severe preeclampsia/eclampsia.**

Pollutant (dichotomized)	Single pollutant model		Multipollutant model	
	HDP adjusted <sup>a</sup> OR (95% CI)	Severe PE/eclampsia adjusted <sup>a</sup> OR (95% CI)	HDP adjusted <sup>a</sup> OR (95% CI)	Severe PE/eclampsia adjusted <sup>a</sup> OR (95% CI)
Arsenic (1.66 µg/L)	0.99 (0.97, 1.00)	0.99 (0.97, 1.01)	1.00 (0.97, 1.03)	0.99 (0.95, 1.04)
Cadmium	1.15 (1.12, 1.17)	1.12 (1.09, 1.16)	1.11 (1.06, 1.17)	1.11 (1.04, 1.18)
DBCP	1.06 (1.05, 1.08)	1.07 (1.05, 1.09)	1.03 (0.99, 1.06)	1.10 (1.06, 1.15)
Hex Chrom (1.57 µg/L)	1.08 (1.07, 1.10)	1.07 (1.05, 1.09)	1.08 (1.05, 1.11)	1.00 (0.96, 1.04)
Lead (0.02 µg/L)	1.08 (1.06, 1.09)	1.09 (1.07, 1.11)	1.16 (1.13, 1.19)	1.20 (1.16, 1.24)
Nitrate (10.82 µg/L)	0.99 (0.98, 1.00)	1.01 (0.99, 1.03)	1.03 (1.00, 1.05)	1.11 (1.07, 1.15)
Perchlorate	0.93 (0.92, 0.94)	0.91 (0.90, 0.93)	0.91 (0.89, 0.93)	0.87 (0.84, 0.89)
PCE (0.09 µg/L)	0.96 (0.95, 0.97)	0.98 (0.96, 0.99)	0.97 (0.94, 1.00)	1.07 (1.03, 1.12)
Radium (0.16 pCi/L)	0.98 (0.97, 1.00)	1.03 (1.01, 1.05)	1.00 (0.98, 1.03)	1.02 (0.99, 1.06)
TCE (0.07 µg/L)	0.95 (0.94, 0.97)	0.97 (0.95, 0.98)	1.03 (1.00, 1.06)	0.95 (0.91, 1.00)
TCP	0.96 (0.95, 0.98)	0.98 (0.96, 1.00)	1.01 (0.99, 1.04)	0.96 (0.93, 1.00)
THM (44.86 µg/L)	0.97 (0.96, 0.98)	0.97 (0.96, 0.99)	1.05 (1.02, 1.07)	1.09 (1.05, 1.13)
Uranium (3.10 pCi/L)	0.95 (0.94, 0.96)	0.95 (0.93, 0.97)	0.95 (0.92, 0.97)	0.92 (0.89, 0.95)
MCL violations <sup>b</sup>	1.00 (0.99, 1.02)	0.99 (0.97, 1.01)		
TCR violations <sup>b</sup>	1.03 (1.02, 1.05)	1.03 (1.01, 1.05)		

<sup>a</sup>Models were adjusted for maternal age (years), race/ethnicity, payment source of birth costs, education, smoking during pregnancy, parity and preexisting diabetes.

<sup>b</sup>TCR and MCL violations were not included in the multipollutant model since these are not measured levels of contaminants

DBCP indicates 1,2-Dibromo-3-chloropropane; HDP, hypertensive disorders in pregnancy; Hex Chrom, hexavalent chromium; PCE, tetrachloroethylene; PE, preeclampsia; TCE, trichloroethylene; TCP, 1,2,3-trichloropropane; THM, trihalomethane.

