

Assessment of Arsenic Metabolism and Diabetes Prevalence using Mendelian Randomization

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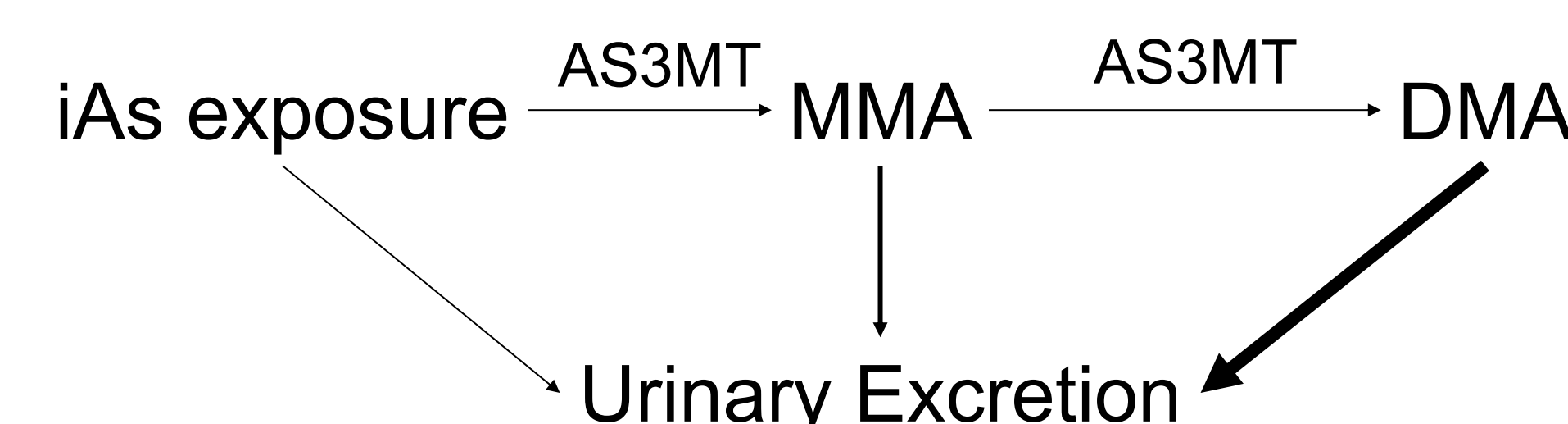


Significance

Arsenic Exposure

- Exposure varies by geographic region
- Starr County, TX: elevated ground water arsenic¹
 - Markedly elevated diabetes prevalence and mortality
 - High percentage of Mexican-American population

