TRI-COUNTY BIRTH OUTCOMES STATISTICAL REVIEW

Study Design

Environmental Epidemiology Program

Bureau of Epidemiology

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A Little History

- June 8, 2013:
  - Vernal midwife notes high number of stillbirths & infant deaths occurring in Vernal, Utah
  - Contacts Natural Resource Management, Inc (NRM) in Salt Lake City
  - NRM forwards the email communication to University of Utah (UU) and others
- June 12, 2013
  - UU contacts Environmental Epidemiology Program (EEP) at the Utah Department of Health
  - EEP responds to UU and contacts Tri-County Health Department (TCHD)
- June 18, 2013
  - EEP provides a case count of still births and infant deaths for Vernal, Utah
- July-September 2013
  - UU asks EEP support to conduct an investigation
  - UU working with EEP determines not feasible for UU to conduct an investigation

A Little History

- January 28, 2014
  - The Governor's Clean Air Action Team (CAAT) asks if an investigation is going to happen
  - EEP responds to CAAT
  - EEP provides an update to TCHD and makes an offer
- March 20, 2014
  - TCHD contacts EEP with approval to conduct an investigation
  - EEP offers to provide TCHD assistance with a stakeholders meeting to design the investigation
- Here we are

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Some Terms

- RISK:
  - Disease Risk: the probability of acquiring a disease (usually defined as a rate or risk ratio)
  - Environmental Risk: a function of (1) exposure and (2) hazard (usually defined as an reference dose)
  - Toxicological Risk: a function of (1) a dose and (2) an effect on the body (usually defined a measure from a dose-response plot)

- INCIDENCE: the number of new cases occurring in a time period (a year)

  Just a fancy word for "count"

- INCIDENCE RATE (or RATE): the number of new cases per time period occurring per a unit (i.e., 1,000) of the population

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Terms about risk

- Risk Factors: Conditions or events that increase one's disease risk
  - Genetics
  - Other health conditions
  - Behaviors and choices
  - Access to health care
  - Home environment
  - External environment

INTRINSIC

EXTRINSIC

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One Last Term

- RISK RATIO (or INCIDENCE RATIO): A ratio created by comparing the study area incidence to a comparison area incidence.

$$RR = \frac{Observed}{Expected}$$

  - The comparison population incidence (the "expected") has been re-proportioned to the same scale as the study population.
  - The "expected" risk is assumed to be the normal random occurrence of disease.

  - Interpretation
    - RR = 1: The risk in the study population and the comparison population are the same
    - RR > 1: The study population has more risk than expected
    - RR < 1: The study population has less risk than expected

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Statistical Review

- Historic trend and current status
  - Provides a measures of the relative risk of a study area
  - Provides an assessment of trends in rates over time
- Is not a cluster investigation – the study area is pre-defined
- Is not an environmental risk assessment
  - Does not link disease risk to environmental risk
  - Will discuss the literature

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Why do this investigation

- Inform the public about the level of disease risk
- Provide education about risk factors
- Support or promote science-based public policy decisions
  - Note: “no action needed” is a public policy decision

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Study Design Issues

- Defining the study population
- Defining the comparison population
- Defining cases
- Defining the analytical periods
- Interpretation rules

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Defining a Study Population

- What data is available?
  - Birth: 1991 – 2012 Utah Birth Records
  - Infant deaths: 1991 – 2012 Utah Death Records
  - Stillborns: 1991 – 2012 Utah Fetal Death Registry
- Is there a risk factor of concern?
  - Air pollution, ozone?
- How big of a population is needed (power)?
  - 2,000 births per study cell (area and/or time) = 80% power
- How is the population tabulated?
  - Area: Census areas, City, ZIP Code, County

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Birth count estimates

Analytical Cell Definition	Average births per cell definition
Vernal city, per year	~ 300
Uintah county, per year	~700
Tri-County Health Department, per year	~1,200

Recommended

Options: Aggregate 2 years

Enhancements: When a health outcome is more frequent, we can do county level analyses as well.

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Defining a comparison population

- What data is available at the same scales?
  - Utah birth, death and fetal death records
  - Scales = year and county
- Should be 2-3 times bigger than the study population (for stability)
- Should be similar in demographic, economic, and other intrinsic risks

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For Example

Metric	Tri-County	Bear-River	South Western	Central	Utah State
Number of births (2012)	1,137	3,326	3,283	1,097	51,230
Teen Pregnancy Rate	74.8	48.4	50.9	85.7	4.8
Maternal Smoking Rate	160.1	54.1	71.6	91.7	61.0
Rate of Inadequate Prenatal Care	12.3	10.8	11.6	24.6	12.4

Etc.

