Perinatal Outcomes and Unconventional Natural Gas Development (UNGD) in Southwest Pennsylvania

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Disclosures: Heinz Endowment

## OUTLINE

- UNGD and Human Health (Bkgd)
- UNGD and Perinatal Outcome
- Biomonitoring maternal exposure
- Summary

## Impact UNGD on Human Health

- Conferences, working groups and commissioned reports (Physicians and Scientists for Health, Society Toxicology, NIEHS Centers Excellence, National Research Council, NY State Department Health, Maryland Dept Environment, Council Canadian Academies, Health Effects Institute)
- Concensus:
  - Current data neither sufficient nor conclusive
  - One size fits all . . . . Won't work
  - Need for transparency
  - Environmental stressors and routes of exposure make adverse effects on human health plausible.

#### Potential Impacts on Human Health

Exposure: contact (inhalation, ingestion, dermal) between substance in environment and human body at specific points in space over specified time.

Stressors: chemical (PM, BETX, metals) or sensory (light, noise, odor) stressors, physical agents (radiation, silica) and hazards (traffic, stress).

# Issues limiting insight into health effects of UNGD

- Lack of baseline studies (natural, anthropogenic, non-specific)
- Some effects take considerable time
- Sparse (statistical power) and dense (non-UNGD) pop
- Life cycle of UNGD (development, production, post-prod)
- Inadequate monitoring
- Toxicology: a) chemical mixtures; b) material recovered (brine, metals, NORM)
- Non-disclosure agreements
- Lack of registries/biorepositories
- Incorporate potential benefits

http://www.healtheffects.org/UOGD/UOGD.htm

#### APPROACHES IN ASSESSING HEALTH EFFECTS OF UNGD

- Worker and Community
- Community based participatory research (perception risk, self-reported symptoms, anecdotal information)
- Epidemiology (retrospective cohorts)

#### Occupational Health and Unconventional Oil and Gas Extraction

- Mortality (automobile, struck tools) oil/gas workers 7X greater than all workers (CDC/NIOSH/programs/oilgas/risks)
- Exposure to respirable crystalline silica 10X (Esswein et al, *J Occ Env Hyg* 2013)
- Exposure to benzene and flammable HC's exceeded OSHA permissible level (Esswein et al, J Occ Env Hyg 2014)

Health Symptoms Associated with NGD – Marcellus Shale

- Upper Respiratory Symptoms; Behavioral mood & energy (Steinzor et al, New Solutions 2013)
- Stress (Ferrar et al, Int J Occ Env Hlth 2013)
- Upper Respiratory; Dermal (Rabinowitz et al, Env Hlth Perspect 2015)

# Epidemiology of Health Effects of NGD

Childhood cancer (leukemia; CNS tumors) incidence did not change after HF in PA (Fryzek et al, *J Occ Env Med* 2013) – obfuscation does not bring comfort (Goldstein and Malone) UNGD and Increased Hospitalization Rates in NE Pennsylvania

Increased hospitalization rates (cardiology, neurology)  $\uparrow$  as function of well density in Bradford and Susquehanna (PA Healthcare Cost Containment Council) – Jemielita et al, **PLoS One 10,** 2015

#### **UNGD** Perinatal Outcomes

- Hill EL. PhD Thesis. Dyson Sch Appl Econ and Management, Cornell Univ 2014
- McKenzie et al. Env HIth Perspect 122, 2014
- Casey et al. *Epidemiology 27*, 2016
- Stacy et al. *PLoS One 10*: e0126425, 2015.

## Perinatal Outcomes and Environmental Health

- Extensive data that they are often sensitive population to environmental exposure
- Association of low birth weight and preterm birth with candidate stressors (PM2.5, heavy metals, benzene, ozone, NOx, SO<sub>2</sub>, PAH)
- Fetal basis of adult disease

# Methods

- Retrospective study of 15,451 births in three counties in Southwest PA (Butler, Washington, and Westmoreland) over 4 years (2007-2010)
- Natural gas well data obtained from the Pennsylvania Department of Environmental Protection (PADEP)
  - Geographic coordinates, drilling commencement dates, status (active, abandoned, etc.), configuration (vertical or horizontal), conventional or unconventional
  - Confined analysis to unconventional, active natural gas wells
- Birth data obtained from Pennsylvania Department of Health (PADOH)
  - Geocoded residential addresses (at birth), birth year, sex of child, birth outcomes, maternal risk factors (age, race, etc.)
  - Confined analysis to singleton births
- Used ArcMap 10.1 to calculate point distances between singleton birth residences and natural gas wells

