US EPA Region 5 summary remarks Health study of airborne manganese (Mn) in Ohio adults – preliminary results East Liverpool Ohio - July 11, 2013

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Key points

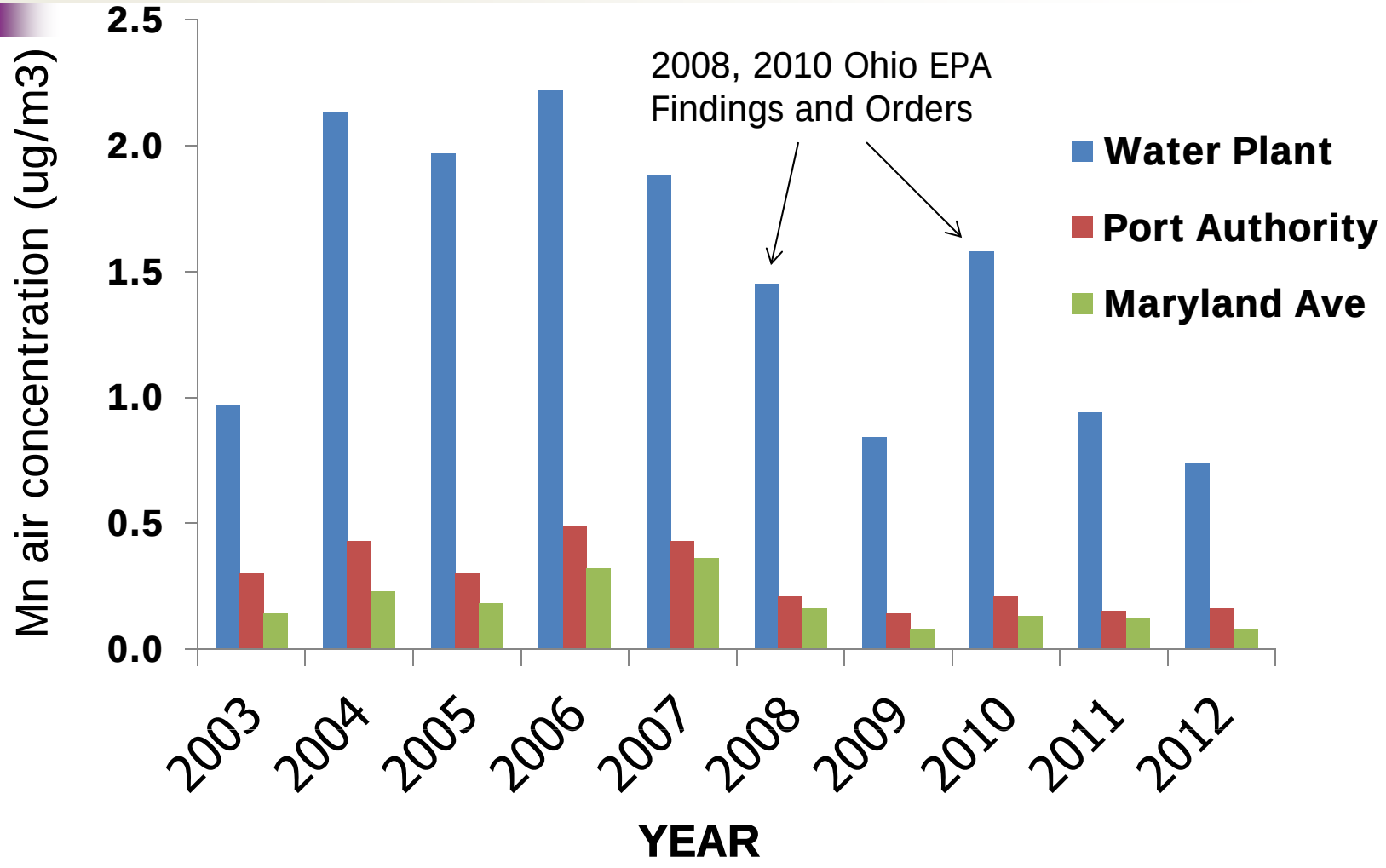
- US EPA funded study looked at potential effects of long term Mn exposure in adults
- Health study found subtle health effects associated with airborne Mn
- Airborne Mn has been high in East Liverpool

Key points (continued):

- SH Bell has made substantial$_c$ hanges to its operations
- Airborne Mn lower now than in past due to long term efforts (SH Bell, Ohio agencies, federal agencies)
- US EPA's most recent SH Bell investigation conducted in summer 2013
- State and federal agencies will continue monitoring and oversight

Annual average airborne Mn concentrations in East Liverpool decreased from 2003-2012

(composite TSP samples; arithmetic mean)



Preliminary Results: An Epidemiologic Health Study of Manganese Exposure in Adult Residents of East Liverpool, Ohio

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East Liverpool, Ohio
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Disclaimer: The views expressed in this Presentation are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency

OVERVIEW

- Research Team
- About the study
- East Liverpool Manganese Exposure
- Results of Neuropsychological and Neurological Function Testing
- Summary & Conclusions
- Q & A

RESEARCH TEAM

- Comprised of scientists:
  - four different universities (in three countries),
  - two federal agencies
  - the state department of health
- Overseen by three scientists from the U.S. EPA Research Triangle Park (North Carolina) and Chicago Region 5 office as well as the Agency for Toxic Substances Disease Registry