Our standard recommendation

Alternative:
(1) Find several counties most similar to Tri-County
(2) Control for these non-environmental risk factors
(3) Exclude pregnancies with non-environmental risk

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Controlling for Non-Environmental Risk Factors

Risks Factors	Tri-County Cases	Tri-County Births	Comparison Area Cases	Comparison Area Births	Adjusted Comparison Case Count
None	40	669	2,817	38,124	**49.4**
Teen-Pregnancy	10	85	313	2,494	10.7
Maternal Smoking	30	182	529	3,124	30.8
Inadequate Prenatal Care	25	201	775	7,488	20.8
TOTAL	**105**	**1,137**	**4,434**	**51,230**	
Scaled to Tri-County	**105**		**98.4**		**111.7**

sum

$$1{,}137\,\frac{4{,}434}{51{,}230} = 98.4$$

$$669\,\frac{2{,}817}{38{,}124} = 49.4$$

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Controlling Risk

Without Adjustment

$$RR = \frac{105}{98.4} = 1.07$$

RR > 1 means higher than normal risk

With Adjustment ← **Recommended**

$$RR = \frac{105}{111.7} = 0.94$$

RR < 1 means lower than normal risk

Exclude At-Risk Pregnancies

$$RR = \frac{40}{49.4} = 0.81$$

RR < 1 means lower than normal risk

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Controlling risk factors

- Mother's age < 19 yrs or > 40 yrs
- Mother's race/ethnicity
- Tobacco or alcohol or drug use during pregnancy
- Concurrent maternal health concerns
  - Cardiovascular disease, respiratory conditions, diabetes, renal disease, eclampsia, blood disorders, insufficient weight gain, incompetent cervix, etc.
- Insufficient prenatal care

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Defining cases

- Utah Mothers (defined by maternal residential address)
- Singleton Births
- Adverse birth outcome
  - Low birth weight (<2,500 grams at birth)
  - Premature (< 38 weeks gestational age)
  - Small-for-gestational age (birth weight < 10th percentile for gestational age)
- Infant death (less than one year of age)
  - Also tabulate major cause of death groupings
- Stillborn (> 19 weeks gestational age)

- What about Birth Defects?

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Necessary exclusions

- Multiparity births
- Out-of-State mothers (based on address)
- Improbable birth weight or gestational age
  - Birth weight < 375 g or > 4,500 g
  - Gestational age < 22 weeks or > 45 weeks
- Missing sex
- Unassignable to a group (insufficient or missing address)

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Defining analytical period

- Recommendation: Bi-annually from 1991 through 2012.
- Alternatives: Multi-year aggregates

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The analysis

- A study area rate per analytical period (i.e., annual) for each health outcome
  - Temporal trend analysis of rates

- A study area study period rate (1991-2012) rate for each health outcome
  - By county
  - By sex
  - By season ?

Or 2007-2012 (last 5 years)?

- A risk ratio for every rate

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Uncertainty

REALITY

Statistical findings

	Increased Risk	Normal Risk
Increased Risk	Correct Finding of Increased Risk	Type I Error False Positive Finding
Normal Risk	Type II Error False Negative Finding	Correct Finding of Normal Risk

Increase the birth count size (by aggregating) to minimize this error [Statistical Power]

Use confidence limits to assess this error [Statistical Significance]

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Confidence Interval

Disease	Year	Rate (per 1,000 births)	Relative Risk (95% Confidence Interval)
		92.3	1.07 (0.87 – 1.28)

- Confidence intervals help determine if 1.07 is essentially 1.
- If the confidence interval includes one (1.00) then the RR is considered to be the same as 1.00.
- So, to be significantly elevated, the lower confidence limit must be greater than 1.00.
- A 95% confidence interval means that a finding of statistical significance will still be wrong 1 in 20 (5%) times.
  - There will be 132 (22 years * 5 health outcomes) different analyses, so expect 6 to be elevated due to random variability in the data
- Alternative: use a 99% confidence interval.

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Privacy and legal concerns

- Suppression requirements
  - 4 or less cases per analytical period
  - Analytical count
  - Marginal counts that could be used to back calculate analytical counts

- Alternative: Aggregate years to increase case count per analytical period

Significance versus Meaningful

Not Significant

Significant
Not Meaningful

Significant
Meaningful

- When does a concern becomes a problem?
- Is it a big enough problem to become a priority?
- Can public health do something about it?

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Interpretation Rules for Meaningful Results

- Proposal:
  - Two or more sequential analytical periods with statistically elevated risk ratios
  - One or more analytical periods with a risk ratio of 5.0 or greater (based on 80% power)
  - Statistically significant last analytical period with an increasing trend

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Study limitations

- Will not link disease risk to environmental risk (but will discuss risk factors as part of the report discussion)
- Cannot discover Utah mothers who give birth outside of Utah
- The population risk can not be applied to the individual ("ecologic fallacy")

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What after completion?

- What to do if the review does not find any public health concern regarding birth outcomes?

- What to do if the review DOES find adverse birth outcome concerns?

How do we stay engaged?

- Your turn!

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