



Trihalomethanes in public drinking water and stillbirth and low birth weight rates: an intervention study

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ABSTRACT

During 2003–2004, United Utilities water company in North West England introduced enhanced coagulation (EC) to four treatment works to mitigate disinfection by-product (DBP) formation. This enabled examination of the relation between DBPs and birth outcomes whilst reducing socioeconomic confounding. We compared stillbirth, and low and very low birth weight rates three years before (2000–2002) with three years after (2005–2007) the intervention, and in relation to categories of THM change.

We created exposure metrics for EC and trihalomethane (THM) concentration change ($n = 258$ water zones). We linked 429,599 live births and 2279 stillbirths from national birth registers to the water zone at birth. We used Poisson regression to model the differences in birth outcome rates with an interaction between before/after the intervention and EC or THM change.

EC treatment reduced chloroform concentrations more than non-treatment (mean $-29.7 \mu\text{g/l}$ vs. $-14.5 \mu\text{g/l}$), but not brominated THM concentrations. Only 6% of EC water zones received 100% EC water, creating exposure misclassification concerns. EC intervention was not associated with a statistically significant reduction in birth outcome rates. Areas with the highest chloroform decrease ($30 - 65 \mu\text{g/l}$) had the greatest percentage decrease in low -9% ($-12, -5$) and very low birth weight -16% ($-24, -8$) rates. The interaction between before/after intervention and chloroform change was statistically significant only for very low birth weight, $p = 0.02$. There were no significant decreases in stillbirth rates.

In a novel approach for studying DBPs and adverse reproductive outcomes, the EC intervention to reduce DBPs did not affect birth outcome rates. However, a measured large decrease in chloroform concentrations was associated with statistically significant reductions in very low birth weight rates.

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1. Introduction

Disinfection by-products in drinking water result from a chemical reaction between treatments such as chlorination and organic and inorganic matter in the water (Rook, 1974). DBPs include over 600 different species such as trihalomethanes (THMs), haloacetic acids (HAAs) and nitrosamines (Richardson et al., 2007). Toxicological studies suggest

that some DBPs may cause adverse reproductive effects in animals, albeit at concentrations several orders of magnitude greater than those to which humans are exposed to in tap water (Colman et al., 2011; IPCS, 2000; Tardiff et al., 2006). Meta-analyses report that exposure to some of the individual THMs is associated with increased stillbirth risk (Nieuwenhuijsen et al., 2010), whilst exposure to total THMs (TTHM) is associated with an increased risk of small-for-gestational age (SGA), but not low birth weight, term low birth weight or preterm delivery (Grellier et al., 2010). However, evidence remains inconclusive as both meta-analyses included few studies ($n = 5$ and $n = 6$ respectively), and recent studies report mixed results for associations between THMs and preterm delivery (Kumar et al., 2014; Patelarou et al., 2011; Rivera-Núñez and Wright, 2013b; Villanueva et al., 2011) and foetal growth outcomes (Danileviciute et al., 2012; Grazuleviciene et al., 2011; Horton et al., 2011; Kumar et al., 2014; Levallois et al., 2012; Patelarou et al., 2011; Rivera-Núñez and Wright, 2013a, 2013b; Summerhayes et al., 2012; Villanueva et al., 2011).

Abbreviations: BDCM, bromodichloromethane; CI, confidence interval; DBCM, dibromochloromethane; DBP, disinfection by-product; EC, enhanced coagulation; GIS, Geographical Information System; HAA, haloacetic acid; ID, Indices of Deprivation; SGA, small-for-gestational age; Tbr THM, total brominated THM; THM, trihalomethane; TTHM, total trihalomethanes.

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In North West England, United Utilities supplies drinking water to almost 7 million customers. A previous study found a 20% statistically significant excess risk of stillbirth, low birth weight and very low birth weight associated with high THM concentrations in the United Utilities water region in 1993–1997, the highest risk and THM concentrations of the three regions investigated (Toledano et al., 2005). During 2003 and 2004, United Utilities changed their treatment methods, introducing enhanced coagulation (EC) to four treatment works. EC is a physical–chemical treatment process that improves the removal of DBP precursors in comparison to conventional coagulation, reducing DBP formation potential. United Utilities defines EC as the destabilisation of colloidal and organic matter in water under optimum conditions (United Utilities, 2004). This intervention provided a unique opportunity to study the possible impact of DBPs on adverse birth outcomes in the water region, since other risk factors such as potential socio-economic confounders were unlikely to change over a short period.

1.1. Objective

We compared stillbirth, low and very low birth weight rates three years before (2000–2002) with three years after (2005–2007) the EC intervention took place. We investigated change in rates in treatment areas with non-treatment areas acting as a control. Since THM concentrations may have changed for reasons other than the intervention, we also studied rate change between the time periods in areas of low, medium and high THM change.