# Methods (continued)

• Calculated an inverse distance weighted (IDW) well count (McKenzie et al., 2014) for each mother living within 10-miles of UGD:

IDW well count = 
$$\sum_{i=1}^{n} \frac{1}{d_i}$$

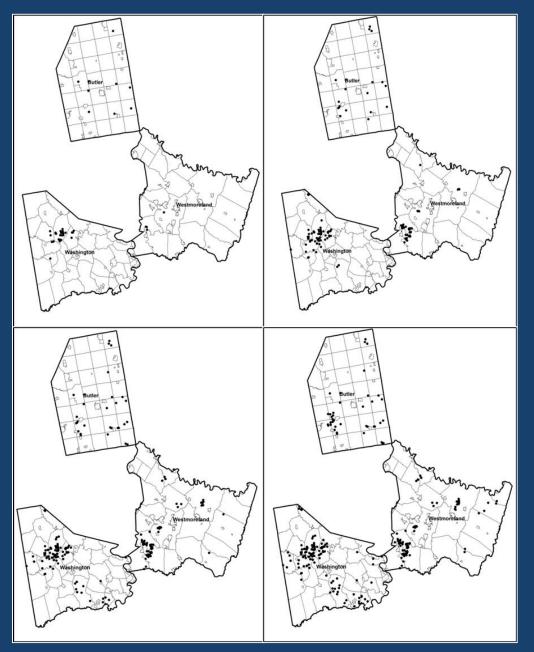
- IDW well count: inverse distance weighted count of active, unconventional natural gas wells within a 10-mile radius of maternal residence in the birth year
- *n*: the number of existing unconventional wells
- *d<sub>i</sub>*: the distance of the ith individual well from the mother's residence

# Methods (continued)

- Categorized mothers into "exposure" quartiles:
  - Group 1: IDW Well Count >0 but <0.87</p>
  - Group 2: IDW Well Count ≥0.87 but <2.60</p>
  - Group 3: IDW Well Count ≥2.60 but <6.00
  - Group 4: IDW Well Count ≥6.00

Groups 2, 3, and 4 (low, medium, and high exposure) compared to Group 1 (the referent)

- Outcomes of interest:
  - Continuous birth weight (g)
  - Small for gestational age (SGA): Birth weight is within 10<sup>th</sup> percentile for given gestational age
  - Premature: Age of gestation <37 weeks</li>
- Adjusted models for sex of the child and a set of *a priori* maternal risk factors: age, race, education, pre-pregnancy weight, smoking during pregnancy, gestational diabetes, WIC (Women, Infants and Children) assistance, prenatal visits, parity (first child, second child, etc.)
- Also adjusted for gestational age in linear birth weight model



Growth of UNGD in three-county area, 2007-2010.