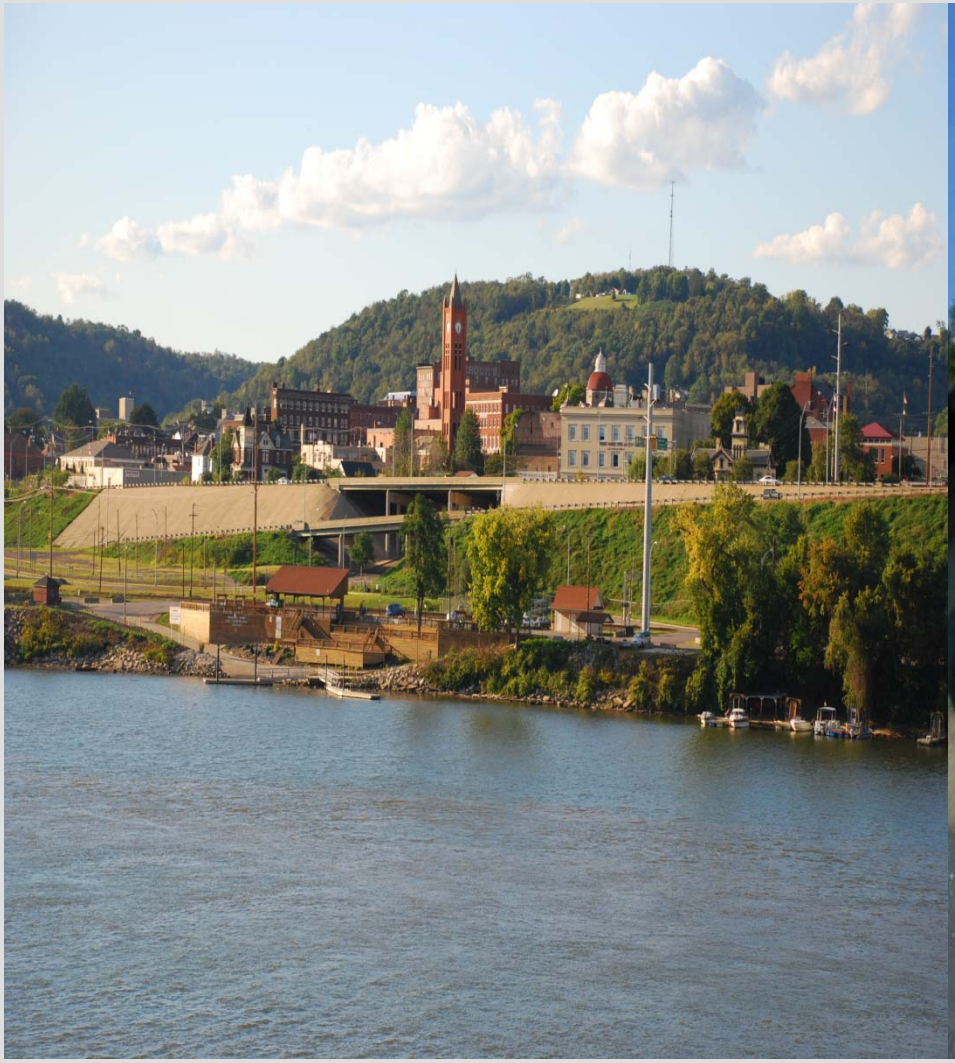
RESEARCH TEAM

- **Dr. Rosemarie Bowler** - Principal Investigator, San Francisco State University
- **Dr. Cheryl Beseler** - Statistician, Colorado State University
- **Dr. Yangho Kim** – Physician, Department of Occupational and Environmental Medicine, Ulsan University Hospital, College of Medicine, South Korea
- **Dr. Danelle Lobdell**– Epidemiologist, U.S. EPA, Office of Research and Development
- **Dr. George Bollweg** – Environmental Health Scientist, U.S. EPA, Region 5
- **Dr. Michelle Colledge** – Environmental Health Scientist, Division of Community Health Investigations, ATSDR Region 5
- 10 doctoral and masters graduate students and psychologists experienced and trained in the methods used in the study

ABOUT THE STUDY

- Conducted in November 2011 to see if manganese exposure from outdoor air could result in measureable health effects in three Ohio towns.
  - The results from East Liverpool were compared to those in Marietta (manganese source from a smelter), and Mount Vernon (no known manganese source)
- Air manganese levels were estimated in East Liverpool and in Marietta by using air monitoring data, distance from the source and years at the residence in the study.
- To evaluate exposures and health effects we looked at:
  - Air monitoring data
  - Biological data (hair, nails, blood)
  - Results from health tests given to each study participant

EAST LIVERPOOL, OH & S.H. BELL LITTLE ENGLAND FACILITY



MARIETTA, OH & ERAMET MARIETTA

STUDY PARTICIPANTS

We included:

- Up to two volunteers per home at randomly selected homes within 2 miles of the S.H. Bell Facility
- People who were 30-75 years old at the time of the study
- People who have lived in the community for at least 10 years

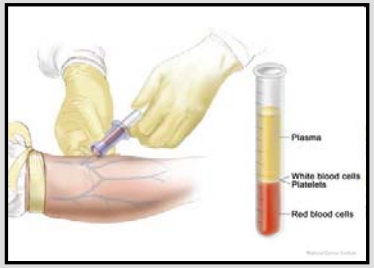
We excluded:

- People who worked at S.H. Bell
- People who have pre-existing exposures or health problems that could result in the person having symptoms like the ones manganese exposure can cause
- People with alcohol or drug dependence

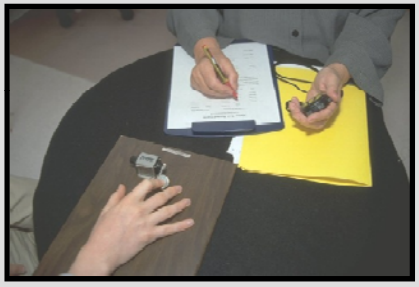
DATA WE COLLECTED

- **Questionnaires:**
  - Residency
  - General Health
  - Sleep
  - Mood
  - Diet
  - Symptoms, Illnesses, and Medication use

- **Medical & Neuropsychological Evaluations**
  - Neurological
  - Small Blood Sample
  - Hair sample
  - Toenail sample
  - Clinical Interview by Principal Investigator



- **Neuropsychological Tests**
  - Cognitive Testing
  - Motor Testing
  - Mood Testing
  - Postural Sway & Tremor Testing