hexavalent chromium, though previous studies were not sourced to water specifically. For example, a systematic review and meta-analysis reported that an increase of 1 µg/dL blood lead level was associated with a 1.6% increase in the likelihood of preeclampsia, making lead exposure one of the strongest known risk factors for preeclampsia.<sup>43</sup> In a study of almost three million pregnant women in the United States, ambient lead levels were associated with hypertensive disorders in pregnancy. They observed a 4% increase in hypertensive disorders in pregnancy per 0.05 mg/m<sup>3</sup> increase in seasonal average lead level at conception and birth.<sup>9</sup> Similarly, these findings are consistent with long-established evidence that lead is associated with risk of hypertension in nonpregnant individuals.<sup>44</sup> Potential mechanisms by which elevated lead may affect hypertensive disorders in pregnancy include its positive association with the vasoconstrictors endothelin,<sup>45</sup> adrenaline, and noradrenaline,<sup>46</sup> and its negative association with nitric oxide<sup>46</sup> and adenosine triphosphatase,<sup>47</sup> which are vasodilators.<sup>22</sup>

Previous studies have shown associations between cadmium and hypertensive disorders in pregnancy. Studies have found associations between urinary cadmium and hypertensive disorders in pregnancy in the United States,<sup>48</sup> China,<sup>19,49</sup> Yugoslavia,<sup>18</sup> and Democratic Republic of Congo,<sup>50</sup> though not in South Africa.<sup>51</sup> Additionally, Liu et al. found a significant interaction between cadmium exposure and maternal socioeconomic status.<sup>19</sup> Cadmium accumulates in the placenta<sup>52</sup> and may affect placental function as a source of reactive oxygen species and oxidative stress<sup>53</sup> and pro-inflammatory cytokines, which may damage placental blood vessels and increase maternal blood pressure.<sup>18,22</sup>

Chromium was found to be higher among those with hypertensive disorders in pregnancy in two studies<sup>50,51,54</sup>; however, the measurements were limited by the inability to distinguish between benign chromium and toxic hexavalent chromium. These studies also examined urinary levels of arsenic in women with and without hypertensive disorders in pregnancy, but produced inconsistent results in Democratic Republic of Congo and South

**Table 5.**  
**Stratification by neighborhood poverty.**

Pollutant (dichotomized)	Hypertensive disorders in pregnancy		Severe preeclampsia/eclampsia	
	Low poverty	High poverty	Low poverty adjusted <sup>a</sup>	High poverty
	Adjusted <sup>a</sup> OR (95% CI)	Adjusted <sup>a</sup> OR (95% CI)	OR (95% CI)	Adjusted <sup>a</sup> OR (95% CI)
Arsenic (1.66 µg/L)	0.97 (0.96, 0.99)	1.01 (0.99, 1.03)	0.98 (0.95, 1.00)	1.03 (1.00, 1.05)
Cadmium	1.18 (1.15, 1.21)	1.05 (1.01, 1.09)	1.15 (1.10, 1.19)	1.03 (0.98, 1.09)
DBCP	1.13 (1.11, 1.15)	0.98 (0.96, 1.00)	1.14 (1.11, 1.16)	1.00 (0.97, 1.02)
Hex Chrom (1.57 µg/L)	1.12 (1.10, 1.14)	1.03 (1.01, 1.06)	1.12 (1.09, 1.14)	1.02 (0.99, 1.04)
Lead (0.02 µg/L)	1.10 (1.08, 1.11)	1.03 (1.02, 1.05)	1.13 (1.10, 1.15)	1.02 (1.00, 1.05)
Nitrate (10.82 µg/L)	1.02 (1.01, 1.04)	0.95 (0.94, 0.97)	1.02 (0.99, 1.04)	1.01 (0.98, 1.03)
Perchlorate	0.93 (0.92, 0.95)	0.90 (0.89, 0.92)	0.92 (0.89, 0.94)	0.89 (0.87, 0.91)
PCE (0.09 µg/L)	0.93 (0.91, 0.95)	1.00 (0.98, 1.01)	0.94 (0.92, 0.97)	1.02 (1.00, 1.05)
Radium (0.16 pCi/L)	1.01 (0.99, 1.03)	0.93 (0.91, 0.96)	1.07 (1.04, 1.10)	0.95 (0.92, 0.99)
TCE (0.07 µg/L)	0.92 (0.90, 0.93)	1.01 (0.99, 1.02)	0.91 (0.89, 0.94)	1.04 (1.02, 1.06)
TCP	0.99 (0.97, 1.00)	0.94 (0.92, 0.96)	0.99 (0.96, 1.01)	0.98 (0.96, 1.01)
THM (44.86 µg/L)	0.90 (0.89, 0.92)	1.06 (1.05, 1.08)	0.90 (0.88, 0.92)	1.08 (1.05, 1.10)
Uranium (3.10 pCi/L)	0.95 (0.93, 0.96)	0.96 (0.94, 0.98)	0.93 (0.90, 0.95)	0.98 (0.96, 1.01)
MCL violations	1.04 (1.02, 1.06)	0.96 (0.94, 0.98)	1.03 (1.00, 1.06)	0.95 (0.92, 0.97)
TCR violations	1.08 (1.05, 1.10)	0.99 (0.97, 1.01)	1.07 (1.05, 1.10)	1.00 (0.98, 1.03)