## Maternal and Child Risk Factors

Factor	Total N = 15,451	Referent (First Quartile) <sup>a</sup> N = 3,604	Second Quartile <sup>a</sup> N = 3,905	Third Quartile <sup>a</sup> N = 3,791	Fourth Quartile <sup>a</sup> N = 4,151
Mother's age (years) <sup>b</sup>	28.6 ± 5.8	28.8 ± 5.8	28.7 ± 5.8	28.6 ± 5.7	28.3 ± 5.8
Mother's Education (% high school graduate/GED) <sup>b</sup>	22.7%	22.1%	22.5%	22.6%	23.6%
Pre-Pregnancy Weight (lbs) <sup>b</sup>	153.8 ± 39.1	152.6 ± 38.2	152.9 ± 38.2	155.2 ± 40.2	154.7 ± 39.9
Race (% African American) <sup>b</sup>	3.0%	2.6%	2.0%	3.4%	4.1%
WIC (% assistance) <sup>b</sup>	32.1%	29.6%	31.0%	33.6%	34.1%
Prenatal care (% at least one visit)	99.5%	99.5%	99.5%	99.5%	99.3%
Presence of gestational diabetes	4.1%	4.7%	3.7%	4.3%	3.9%
Cigarette smoking during pregnancy <sup>b</sup>	20.0%	19.6%	18.8%	19.9%	21.7%
Gestational age (weeks) <sup>b</sup>	38.7 ± 1.9	38.6 ± 1.9	38.8 ± 1.8	38.7 ± 1.9	38.7 ± 1.9
Birth weight (g) <sup>b</sup>	3345.8 ± 549.2	3343.9 ± 543.9	3370.4 ± 540.5	3345.4 ± 553.5	3323.1 ± 558.2
Small for gestational age <sup>b</sup>	5.5%	4.8%	5.2%	5.6%	6.5%
Premature <sup>b</sup>	7.7%	8.0%	6.7%	8.4%	7.9%
Congenital anomalies <sup>b</sup>	0.5%	0.3%	0.7%	0.4%	0.5%
Percent female	48.5%	48.7%	48.3%	48.6%	48.5%
Birth parity (first)	42.7%	42.8%	41.7%	42.2%	44.1%

<sup>a</sup>Referent (First quartile), <0.87 wells per mile; Second quartile, 0.87 to 2.59 wells per mile; Third quartile, 2.60 to 5.99 wells per mile; Fourth quartile, ≥6.00 wells per mile.

<sup>b</sup>Difference between quartiles is significant (p<0.05).

doi:10.1371/journal.pone.0126425.t001

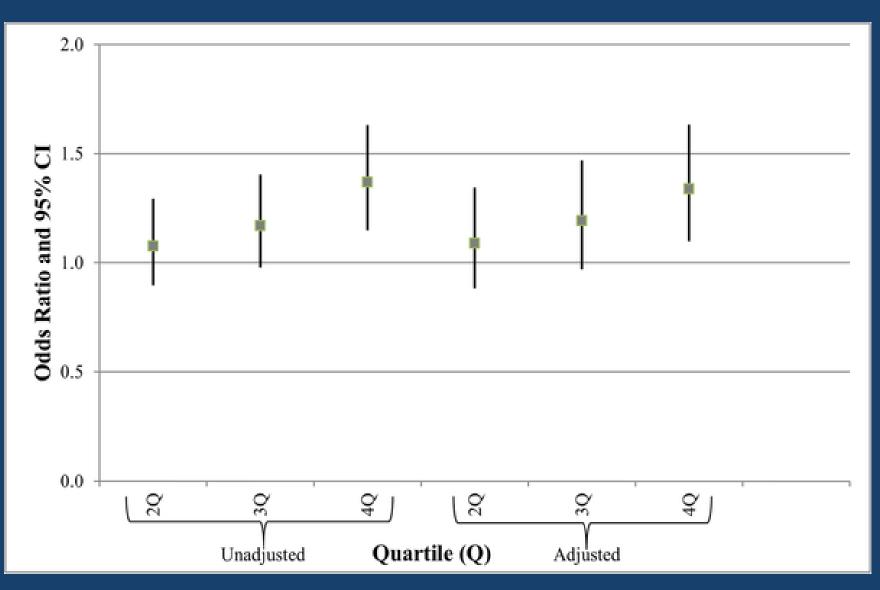
#### Multivariate Linear Regression of Birthweight and Proximity

Model	Unstandardized Coefficients		Standardized Coefficients	t	Significance (P)
	В	Standard Error	Beta		
Constant	-3711.86	93.06	-39.88		<0.01
Mother's Age	-2.95	0.77	-0.03	-3.82	<0.01
Mother's Education	17.88	2.72	0.05	6.58	<0.01
Pre-Pregnancy Weight	2.01	0.09	0.15	23.37	<0.01
Gestational Age	172.64	1.97	0.56	87.51	<0.01
Female	-133.90	6.63	-0.12	-20.19	<0.01
Prenatal Care	127.07	51.53	0.02	2.47	0.01
Smoking During Pregnancy	-184.69	9.07	-0.14	-20.37	<0.01
Gestational Diabetes	33.57	16.82	0.01	2.00	0.05
wic	-27.44	8.62	-0.02	-3.18	<0.01
Race	-146.22	19.88	-0.05	-7.36	<0.01
Birth parity	65.89	4.01	0.12	16.41	<0.01
Low <sup>a</sup>	10.55	9.52	0.01	1.11	0.27
Medium <sup>a</sup>	-0.48	9.59	0.00	-0.05	0.96
High <sup>a</sup>	-21.83	9.39	-0.02	-2.32	0.02