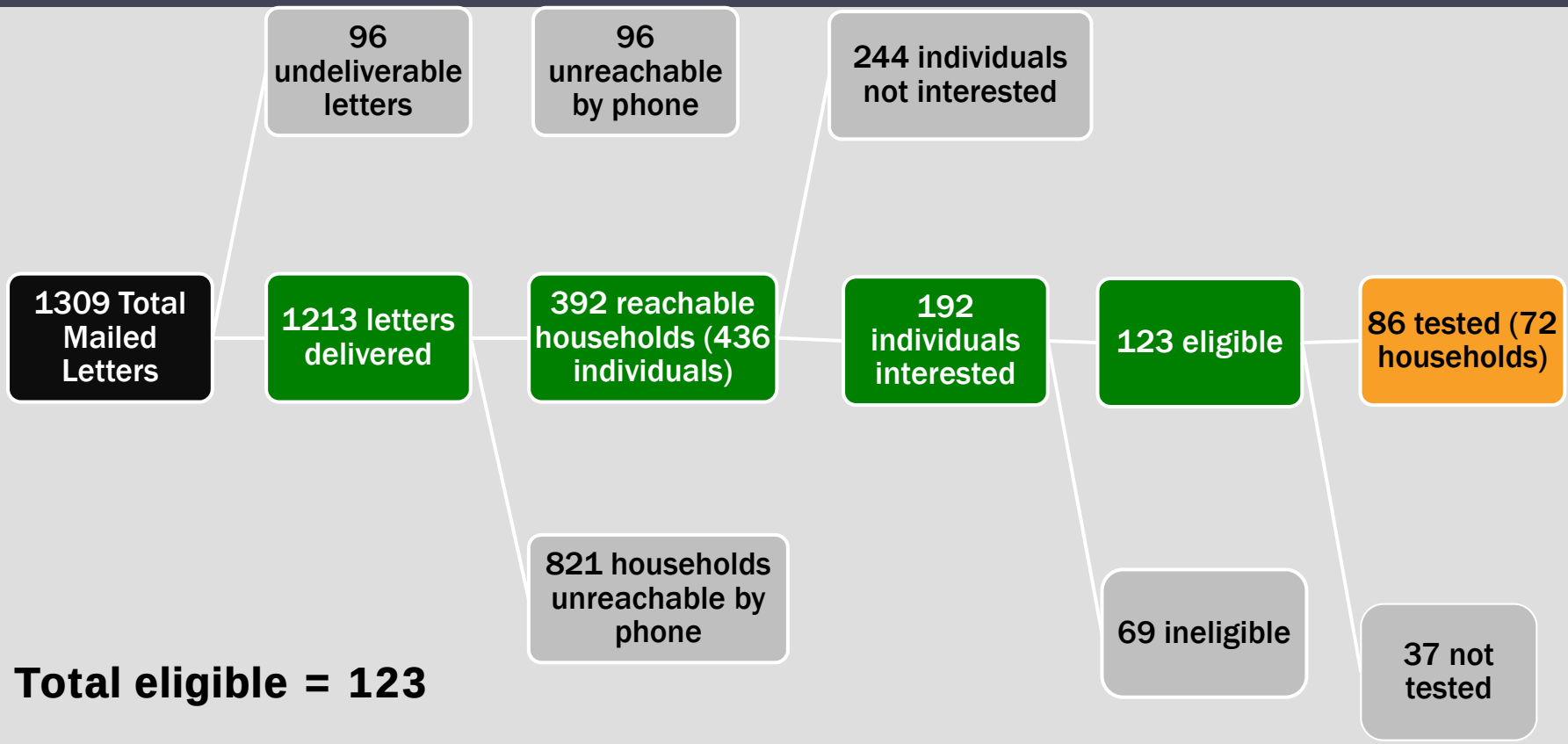


MAINTAINING CONFIDENTIALITY

- All the information we collected was combined in group results
- Personal information remains confidential
- ID numbers were assigned the each participant, and were used on all tests and the questionnaires
- Only the principal investigator has access to both the participant name and their ID #