<sup>a</sup>Models were adjusted for maternal age (years), race/ethnicity, payment source of birth costs, education, smoking during pregnancy, parity, preexisting diabetes, and census tract poverty. DBCP indicates 1,2-Dibromo-3-chloropropane; Hex Chrom, hexavalent chromium; PCE, tetrachloroethylene; TCE, trichloroethylene; TCP, 1,2,3-trichloropropane; THM, trihalomethane.

Africa.<sup>50,51</sup> An additional study in Mexico was similarly inconclusive.<sup>54</sup> To our knowledge this is the first study to find associations between risk of hypertensive disorders in pregnancy and additional contaminants such as trihalomethane, trichloroethylene, 1,2-dibromo-3-chloropropane, nitrate and tetrachloroethylene.

It is unclear why several contaminants were inversely associated with hypertensive disorders in pregnancy (perchlorate, tetrachloroethylene, uranium). Similarly, the results of the violations (MCL and TCR) were in the unexpected direction. Our results should be interpreted with caution, both positive and negative, given the novelty of results and limitations of exposure assessment. Our study serves as a first step to examine multiple water contaminants over a large geography and study population, to seek areas for further research in a more targeted approach.

Our study is limited by its lack of measurement in biospecimens and unknown consumption of drinking water or water from nonresidential sources. The cross-sectional design precludes assessment of the timing of exposure in relation to the outcomes assessed. The lack of temporal data did not allow for examination of trimester specific effects or critical windows, and in some cases the data on water contaminants may have not aligned with the pregnancy period. The frequency of the measurements is not regular nor uniform across different water systems. Additionally, sparse data are currently available from smaller, unregulated wells, though an estimated 98% of Californians received their water from public sources in 2013,<sup>55</sup> and the quantity of consumption by individuals in this study is unknown. Resulting exposure measurement error would likely lead to attenuation of our estimates; however, there is a possibility the measurement error could be related to conditions which are related to hypertensive disorders in pregnancy and thereby biasing our estimates.

Despite these limitations, this study provides a first examination of an area with minimal current knowledge and important health implications. This study has several strengths including a large study population of pregnant women. It covers a wide geography of the entire state of California over several years and thorough outcome ascertainment with ICD-9 codes from hospital discharge records with reduced selection bias. Additionally, the CalEnviroScreen drinking water contamination data allowed us to examine multiple contaminants separately and in combination.

This study identifies contaminants that could be explored further for more time-sensitive exposure periods during pregnancy that may be critical for hypertensive disorders. In areas with high contamination or more unregulated wells, further water sampling is needed. Additionally, exploration of variation by

water system size (as a proxy for water treatment) may provide additional insight to areas of concern. Finally, future studies may benefit from information about the quantity of consumption of drinking water consumption (as opposed to bottled water) or regular measurement of contamination at the home.

The differences observed in the association between drinking water contaminants and hypertensive disorders in pregnancy by neighborhood poverty were not in the hypothesized direction. The associations between water contamination and hypertensive disorders in pregnancy are driven by the populations living in neighborhoods with lower poverty. Additional post-hoc analyses revealed this stratified results were similar with individual socioeconomic status, and stronger in White, non-Hispanic mothers. Further explorations of socioeconomic inequality and/or racial segregation in relation to health disparities is needed.

In conclusion, drinking water contamination continues to pose a threat to public health, particularly to vulnerable populations such as pregnant women. Additional sampling both in water and in people is warranted as is further research on health effects.

### Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

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