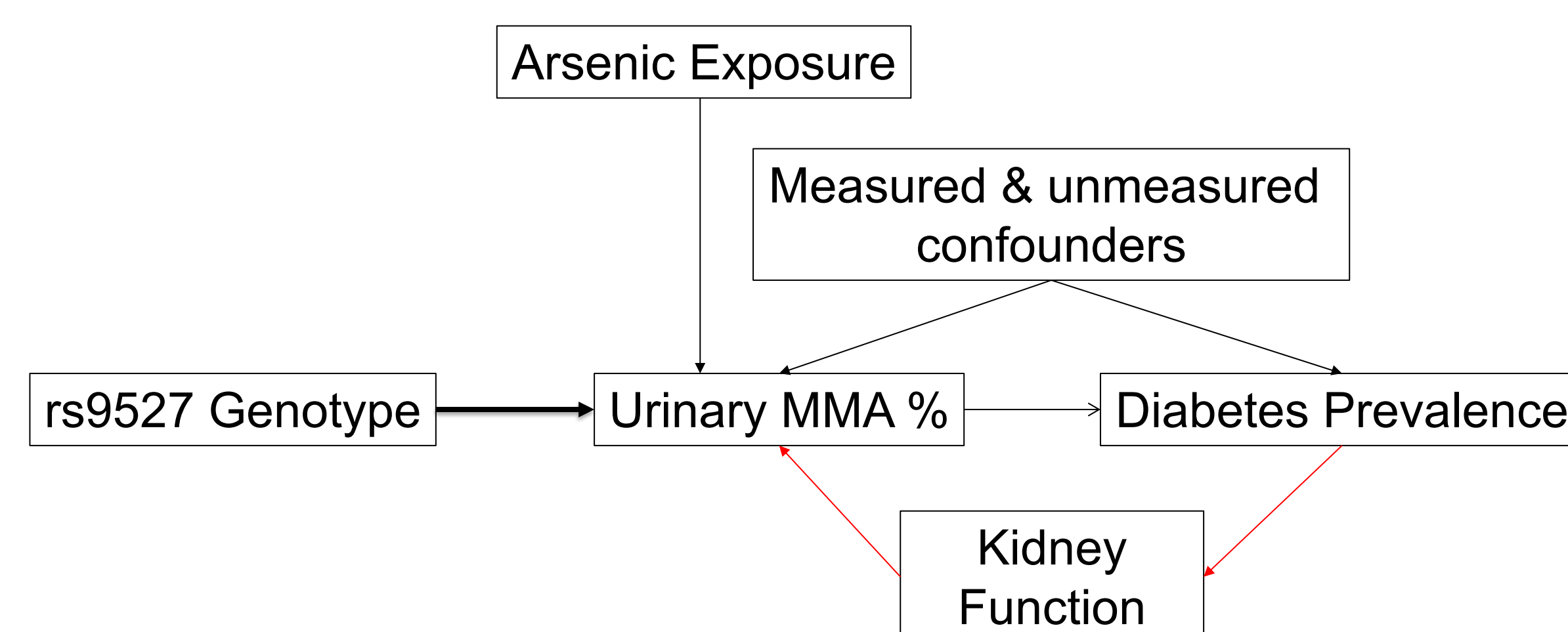
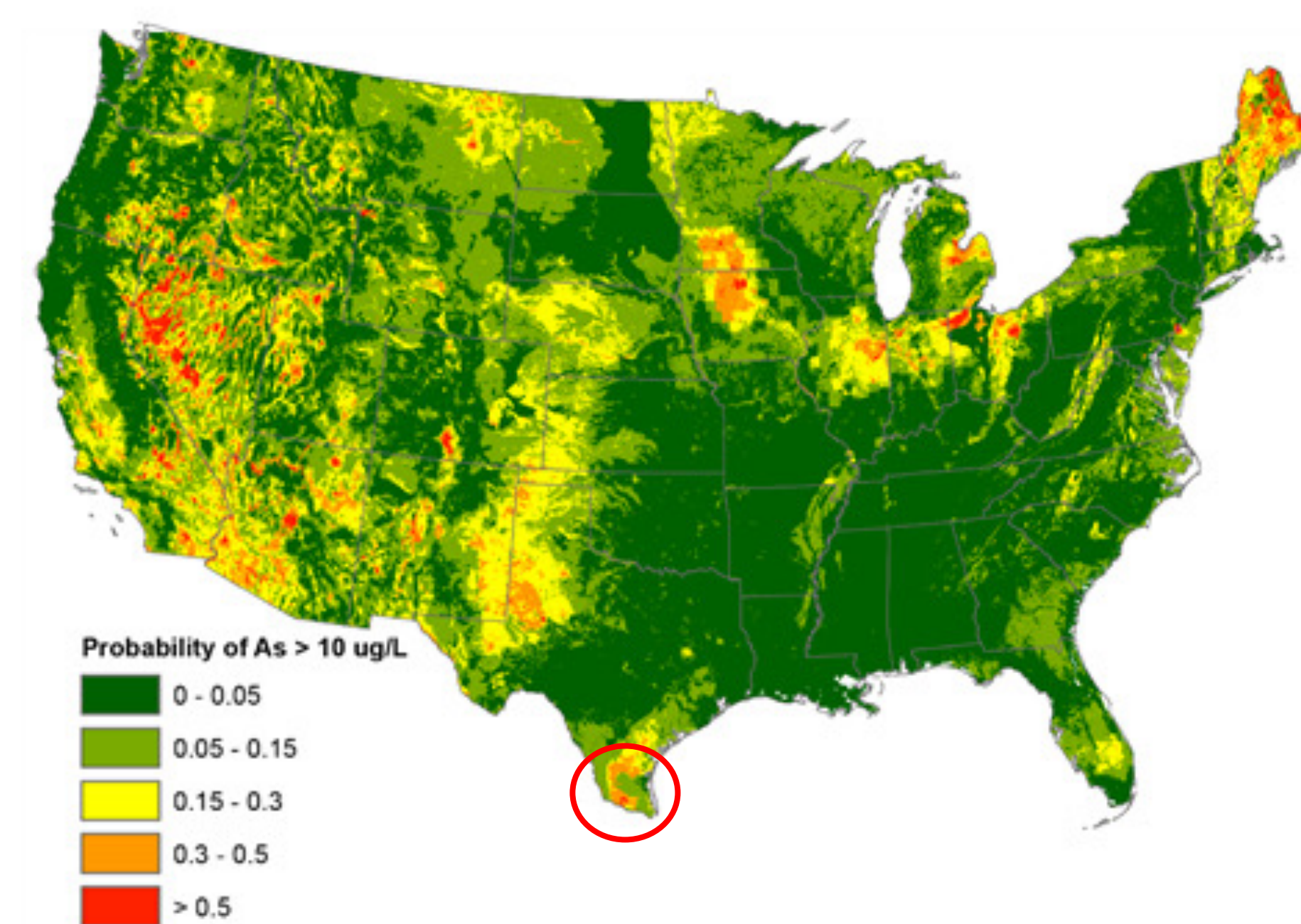
Arsenic Metabolism



