



# Impact of Prematurity and Neonatal Stress Measured by Apgar Score on Analyte Concentrations Used for Newborn Screening

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# Outline

- Background
- Research question
- Methods
- Results
- Conclusions
- Public Health Implications

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# Background

- Analytes used for newborn screening (NBS) vary by gestational age and/or neonatal stress
  - Congenital hypothyroidism (CH)
  - Congenital adrenal hyperplasia (CAH)
  - Cystic fibrosis (CF)
- Variations in other analyte concentrations by gestational age or neonatal stress have not been assessed
  - Phenylketonuria (PKU)
  - Galactosemia (GALT)

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# Research Question

- Do the following analytes used for NBS vary by Apgar score and/ or gestational age after adjustment for potential confounders?
  - Thyroid stimulating hormone (CH)
  - 17-Hydroxyprogesterone (CAH)
  - Immunoreactive trypsinogen (CF)
  - Galactose (GALT)
  - Phenylalanine (PKU)

# Methods

- Study Design
  - Retrospective cohort
- Study Population
  - Infants born in Michigan in 2008 with NBS records matched to birth certificate records
    - 119,386 infants screened
    - 117,473 matched to birth certificate
  - Excluded 237 confirmed cases

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# Methods

- Data Sources
  - NBS
  - Birth certificate
- Analytic method
  - Crude and adjusted generalized linear models (GLM) of the association between analyte concentrations and gestational age/5 minute Apgar score
  - Least squares means and p-values are reported
  - Adjusted analyses: birth weight, race, sex, and age at specimen collection

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# Results

## Demographic and Perinatal Characteristics of Study Population, Michigan 2008

Characteristic		N	%
Birth Weight	<1800 g	1,244	1.1
	1800-2499 g	6,218	5.5
	≥2500 g	105,760	93.4
Gestational Age	<32 weeks	245	0.2
	32-37 weeks	9,534	8.6
	≥37 weeks	101,846	91.2
Sex	Female	60,121	51.2
	Male	57,352	48.8
Race	White	73,425	70.8
	Black	20,364	19.6
	American Indian	519	0.5
	Asian/Pacific Islander	2,409	2.3
	Middle Eastern	2,593	2.5
	Multi-racial	4,389	4.2
5 Minute Apgar Score	<7	2,754	3.2
	7-10	83,918	96.8

# Results-CH

## Generalized Linear Models of the Crude & Adjusted Associations between NBS TSH Values & Gestational Age or 5 Minute Apgar Score, Michigan Newborn Screening, 2008

Characteristic		Crude		Adjusted*		Mutually Adjusted**	
		TSH (LS Mean)	P-value	TSH (LS Mean)	P-value	TSH (LS Mean)	P-value
Gestational age	<32 weeks	5.5	<0.001	6.0	<0.001	4.9	<0.001
	32-37 weeks	10.4		9.9		10.1	
	≥37 weeks	11.4		11.1		11.1	
5 Minute Apgar Score	<7	11.2	0.2	10.3	0.02	9.2	<0.001
	7-10	11.0		10.1		8.8	

\*Adjusted for birth weight, race, sex, and age at specimen collection

\*\*Adjusted for gestational age and 5 minute apgar score

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# Results-CAH

## Generalized Linear Models of the Crude & Adjusted Associations between NBS 17-OHP Values & Gestational Age or 5 Minute Apgar Score, Michigan Newborn Screening, 2008

Characteristic		Crude		Adjusted*		Mutually Adjusted**	
		17-OHP (LS Mean)	P-value	17-OHP (LS Mean)	P-value	17-OHP (LS Mean)	P-value
Gestational age	<32 weeks	122.2	<0.001	104.1	<0.001	105.5	<0.001
	32-37 weeks	35.6		41.8		34.7	
	≥37 weeks	16.1		27.0		16.0	
5 Minute Apgar Score	<7	27.2	<0.001	41.8	<0.001	55.4	<0.001
	7-10	17.3		35.6		50.2	

\*Adjusted for birth weight, race, sex, and age at specimen collection

\*\*Adjusted for gestational age and 5 minute apgar score



# Results-CF

## Generalized Linear Models of the Crude & Adjusted Associations between NBS IRT Values & Gestational Age or 5 Minute Apgar Score, Michigan Newborn Screening, 2008

Characteristic		Crude		Adjusted*		Mutually Adjusted**	
		IRT (LS Mean)	P-value	IRT (LS Mean)	P-value	IRT (LS Mean)	P-value
Gestational age	<32 weeks	41.9	<0.001	38.7	<0.001	42.6	<0.001
	32-37 weeks	29.1		29.0		29.8	
	≥37 weeks	27.9		28.9		28.6	
5 Minute Apgar Score	<7	30.6	<0.001	31.3	<0.001	34.9	<0.001
	7-10	27.5		28.8		32.4	

\*Adjusted for birth weight, race, sex, and age at specimen collection

\*\*Adjusted for gestational age and 5 minute apgar score

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# Results-GALT

Generalized Linear Models of the Crude & Adjusted Associations between NBS Galactose Values & Gestational Age or 5 Minute Apgar Score, Michigan Newborn Screening, 2008

Characteristic		Crude		Adjusted*		Mutually Adjusted**	
		Galactose (LS Mean)	P-value	Galactose (LS Mean)	P-value	Galactose (LS Mean)	P-value
Gestational age	<32 weeks	10.2	<0.001	10.3	<0.001	10.0	<0.001
	32-37 weeks	10.4		10.3		10.3	
	≥37 weeks	10.7		10.6		10.7	
5 Minute Apgar Score	<7	10.6	0.2	10.5	0.91	10.4	0.98
	7-10	10.7		10.5		10.4	

\*Adjusted for birth weight, race, sex, and age at specimen collection

\*\*Adjusted for gestational age and 5 minute apgar score

# Results-PKU

## Generalized Linear Models of the Crude & Adjusted Associations between NBS Phenylalanine Values & Gestational Age or 5 Minute Apgar Score, Michigan Newborn Screening, 2008

Characteristic		Crude		Adjusted*		Mutually Adjusted**	
		Phe (LS Mean)	P-value	Phe (LS Mean)	P-value	Phe (LS Mean)	P-value
Gestational age	<32 weeks	82.5	<0.001	76.2	<0.001	80.4	<0.001
	32-37 weeks	66.6		69.9		65.1	
	≥37 weeks	60.6		66.0		59.9	
5 Minute Apgar Score	<7	63.5	<0.001	68.7	<0.001	70.5	<0.001
	7-10	60.2		67.0		68.5	

\*Adjusted for birth weight, race, sex, and age at specimen collection

\*\*Adjusted for gestational age and 5 minute apgar score

# Conclusions

- After adjustment for potential confounders, analyte concentrations used for NBS do vary by neonatal stress, measured by Apgar score, and prematurity.
- Gestational age and neonatal stress are independently associated with analyte concentrations.

# Limitations

- Apgar score
- Biological confounders

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# Public Health Implications

- NBS guidelines for premature and/ or sick neonates
- Gestational age-specific cut-offs

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# Acknowledgments

- Co-author of abstract:
  - Steven Korzeniewski, MA, MSc
- Violanda Grigorescu, MD, MSPH
  - Michigan Department of Community Health
- NBS Program Staff
  - Follow-up
  - Laboratory

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# Thank You!

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