Preliminary Results
Participants

RESULTS OF RECRUITMENT: EAST LIVERPOOL

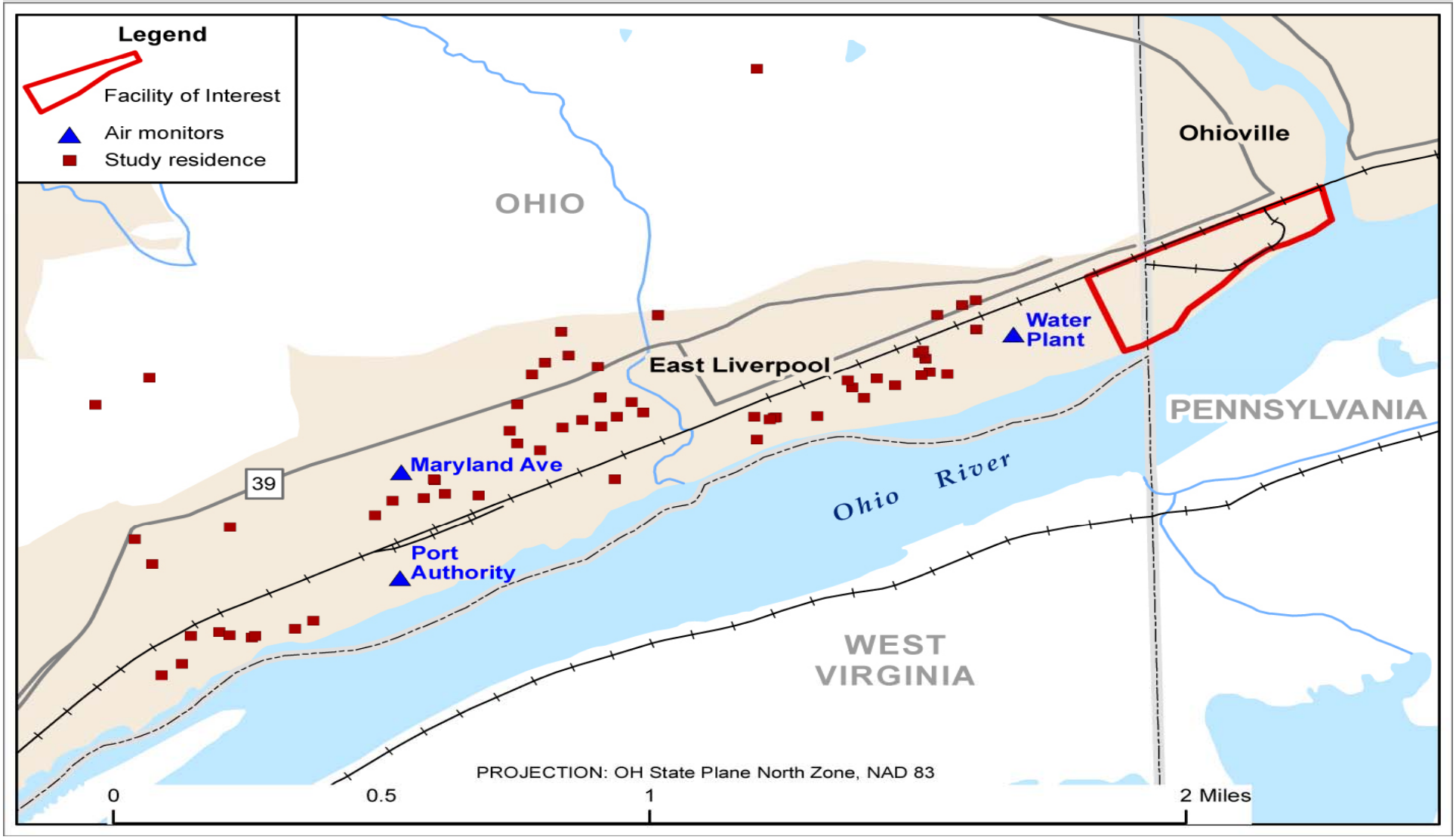


Total eligible = 123

Total tested = 86

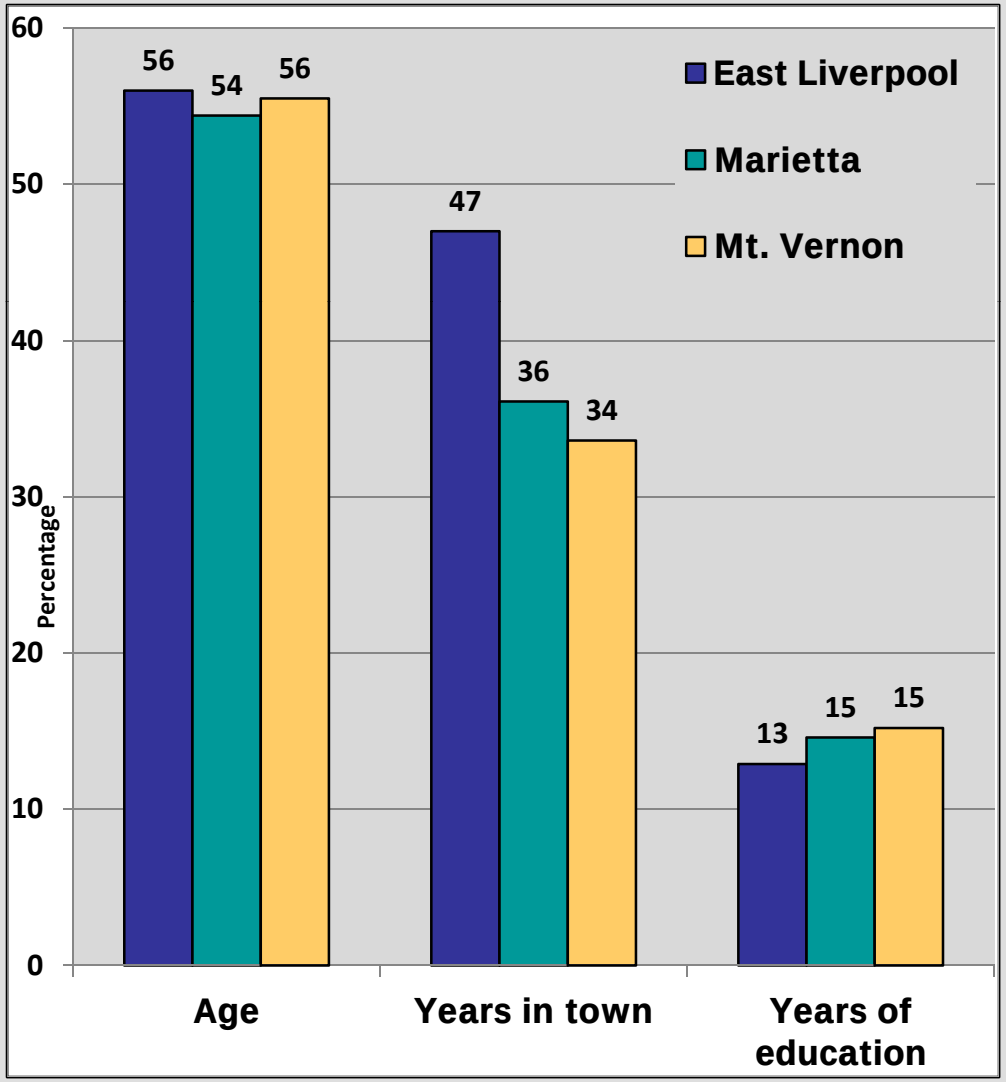
Percentage of eligible tested: 70%

2 MILE STUDY INCLUSION AREA



MORE ABOUT THE STUDY PARTICIPANTS

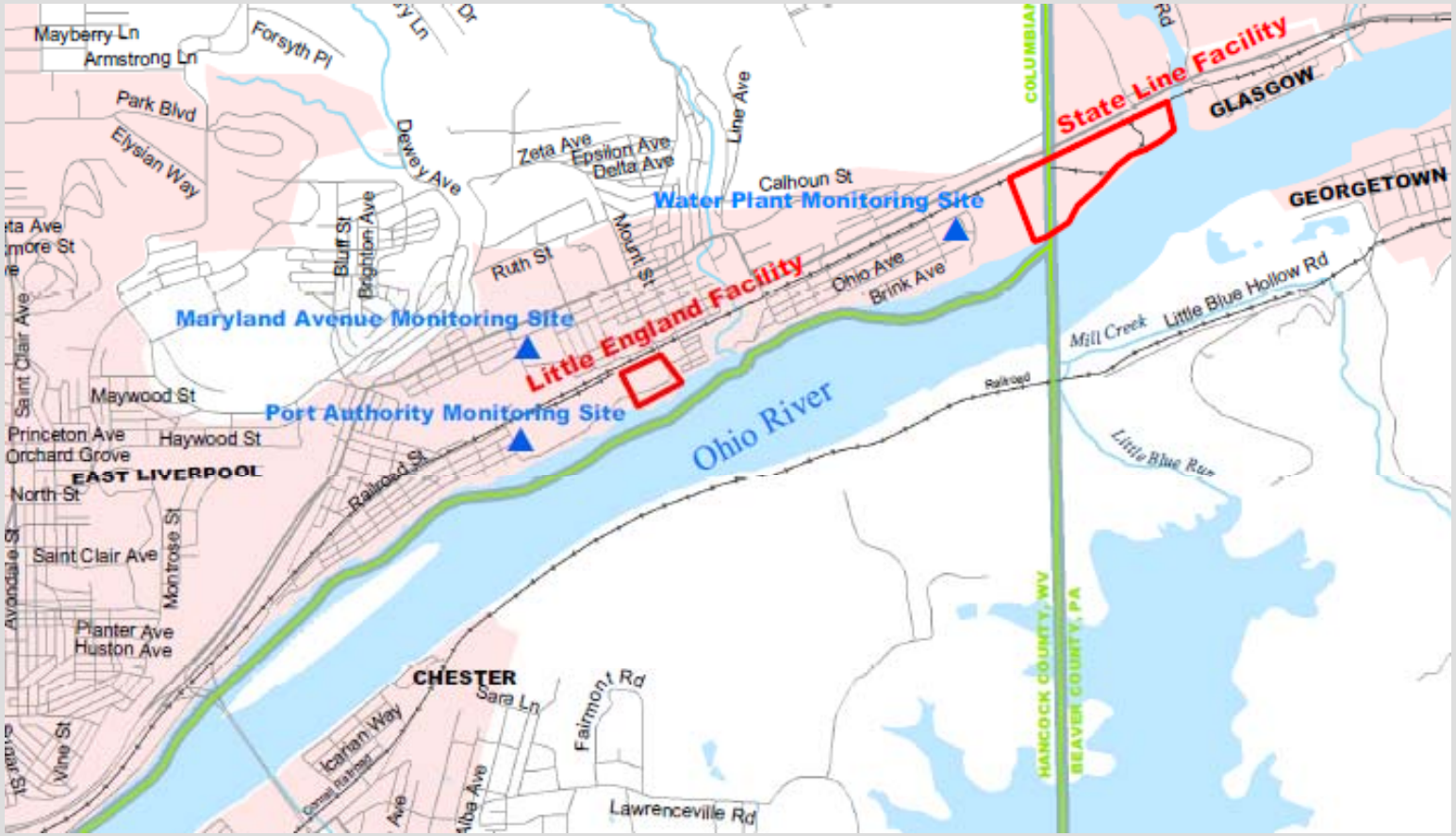
- **Sex:**
  - East Liverpool participants: 36% men and 64% women
  - Marietta participants: 45% men, 55% women
  - Mount Vernon participants: 44% men, 56% women)
- **Years of Residency:** Even though the average age of participants in the mid-50s for all cities, East Liverpool participants generally live longer in their town (average 47 years) than both Marietta (36 years) and Mt Vernon (34 years)
- **Education:** East Liverpool participants have fewer years of schooling (13 yrs) than both Marietta and Mt Vernon (15 yrs)
- **Income:** East Liverpool participants have lower annual income than participants in Marietta and Mount Vernon



