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#### Birth outcomes and water: A multidisciplinary study

Moses New-Aaron University of Nebraska Medical Center, moses.newaaron@unmc.edu

Jane L. Meza University of Nebraska Medical Center, jmeza@unmc.edu

Patrick J. Shea University of Nebraska - Lincoln, pshea1@unl.edu

Martha Rhoades University of Nebraska - Lincoln

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## Background

Birth defects are a known cause of infant death in the United States<sup>1</sup>. Nitrate and atrazine are widely used agrichemicals found in U.S. drinking water and frequently occur as mixtures<sup>2</sup>. While studies explore the risk of adverse pregnancy outcomes associated with exposure to these agrichemicals as single compounds<sup>3,4</sup>, we hypothesize the mixture is more toxic. Nitrate and atrazine can react in vivo to form N-nitrosoatrazine (NNAT), a nitrosamine. Many nitrosamines are known or suspected teratogens. Avian embryos exposed to NNAT showed increased incidence of neural tube defects, microphthalmia, craniofacial hypoplasia, heart defects, gastroschisis and caudal regression compared to embryos exposed to nitrate or atrazine.<sup>5</sup> Our objective is to further examine the risk of adverse health outcomes associated with exposure to nitrate and nitrosatable agrichemicals in drinking water. To date Nebraska and NNAT have been the focus of our population and laboratory studies. Presented here are some preliminary findings illustrating the multidisciplinary nature of this type of research.

### Methods

#### Outcome

Birth defect rates for each of the 93 Nebraska counties were obtained from Nebraska Department of Health and Human Services (2005-2014) and expressed as case rate per 10,000 live births.