2. Methods

2.1. Study population

We extracted all live and stillbirths within the United Utilities water region from 2000 to 2002 and 2005–2007 from the National Birth and Stillbirth Registers. Birth weight, maternal age, sex of baby, information on multiple births and maternal residence at birth postcode were available. Routine birth data in the UK does not contain information on gestation weeks, socioeconomic deprivation, or ethnicity, however, for descriptive purposes area-level 2001 Census data on deprivation and ethnicity were available. Stillbirth refers to foetal deaths after 24 completed weeks of gestation. Live births were categorised: normal (≥ 2500 g), low birth weight (< 2500 g, i.e. including very low birth weight births) and very low birth weight (< 1500 g).

2.2. Exposure assessment

United Utilities provided information on chloroform, bromodichloromethane (BDCM), dibromochloromethane (DBCM), bromoform and water zone boundaries for each water zone, 2002–2007. For regulatory purposes, a water zone is a designated supply area within which water quality should be approximately uniform and whose population does not exceed 100,000. In each water zone, geographically random samples must be collected on regular occasions (i.e. scheduled at similar dates and times each year), a minimum four times per annum. Between zone variation is greater than within zone variation for chloroform and BDCM but not DBCM (Keegan et al., 2001). Digital information on water zone boundaries plus THM data for 2000–2001 was available from a previous study (Nieuwenhuijsen et al., 2008). We linked water zone boundary information to THM concentrations using ArcMap, version 9.1 Geographical Information System (GIS). We excluded water zones with boundaries that had been incorporated into other water zones during 2000–2007 ($n = 52$), leaving 258 water zones for study.

We constructed two exposure metrics for each water zone. EC identified treatment status (No/Yes). We also calculated concentration change for TTHM (the sum of chloroform, BDCM, DBCM and bromoform), total brominated THMs (the sum of BDCM, DBCM and

bromoform) and the individual THMs, based on the difference in average concentration in each water zone during the three years (2000–2002) before and the three years (2005–2007) after EC was introduced. We categorised TTHM concentration change to give distribution-based cutpoints as follows: areas with high TTHM decreases (30–65 $\mu\text{g/l}$), medium TTHM decreases (10–<30 $\mu\text{g/l}$), areas with low TTHM decreases/increases (decrease < 10 $\mu\text{g/l}$ to increase ≤ 10 $\mu\text{g/l}$) and, (Supplementary data 1 only), areas with moderate TTHM increases (11–26 $\mu\text{g/l}$). As the TTHM composition in England is dominated by chloroform, we used the TTHM category cutpoints for chloroform as well.

In order to assign the birth to the correct water zone where the majority of exposure would have occurred, we linked the postcode of maternal residence at birth to the water zone boundary in use during the year of birth using point-in-polygon methods in GIS. Births occurring during the first six weeks of the year were linked to the water zone boundary of the preceding year when the majority of the pregnancy (i.e. up to and including the majority of the third trimester), would have occurred, ensuring that the exposure metrics based on annual average THM data covered the entire pregnancy that may be relevant for stillbirth and the birth weight outcomes (Pedersen et al., 2013). We extracted 472,526 live births and 2631 stillbirths for the United Utilities region. Before linking to water zones, we excluded births during the first six weeks of 2000 (before) or 2005 (after) ($n = 18,896$ live, $n = 102$ stillbirths) and multiple births ($n = 12,414$ live, $n = 190$ stillbirths). A total of 441,216 live and 2339 stillbirths were available for exposure assessment. Of these, we georeferenced and linked 432,019 (98%) live births and 2293 (98%) stillbirths to 258 water zones. Finally, we excluded births in four water zones with a large chloroform increase 11–26 $\mu\text{g/l}$ due to small numbers of stillbirths ($n = 2420$ live, $n = 14$ stillbirths), and births from the birth weight analyses with unreliable birth weights recorded i.e. < 200 g ($n = 895$). This left 429,599 live births and 2279 stillbirths for the stillbirth analysis and 27,664 low, 4209 very low and 401,040 normal weight births in the birth weight analyses.

2.3. Analysis of socioeconomic confounders in water zones

We analysed income deprivation sub-scores from the English Indices of Deprivation (ID) at the water zone level to test the assumption that there was little change in socioeconomic factors between 2000–2002 and 2005–2007. At lower level super output area (a super output area is typically an aggregation of 4 to 6 census output areas and the lower level contains about 1500 people), ID were available for 2004 and 2007, based on data collected in 2001 and 2005 respectively (Noble et al., 2004, 2007) and covering 7 domains of deprivation. The income domain of the ID, reflecting means tested state-provided benefits, is expressed as a proportion, which we converted from super output area to water zone level using postcode-weighting methods (Briggs et al., 2008). For ID 2004, income was highly correlated with employment ($r = 0.90$) and the composite index of multiple deprivation that combines the 7 domains ($r = 0.96$) (Briggs et al., 2008). We calculated income deprivation scores for 'before' and 'after' intervention periods, as well as calculating income deprivation change from 2000–2002 to 2005–2007.

We also had deprivation information at a more refined resolution that has been calculated at the postcode sector level (Carstairs Index), but was only available for 2001 (Census is every 10 years) and would not capture change over time. We assigned each woman the Carstairs score for her postcode sector and used this in the descriptive statistics.

2.4. Statistics

We tested correlations between EC, THM, and income deprivation variables before and after the intervention, using Spearman's rho or Pearson's R as appropriate. We examined rates of stillbirth, low and

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