Estimating Individual Manganese Inhalation

EAST LIVERPOOL MANGANESE SOURCES AND OUTDOOR AIR MONITORING SITES

- Three community monitoring stations have measured metals in air for over 10 years in East Liverpool

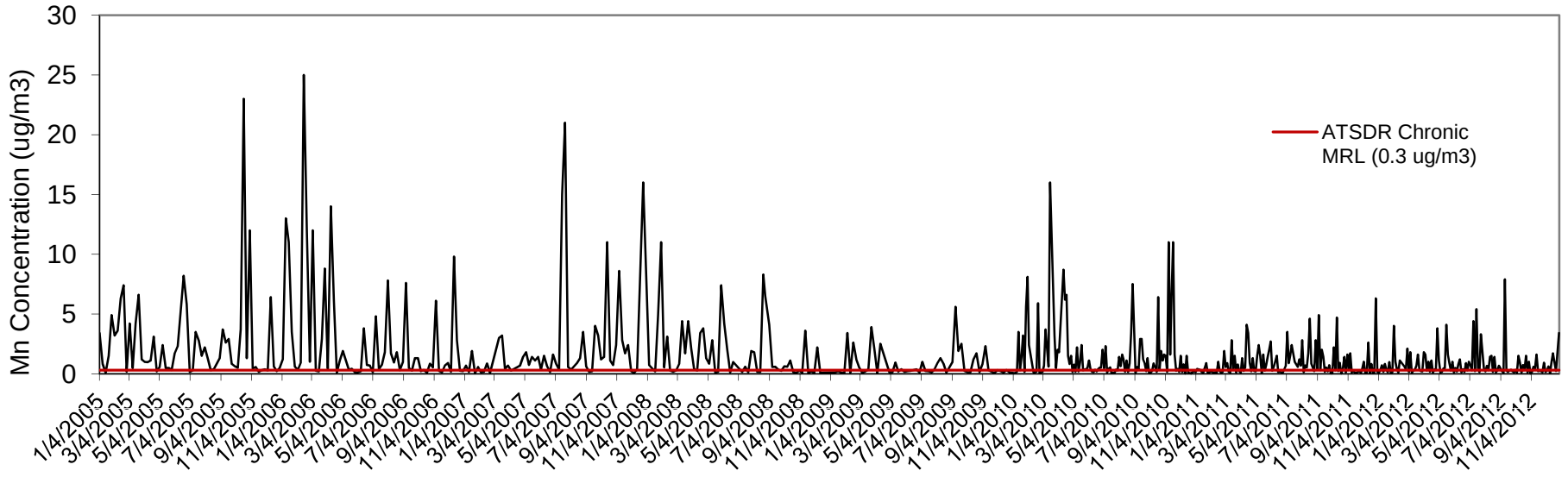


OUTDOOR AIR DATA

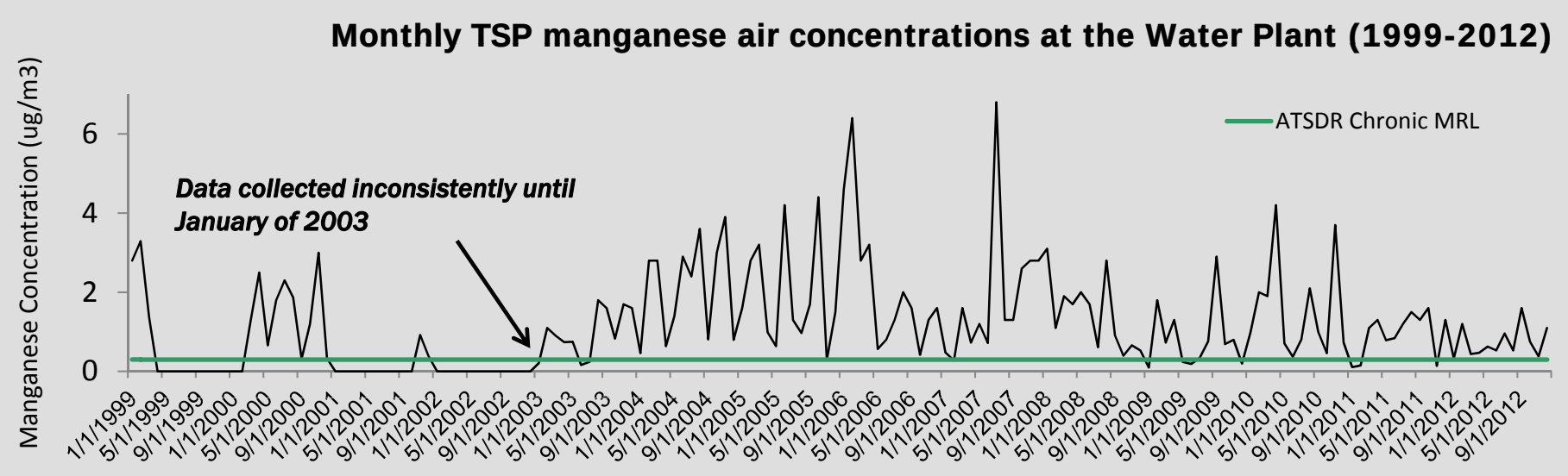
Air Manganese Summary Statistics for EL Monitoring Sites (Jan. 2003-Dec. 2012)*, µg/m³