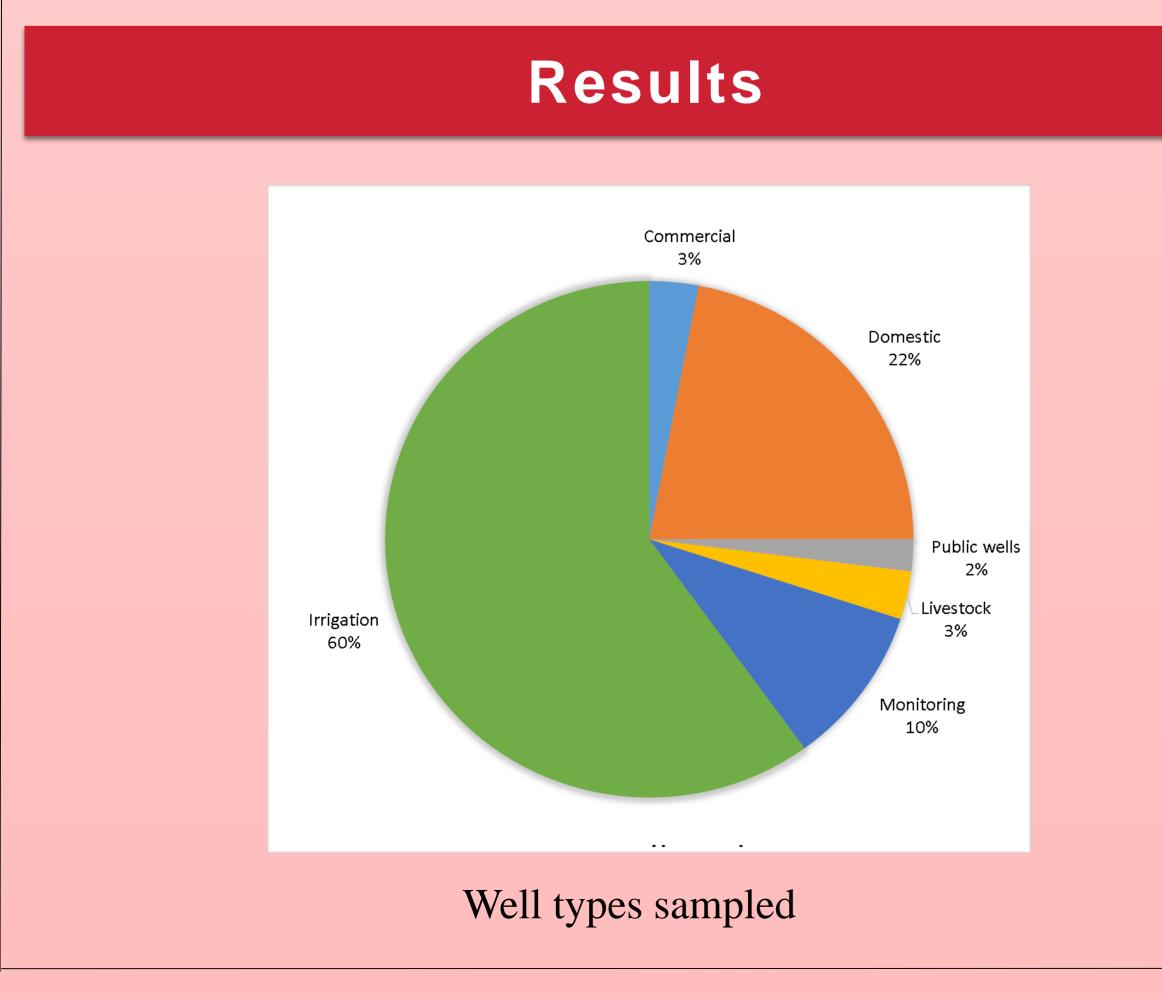
#### Exposure

Contaminant data for nitrate and nitrosatable agrichemicals were obtained from the Quality-Assessed Agrichemical Contaminant for Nebraska Ground Water database (1977-2014).

- Contaminants include nitrate and nitrosatable compounds (NCs).
- Well types include commercial, domestic, irrigation, public water system, monitoring and livestock.