- Toxicity varies by arsenic metabolite

Mendelian Randomization

- Genetic polymorphisms are independent predictors of arsenic metabolism
- Rs9527 is intron variant in arsenic methyltransferase



Overall Objective

Evaluate the association of arsenic on diabetes prevalence among Mexican American adults from Starr County using Mendelian Randomization.

Study Population & Demographics

- Cross-sectional study design from 2010-2014
- 475 participants: 127 with type 2 diabetes, 348 without
- Most participants were female, overweight, never smokers

Characteristics of study participants (N=475)

Age, years mean ± SD	51 ± 10
Gender, n (%)	
Male	138 (29)
Female	337 (71)
BMI, kg/m ² mean ± SD	32 ± 6
Smoking status, n (%)	
Current	80 (17)
Former	77 (16)
Never	318 (67)

Conclusion

Differences in MMA % imply differences in arsenic methylation efficiency:

- High MMA % indicates lower efficiency
- Low MMA % indicates higher efficiency

These data indicate higher methylation efficiency is a potential risk factor for arsenic associated diabetes in this high-risk Mexican American population

Acknowledgements

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Arsenic Exposure & Diabetes Prevalence

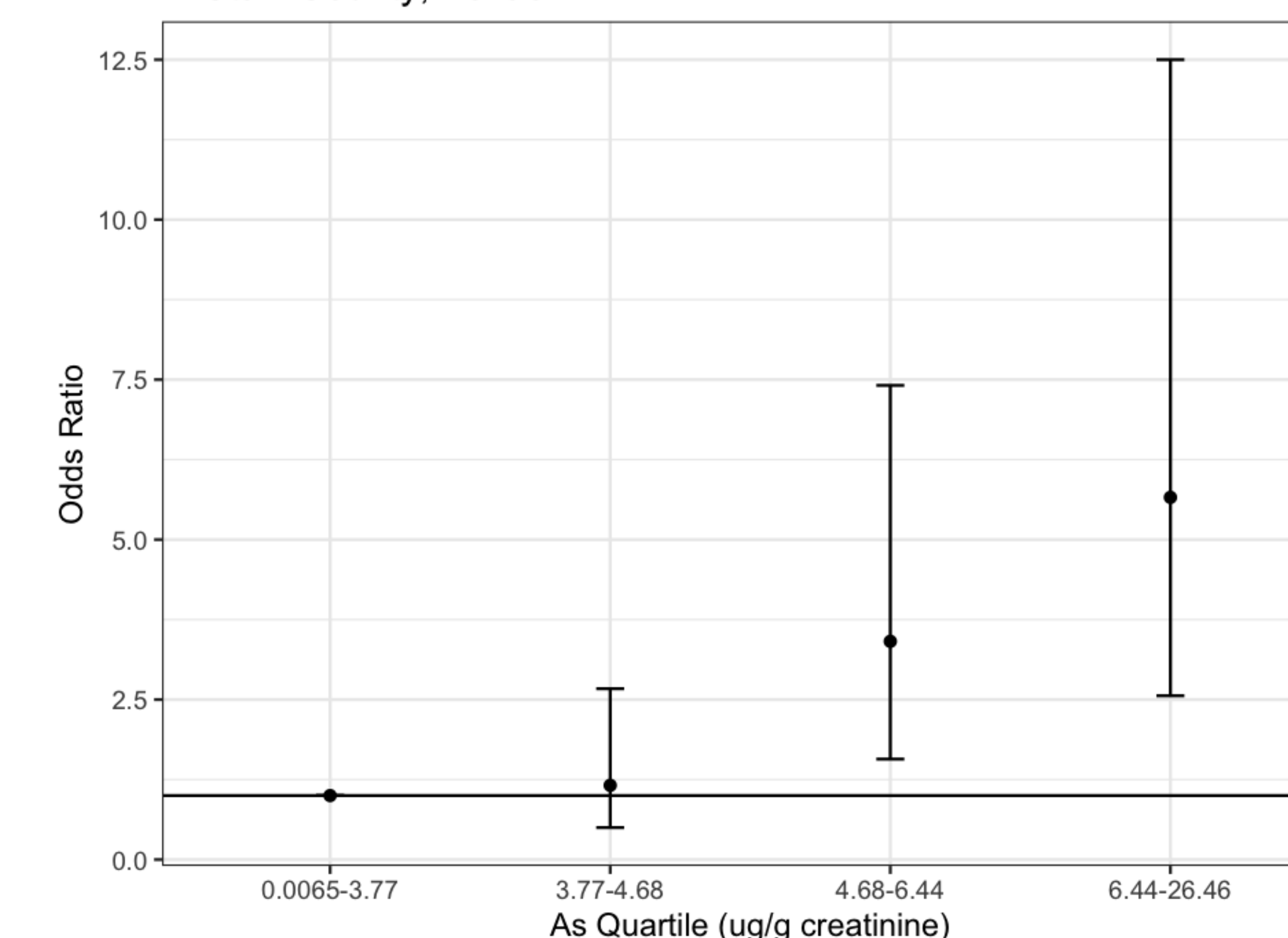
Statistical analysis

- Multivariable logistic regression for association between total As exposure and diabetes prevalence
- Urinary arsenic adjusted for seafood consumption and standardized to urine creatinine
- Adjusted for age, sex, body mass index, smoking, alcohol consumption, socioeconomic status

Results

- Median (IQR) total arsenic: 4.68 (2.96) µg/g Cr
- Highest quartile of urinary arsenic is associated with a 566% increased odds of type 2 diabetes
- Significant linear trend of increasing arsenic exposure with type 2 diabetes prevalence