Monitoring Site	(2005-2012*) Water Plant (24 hr avg)	Water Plant (monthly avg)	Port Authority (monthly avg)	Maryland Ave (monthly avg)
Distance to SH Bell Stateline Facility	0.08 km	0.08 km	2 km	2.1 km
# of observations	525	125	124	112
Average	1.57	1.55	0.30	0.19
Minimum observation	0.02	0.10	0.02	0.01
Maximum observation	25.00	6.80	1.90	1.00
% greater than U.S. EPA RfC (0.05 µg/m³)	**100.0**	**100.0**	**93.38**	**84.68**

Daily TSP manganese air concentrations at the Water Plant (2005-2012)



Monthly TSP manganese air concentrations at the Water Plant (1999-2012)



ESTIMATING EXPOSURE

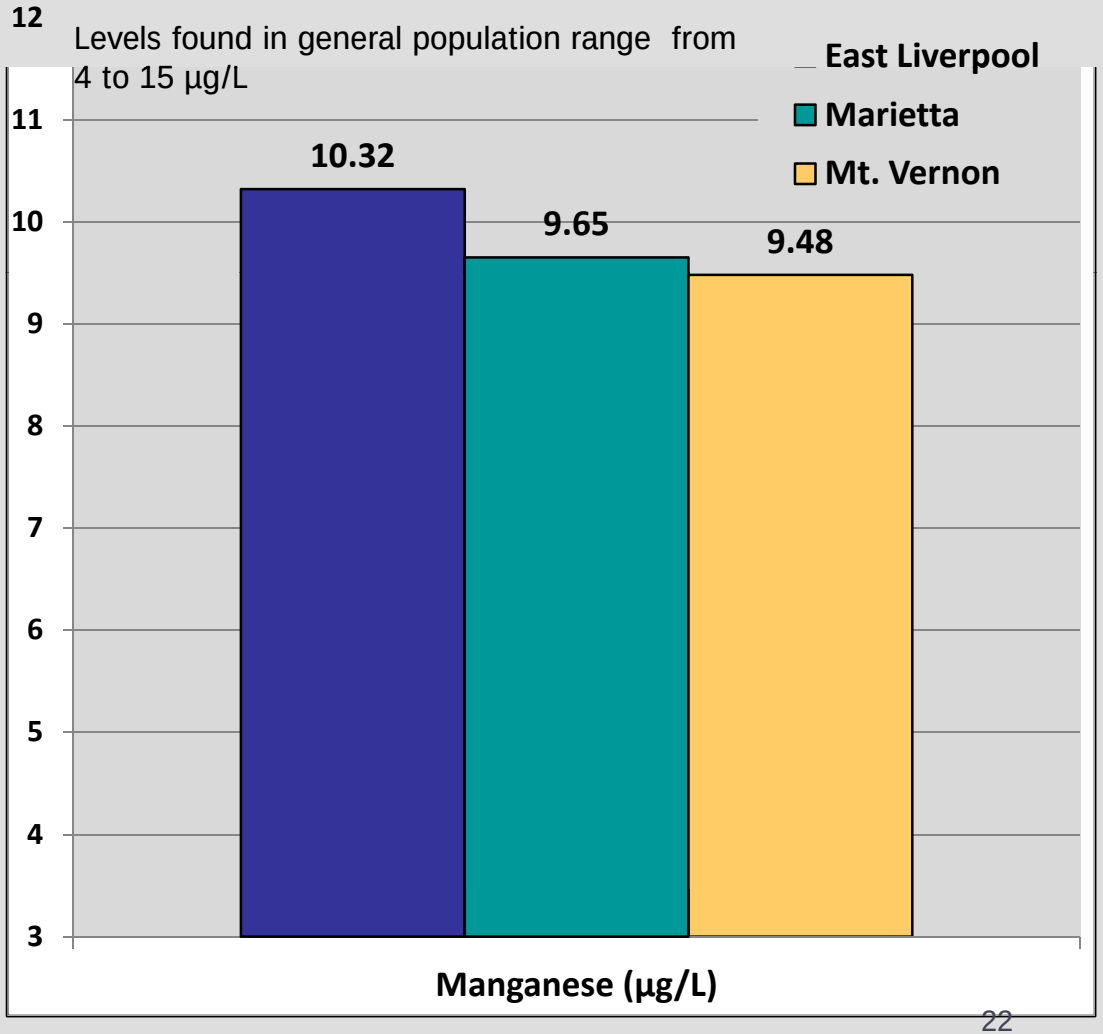
1. A computer air model (AERMOD) and measured data were used to estimate long term average air manganese concentrations at the residence of each study participant
2. The long-term estimated air manganese concentration for each residence, the distance from the source, and years living in East Liverpool were used to calculate a "cumulative exposure index" (we will refer to as exposure index)
3. The exposure index was used to look at the relationship of estimated long-term air manganese exposure with
   - Neuropsychological health outcomes
   - Manganese levels in blood, hair, and toenails

Preliminary Test Results of the Three Towns Compared to Each Other

PRELIMINARY RESULTS: BLOOD

Manganese is an essential nutrient and we get most of our manganese from our diet. Manganese can be found in our blood

- No significant differences in blood manganese between the three towns and all were within normal ranges
- East Liverpool participants had higher levels of cadmium and lower levels of mercury in their blood than the other two towns
  - All levels were within normal population ranges
- There was no difference in blood lead or iron stores in the body in the three towns



NEUROPSYCHOLOGICAL TESTS

- Neuropsychological tests are COGNITIVE (thinking, communicating, remembering) and MOTOR tests (speed of movement, grip strength, accuracy) designed to measure a psychological function known to be linked to a particular part of the brain

- Exposures to some kinds of heavy metals, like manganese, can cause deficits in brain function indicating impairment of motor skills or thinking/communicating