#### Statistical analysis

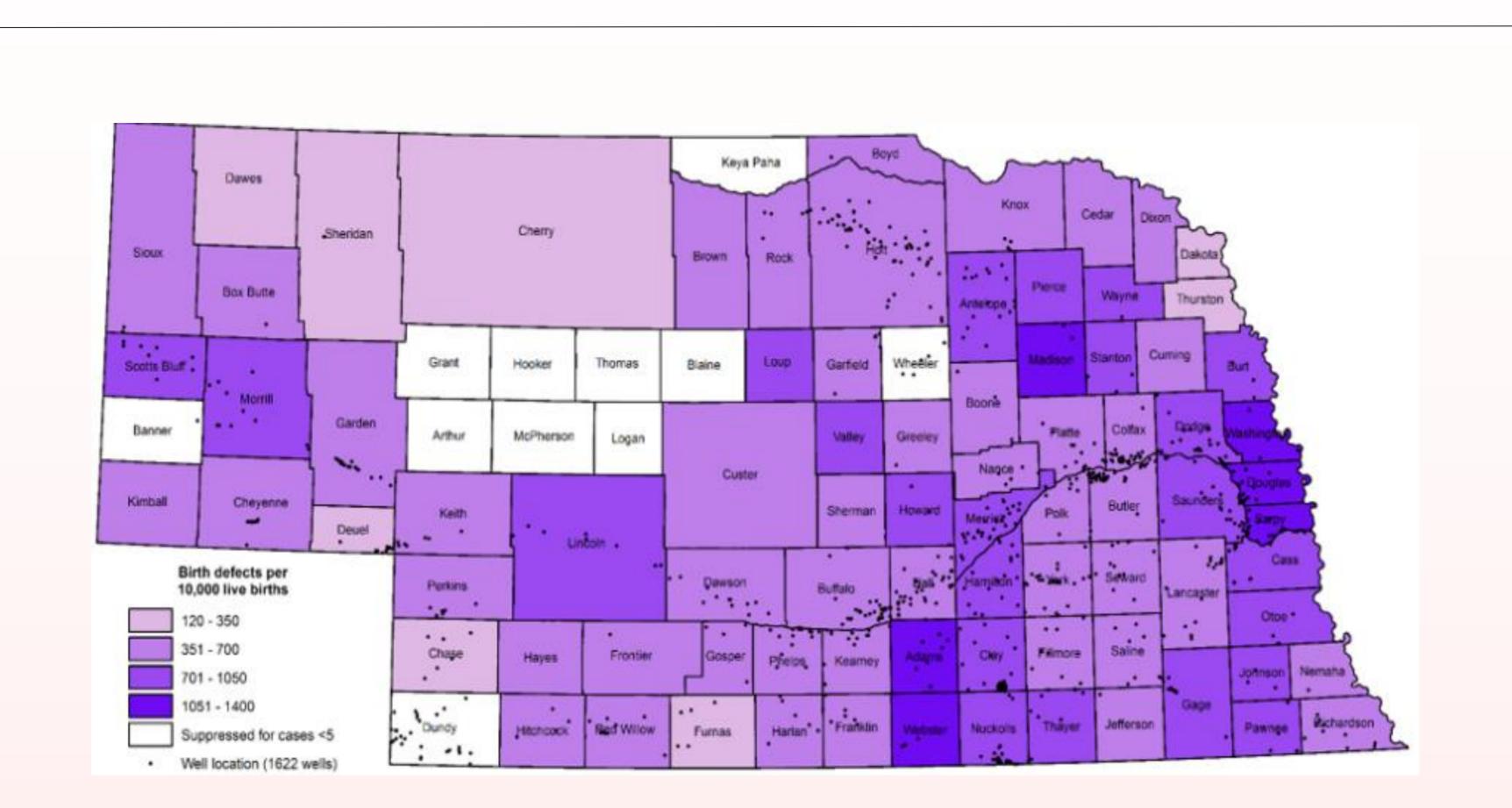
Percentage of wells positive for each agrichemical was calculated. A linear regression model was fitted for nitrate and NCs in different well types to determine if there was a relationship between percent positive agrichemical wells and birth defect rates. All analyses were conducted using SAS version 9.4.