Association of Total Arsenic Exposure with Diabetes Prevalence in Starr County, Texas



Arsenic Metabolism & Diabetes Prevalence

Statistical analysis

Multivariable stepwise adjusted linear and logistic regression for associations between:

- Rs9527 and MMA %
- MMA % and diabetes status
- Rs9527 and diabetes status

Results

- Higher urinary MMA% is associated with reduced diabetes prevalence
- In high total arsenic group (top 50%ile), the T allele of rs9527 is associated with increased urinary MMA%
- In high total arsenic group (top 50%ile), the T allele of rs9527 is associated with reduced diabetes prevalence

Model	Exposure	Outcome	Overall (N=475)		Low Total Arsenic (n=238)		High Total Arsenic (n=237)		P value Interaction
			Beta/OR (95% CI)	P value	Beta/OR (95% CI)	P value	Beta/OR (95% CI)	P value	
Model 1	rs9527	MMA %	0.02 (0.008, 0.04)	0.003	0.01 (-0.009, 0.03)	0.300	0.04 (0.02, 0.06)	<0.001	0.08
	MMA%	Diabetes	0.53 (0.39, 0.73)	<0.001	0.61 (0.37, 0.98)	0.040	0.54 (0.35, 0.83)	0.005	0.71
	rs9527	Diabetes	0.89 (0.57, 1.41)	0.63	1.81 (0.94, 3.50)	0.080	0.50 (0.24, 0.90)	0.02	0.004
Model 2	rs9527	MMA %	0.03 (0.01, 0.04)	0.001	0.01 (-0.007, 0.03)	0.200	0.04 (0.02, 0.06)	<0.001	0.02
	MMA%	Diabetes	0.44 (0.30, 0.64)	<0.001	0.43 (0.24, 0.76)	0.003	0.49 (0.30, 0.81)	0.005	0.70
	rs9527	Diabetes	0.80 (0.49, 1.33)	0.40	1.30 (0.63, 2.71)	0.500	0.54 (0.27, 1.10)	0.09	0.09
Model 3	rs9527	MMA %	0.03 (0.01, 0.04)	0.001	0.01 (-0.007, 0.03)	0.200	0.04 (0.02, 0.06)	<0.001	0.11
	MMA%	Diabetes	0.44 (0.30, 0.64)	<0.001	0.41 (0.23, 0.74)	0.003	0.50 (0.31, 0.83)	0.007	0.63
	rs9527	Diabetes	0.79 (0.48, 1.33)	0.38	1.27 (0.61, 2.67)	0.520	0.55 (0.27, 1.10)	0.09	0.13

Model 1: Adjusted for seafood consumption

Model 2: Adjusted for seafood consumption, age, and sex

Model 3: Adjusted for seafood consumption, age, sex, body mass index, and smoking status