PRELIMINARY RESULTS: NEUROPSYCHOLOGICAL TESTS

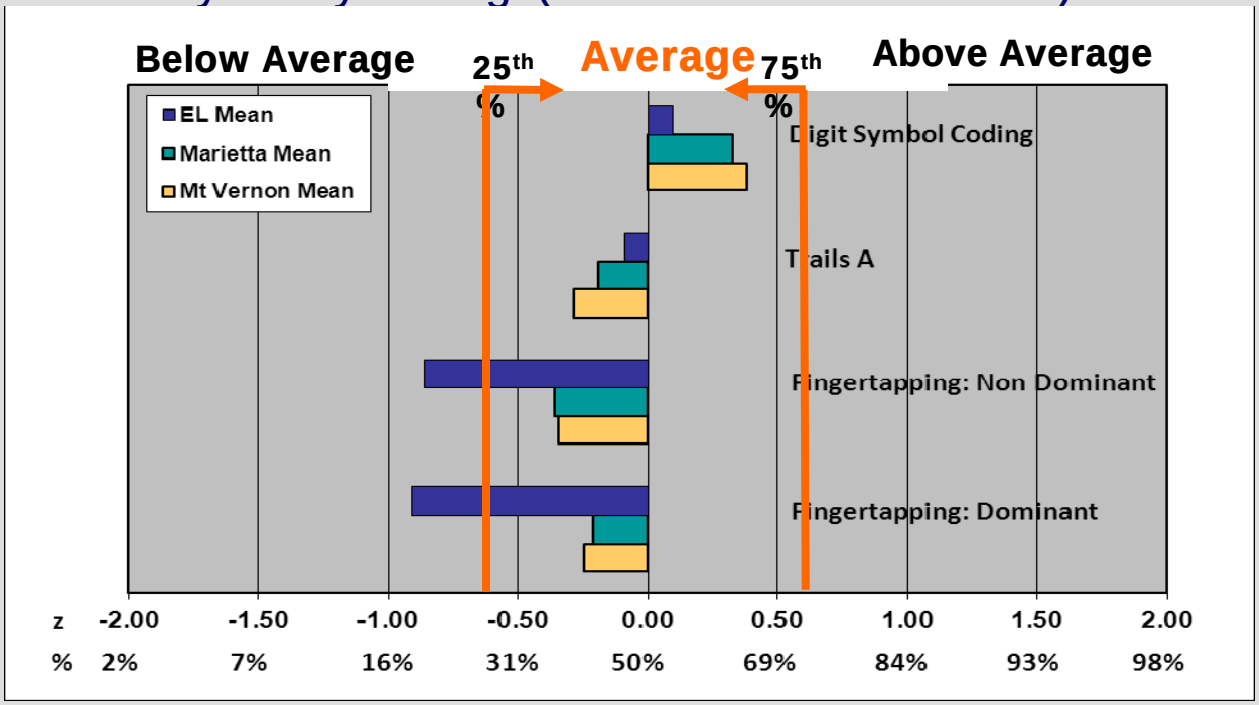
*There were **NO** significant differences between the 3 towns on tests of:*

- Attention
- Switching categories and divided attention
- Visual delayed memory
- Verbal delayed memory

PRELIMINARY FINDINGS: NEUROPSYCHOLOGICAL TESTS

Significant differences between the 3 towns

- East Liverpool scored worse than Marietta and Mount Vernon on: Word reading; Motor speed; Motor strength, and Motor tactile
- East Liverpool participants also scored worse than one of the other towns on: Naming animals (worse than Mt. Vernon) and immediate memory-daily living (worse than Marietta)



*** p< 0.05 (EL < Marietta & Mt. Vernon)

NOTE: Most of the participants' test scores in all three towns were within the normal range (between 25th and 75th percentile) with the exception of the following in East Liverpool:

1) divided memory
2) visual memory
3) motor speed and strength

NEUROLOGICAL TESTS

- Neurological tests are PHYSICAL tests done to evaluate the presence and severity of postural sway, tremor, sensory and motor responses (i.e. reflexes) to determine whether a person's nervous system is impaired

- Exposures to some kinds of heavy metals, like manganese, can cause deficits in brain function indicating impairment of motor skills or thinking/ communicating

PRELIMINARY FINDINGS: NEUROLOGICAL TESTS

- **Postural Sway:** Men and women in EL had more postural sway on the Eyes Open conditions than Marietta and Mt. Vernon men and women

- **Hand Tremor :** EL participants had more tremor than Marietta on both dominant and non-dominant hand (NOTE: Mt. Vernon not measured for tremor)
- EL participants showed slowed **Movement Initiation** compared to Mt. Vernon, but slightly better movement initiation than Marietta
- There were no difference on **Activities of Daily Living & Motor scores** between the three towns

PRELIMINARY FINDINGS: MOOD AND PHYSICAL HEALTH

- People in East Liverpool had less physical illness from stress and anxiety than Marietta (*somatization*)

No significant difference between the towns on:

- Poor physical or mental health days reported in a month
- Percent of current smokers; number of obese participants

Significant difference between the towns:

- More people in East Liverpool reported fair or poor health than Mount Vernon (but not Marietta)
- East Liverpool participants reported more visual and

Preliminary Results

Combined Data from Marietta and East Liverpool Compared to Exposure Index/Distance

PRELIMINARY RESULTS: MOOD, NEUROPSYCHOLOGICAL PERFORMANCE, AND NEUROLOGICAL EXAM

When Marietta and EL are combined:

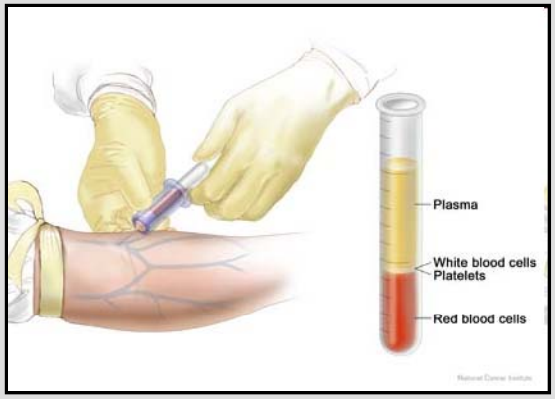
- **Exposure Index**- higher exposure was related to:
  - Mood: Higher scores on generalized anxiety
  - Neuropsychological Performance: Immediate and delayed memory (daily living), Delayed visual memory, Divided attention, Word reading, Cognitive flexibility, Naming, Abstract thinking, Processing speed
  - Neurological Exam
    - Increase in tremors
    - Lower scores motor speed and strength
- **Distance from source** – living closer to the manganese source was related to:
  - Increase in tremors
  - Lower scores motor speed and strength