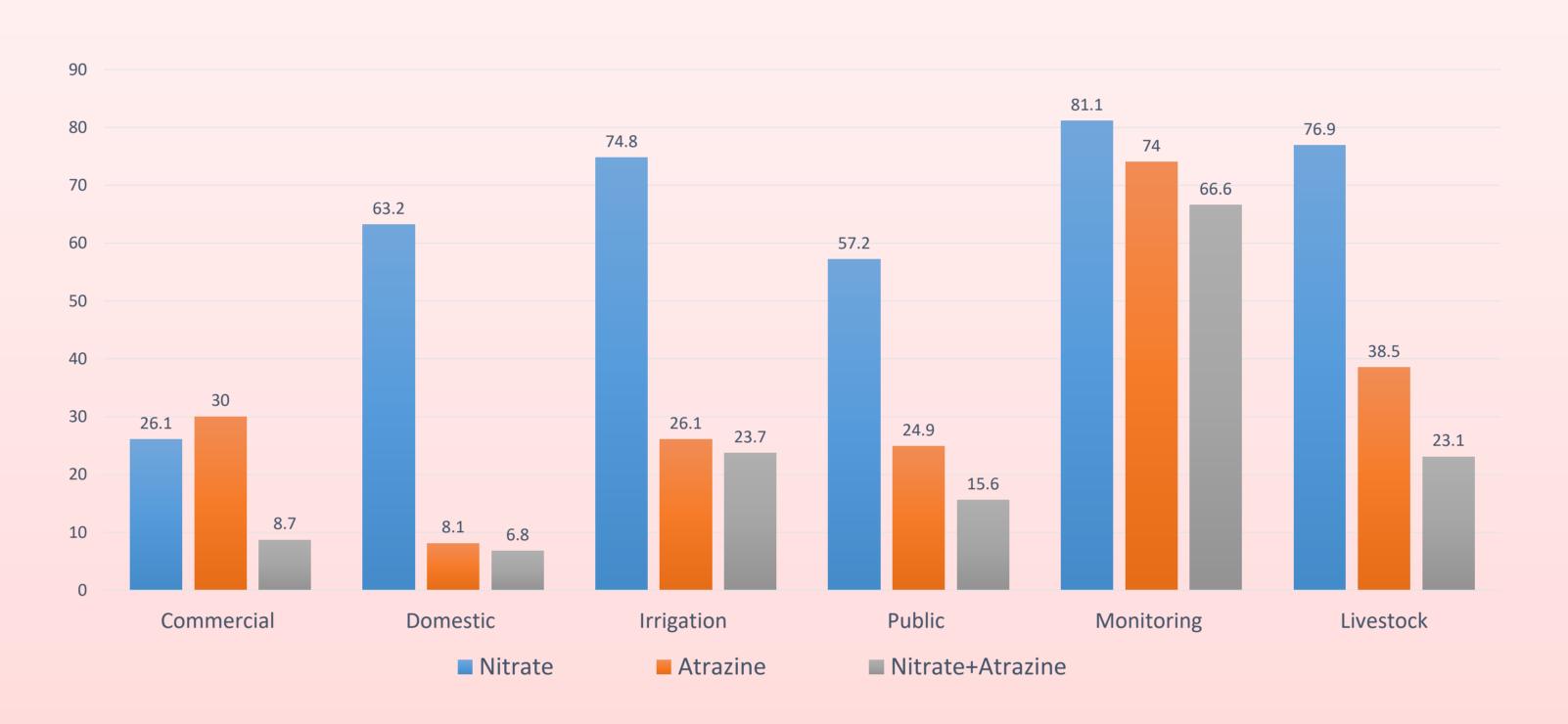


# **Birth Outcomes and Water: A Multidisciplinary Study**

Moses New-Aaron, Jane L. Meza, Patrick J. Shea, Martha G. Rhoades **University of Nebraska-Lincoln and University of Nebraska Medical Center** 







## Percent wells positive for nitrate, atrazine and combination by well type

#### Association between domestic wells and other well types.

Percent Domestic Wells	Correlation Coefficient (p-value)	
Nitrate Positive		
Livestock	0.77 (0.0008)	
Public	0.59 (0.0001)	
Commercial	0.61 (0.03)	
Percent Domestic Wells		
Atrazine Positive		
Public	0.32 (0.04)	
Monitoring	0.55 (<0.0001)	
Irrigation	0.45 (<0.0001)	

### References

1. Mburia-Mwalili A., Yang W (2014). Birth defects surveillance in the United States: Challenges and implications of international classification of diseases, tenth revision, clinical modification implementation. International Scholarly Research Notices, 2014. 2. Brender JD, Weyer PJ (2016). Current Environmental Health Reports 3.2, 44-152.

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### Linear regression between birth defect rates and percent of agrichemical positive wells.

Agrichemical (%)*	Slope	p value
Any NCs	3.12	0.02
Only Parent (P) NCs	2.92	0.03
Only Degradate (D) NCs	2.16	0.26
Nitrate	-4.33	0.07
Atrazine	3.03	0.03
Nitrate D	-2.71	0.14
Atrazine D	5.7	0.02
Nitrate P	-6.37	0.02
Atrazine P	1.87	0.05
Nitrate P+D	-2.45	0.19
Atrazine P+D	6.44	0.002
Nitrate+Atrazine D	5.73	0.03
Nitrate+Atrazine P+D	6.9	0.005

\*Percent positive of wells tested; D=Domestic wells; P=Public wells; NCs=Nitrosatable compounds

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### Acknowledgments

- and domestic wells (23%).

- from the same aquifer.
- same aquifer.

# **Conclusions and Limitations**

- individual exposures.

# BOW Study (bow.unl.edu)

A related multidisciplinary project is underway to design and evaluate the feasibility of conducting a case control study in Nebraska. Our overall objective is to assess the risk of adverse fetal outcomes associated with maternal exposure to nitrate and nitrosatable compounds in drinking water. Protocol:

- Identify participants
- Questionnaire
- Health history
- Demographics
- Blood sample
- Water sample
- Participant perception

Future work: Fully powered case control study



## Discussion

• Majority of wells tested for agrichemicals were irrigation (62%)

Sixty three percent of domestic wells tested positive for nitrate and 25% of public wells tested positive for atrazine.

• Nitrate-positive domestic wells were correlated to nitrate-positive livestock wells. Atrazine-positive domestic wells were correlated to atrazine-positive irrigation wells.

• This suggests that if a livestock well is contaminated with nitrate, a nearby domestic well could be contaminated if the water is

• And if an irrigation well is contaminated with atrazine, a nearby domestic well could be contaminated if the water is from the

• The basis for a negative relationship between nitrate contaminated wells and birth defect rates is less apparent, but if nitrate induces miscarriage it reduces the incidence of birth defects because the fetus does not survive to delivery.

• The largest effect of agrichemicals on birth defect rates was found with nitrate + atrazine in public and domestic wells.

• This study suggests that the association between birth defect rates and wells positive for both nitrate and atrazine is stronger than with wells positive for a single contaminant.

• This is an ecological study; the contaminant data do not represent

• The study did not control for other exposures that can impact development, resulting in birth defects.

• 20 cases and 20 controls

• 5 from each water system: Public, private, bottled, filtered

Residential/water history

• Saliva sample to measure NO<sub>2</sub> and NO<sub>3</sub> • Evaluate maternal nitrosation potential

• Genetic and chromosomal factors

• Estimate maternal exposure • Three years prior to conception

• Motivation and barriers to participate in BOW study