<sup>a</sup>Low, Second quartile to referent; Medium, Third quartile to referent; High, Fourth quartile to referent.

doi:10.1371/journal.pone.0126425.t002

#### ODDS RATIO for SMALL FOR GESTATIONAL AGE INCREASED AS A FUNCTION OF WELL DENSITY



#### Limitations

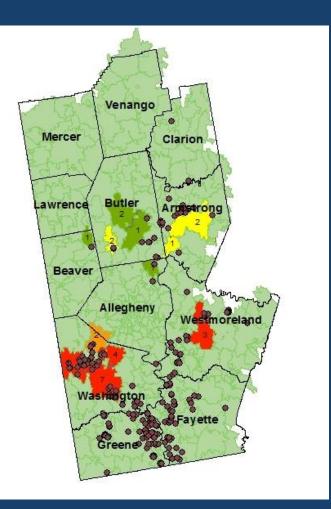
- Associations do not imply causation and could be due to unknown confounding factor or chance (as well as stressor from UNGD).
- Proximity is primitive surrogate for exposure and simple metrics from PADEP modest information regarding heterogeneity of UNGD
- Birth certificate: birthweight, gestational age, risk factors, residence of mother,

#### Summary

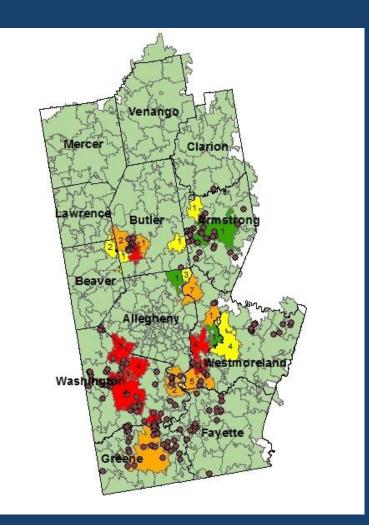
 Although clinical significance of difference in birth weight among exposure groups is unclear, there is need for larger studies, in region-specific fashion, with more precise characterization of exposure over an extended period of time to evaluate public health significance of UNGD. Biomonitoring of maternal exposure to chemical stressors near UNGD in SW PA

- Banked prenatal aneuploidy screening samples from future deliveries at Magee-Women's Hospital of UPMC (with IRB approval)
- UNGD locations obtained from PADEP and initial proximity to wells from zip code of patient (Washington, Westmoreland, Butler, Green, Fayette, Armstrong)

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#### Biomonitoring

- Metals (Cd, Hg, Pb, Ar, and Ag, Al, B, Ba, Ca, Ce, Co, Cr, Cs, Cu, Fe, Ge, In, K, La, Li, Mg, Mn, Mo, Na, Ni, P, Rb, Sb, Sc, Se, Si, Sn, Sr, Ti, U, V, W, Zn, Zr) by Inductive coupled plasma mass spectrometry)
- Benzene oxide adduct albumin by nano-chip LC-QQQ MS
- Cotinine metabolite of nicotine

#### **Future Directions**

- Unfocused adducts on serum albumin
- Newborn dried blood spots and/or cord blood
- Association of pregnant women and newborn health outcomes with level of exposure in larger population affected by UNGD in Southwest PA

#### ACKNOWLEDGMENTS

#### • EOH

- Shaina Stacy, PhD Bernard Goldstein, MD
- EPIDEMIOLOGY
  Evelyn Talbott, PhD
  LuAnn Brink, PhD
- CRITICAL CARE MED Murat Kaynar, MD Veli Bakalov, MD
- GEOLOGY
  Dan Bain, PhD

- Magee Womens
  Yoel Sadovsky, MD
  Hy Simhan, MD
  Jacob Larkin, MD
  Janet Catov, PhD
- Children's Hospital Jerry Vockley, MD, PhD
- Northwestern Sch Med William Funk, PhD