Preliminary Results
Biomarkers in East Liverpool

PRELIMINARY FINDINGS: BIOMARKERS

Manganese in blood: no consistent relationship with neuropsychological tests or mood, but participants with higher blood Mn reported more symptoms associated with daily living including:

- Changes in handwriting
- Difficulty turning in bed
- Difficulty with skilled movement
- Difficulty writing
- Excessive salivation
- Slurred speech



Manganese /Toenails: no consistent relationship with neuropsychological tests or mood in East Liverpool

Summary & Conclusions

SUMMARY OF PRELIMINARY FINDINGS

- Closer distance from manganese source was associated with differences in neuropsychological and motor test scores
- Higher exposure index associated with differences in neuropsychological and motor test scores
- No differences between towns:
  - Levels of manganese in blood did not differ statistically between the towns.
  - General health categories
  - Activities of Daily Living and motor scores
  - Tests of attention, visual delayed memory, verbal delayed memory
  - Mood disturbance

SUMMARY OF PRELIMINARY FINDINGS CONTINUED

- Differences between towns:
  - More tremors were observed in East Liverpool participants than Marietta participants
  - East Liverpool participants had more postural sway/instability than Mount Vernon participants
  - East Liverpool participants had slower initiation of movement than Mount Vernon participants but faster than Marietta participants
  - Differences in neuropsychological testing were noted between East Liverpool and the other two towns of Marietta and Mount Vernon

CONCLUSIONS

- Both exposed towns had elevated manganese air exposures, but effects potentially due to manganese exposure were fewer and more subtle than in occupational studies of much higher exposures
- Neuropsychological and mood test scores of the 3 towns were mostly within the average range of the general population
- When comparing test scores with the exposure index, there were significant relationships with tests of: Immediate and delayed memory (daily living), Delayed visual memory, Divided attention, Word reading, Switching Categories, Naming, Abstract thinking, Processing speed
- An association between low test scores and higher exposure index and closer distance suggests living closest to the manganese source for a longer time at times results in subtle differences, lower neuropsychological and psychomotor performance

NEXT STEPS

- Blood manganese - may not be an ideal biomarker, so we will continue with an evaluation of hair and toenails
- Manganese in hair is being analyzed for East Liverpool and compared with air manganese, the distance from the manganese source, and the modeled exposure index (which includes distance in the calculation)
- Manganese in toenails will be analyzed by distance from the manganese source, and the modeled exposure index
- Further data analyses will be performed
- Publications – which will be added to the EPA website when published ***http://www.epa.gov/nheerl/mnstudy***

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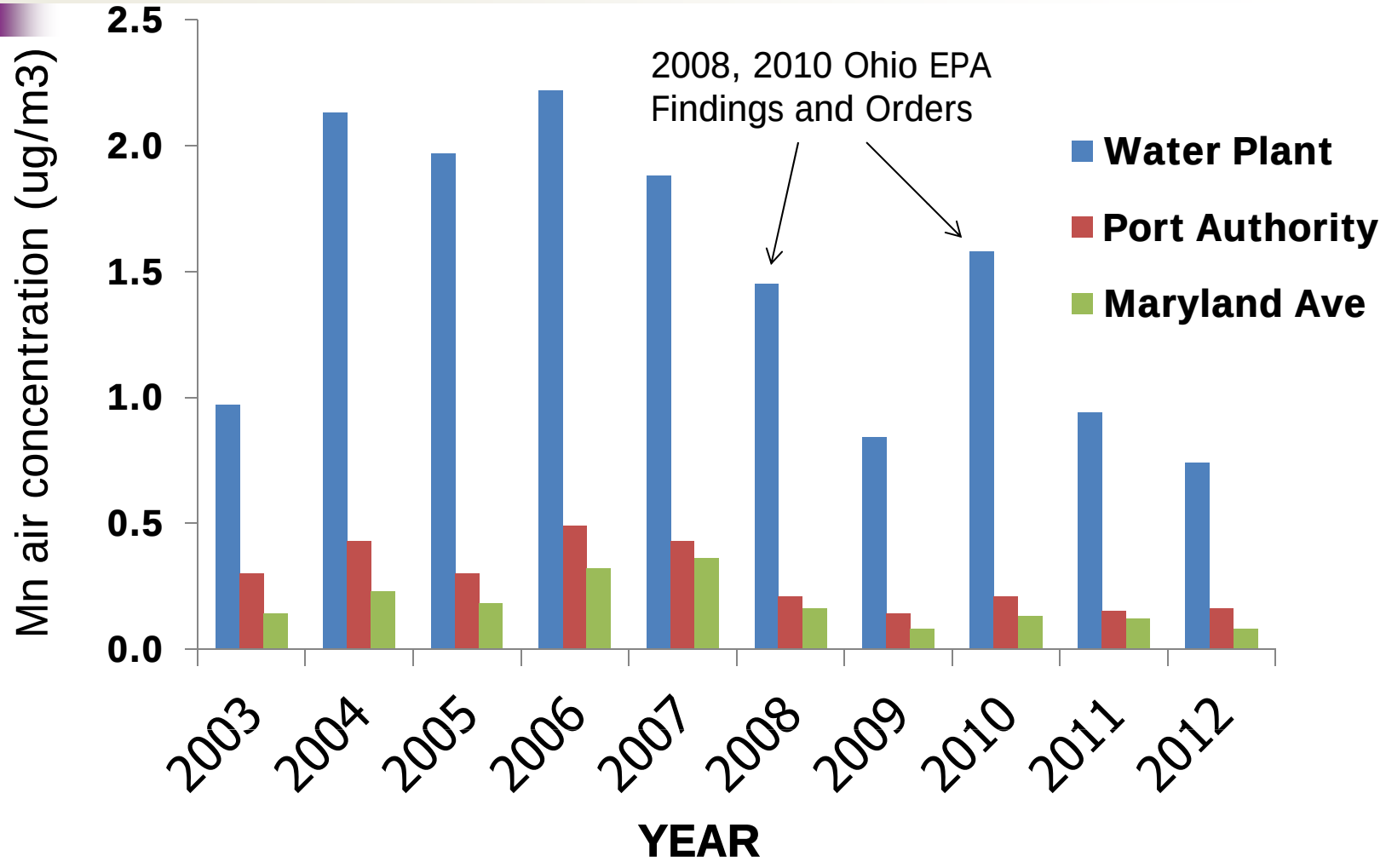

THANK YOU!

San Francisco, CA

East Liverpool, OH

ANY QUESTIONS?