

# Exposure to Volatile Organic Compounds in Drinking Water and Specific Birth Defects and Childhood Cancers at U.S. Marine Corps Base Camp Lejeune, North Carolina

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# ATSDR DHS Project Team

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# 1998 ATSDR Study on Adverse Pregnancy Outcomes

- Evaluated potential maternal exposure to drinking water contaminants on base and
  - Preterm birth
  - Small for gestational age (SGA)
  - Mean birth weight deficit
- Only used available databases
  - Electronic birth certificates beginning in 1968
  - 12,493 singleton live births on base during 1968-1985
  - Base family housing records linked to mother's address at delivery and father's name in most cases
  - Could not evaluate birth defects and childhood cancers

# 1998 ATSDR Study on Adverse Pregnancy Outcomes: Results

- Exposure to TT water (PCE)
  - Elevated risk for SGA among infants born to
    - Mothers aged >35 years
    - Mothers with  $\geq 2$  prior fetal losses
- Exposure to HP water (TCE)
  - Elevated risk for SGA only among male infants
- Recently discovered exposure misclassification requires reanalysis of study data

# Current ATSDR Case-Control Study

- Exposure to VOCs in Drinking Water and Specific Birth Defects and Childhood Cancers
- Multi-step process
  - Review scientific literature to identify specific birth defects and childhood cancers associated with drinking water contaminated with chlorinated solvents
  - Conduct telephone survey to ascertain potential cases
  - Obtain medical records to verify diagnoses of reported cases
  - Conduct a case-control study

# Current ATSDR Case-Control Study

- The following outcomes were selected for further study based on the scientific literature
  - Neural tube defects (NTD)
  - Oral cleft defects (cleft lip and cleft palate)
  - Conotruncal heart defects
    - tetralogy of Fallot
    - D-transposition of the great arteries
    - truncus arteriosus
    - pulmonary valve atresia with ventricular septal defect
    - double outlet right ventricle
  - Choanal atresia (a nasal defect)
  - Childhood leukemia
  - Childhood non-Hodgkin's lymphoma

# Current ATSDR Case-Control Study

- Telephone survey conducted to identify potential cases of the selected adverse childhood outcomes among births occurring during 1968-1985 to mothers residing on base any time during their pregnancy
  - 16,000-17,000 estimated births
- Parents of 12,598 eligible children were surveyed
  - Overall participation rate of 74%-80%

# Current ATSDR Case-Control Study

- Sufficient numbers of NTDs, oral clefts, and childhood cancers reported
  - 106 reported cases
    - 35 NTDs
    - 42 oral cleft defects
    - 29 childhood hematopoietic cancers
- Verification of diagnoses of cases ascertained by survey has been completed

# Current ATSDR Case-Control Study

- 52 confirmed cases (51 parents interviewed)
  - 15 NTDs
  - 24 clefts
  - 13 hematopoietic cancers
- 32 confirmed not to have the reported diseases
- 8 refused to participate
- 7 could not be verified (no medical records)
- 7 were ineligible

# Current ATSDR Case-Control Study

- Parents of 548 controls were interviewed
- Parental interviews conducted in 2005 to obtain information on
  - Maternal water consumption habits
  - Maternal residential history
  - Maternal exposures during pregnancy
  - Parental risk factors
- Review of base family housing records to verify dates and location of mother's reported residence on base

# Data Analysis

- Separate analyses will be conducted
  - NTDs
  - Oral clefts
    - cleft lip (with or without cleft palate)
    - cleft palate
  - Childhood leukemia/NHL

# Data Analysis

- Analyses will evaluate both continuous and categorical drinking water contaminant variables
  - Smoothing methods will be used to suggest categorical variable cutpoints
  - Each contaminant will be analyzed separately
  - Joint effects of contaminants will also be evaluated

# Data Analysis

## Confirmed cases of NTDs

- Average and maximum contaminant level over the first trimester
- Average and maximum contaminant level during the period 3 months prior to date of conception (DOC)
- Average level in the first month of pregnancy

# Data Analysis

## Confirmed cases of oral cleft/oral palate defects

- Average and maximum contaminant level over the first trimester
- Average and maximum contaminant level during the period 3 months prior to DOC
- Average level in the second month of pregnancy

# Data Analysis

Confirmed cases of childhood cancers  
(leukemia and non-Hodgkin's lymphoma)

- Average and maximum contaminant level over each trimester
- Average and maximum contaminant level over the first year of child's life
- Average and maximum contaminant level during the period 3 months prior to DOC
- Cumulative exposure over the pregnancy and first year of child's life

# PCE Contamination Levels (ppb) from Tarawa Terrace by Gestational Month: Example

	Child #1	Child #2	Child #3	Child #4	Child #5	Child #6	Child #7	Child #8	Child #9
-3DOC	118	174	108	0	121	0	55	0	0
-2DOC	120	173	109	0	121	0	54	0	93
-1DOC	132	176	110	103	0	0	54	0	94
month1	180	4	111	104	0	0	53	0	95
Month2	183	9	111	105	0	182	0	0	96
month3	151	8	0	107	0	156	0	82	97

# Data Analysis

- Compute unadjusted and adjusted results using logistic regression and calculate 90% confidence intervals
  - If data too sparse, conditional or exact logistical regression may be used
- Include in final model potential confounders that contribute to a  $\geq 10\%$  change in the parameter estimate for the exposure variable
- Evaluate categorical variables for water usage obtained from interviews, alone and in combination with the contaminant levels

# Data Analysis

- Sensitivity analysis to assess the impact of exposure misclassification
- Consider secondary analyses including cases and controls with incomplete residential history or cases that could not be confirmed by medical records
- Interpretation of results based on
  - Magnitude of association
  - Exposure-response relationship
  - Biological plausibility
  - Consistency with other studies