

Flint Perinatal Metrics Analyses

(Methods 1-3)

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Data source: Division of Vital Records and Health Statistics, MDHHS

Final geocoded Michigan resident live birth files (received 7/27/17), infant mortality files (received 3/3/17) and fetal death files (received 10/2/17)

Background

- In April, 2014, the city of Flint, Michigan, changed its water supply from Detroit-supplied Lake Huron water to the Flint River water, an aging water system without adequate corrosion control.
- A previous study showed that exposure to lead-contaminated drinking water has been associated with adverse pregnancy outcomes (Edwards, 2014).
- We used three methods to assess the rates of stillbirth, infant mortality, preterm birth and low birthweight in the city of Flint, Michigan before and after the water source change.

Methods

- Data source – Michigan Vital Records
 - Vital Records are legal records of Michigan resident live births, fetal deaths and infant deaths and as such are subject to change as new records are submitted or existing records modified or corrected. The data sets used in this analysis are the most current available.
 - Statistical files were prepared by Vital Records statisticians prior to our analysis, including standard de-duplication and removal of voided records.
- Flint definition
 - Geocode of residence was used to determine the minor civil division
- Statistical methods used
 - Statistical test for comparing two proportions
 - Poisson Regression Model (Proc Genmod in SAS)
 - Bayesian Poisson Regression Model (Openbugs)

Method 1

The test statistic for testing the difference of two proportions in the two periods, that is, for testing the null hypothesis $H_0 : p_1 - p_2 = 0$

$$Z = \frac{(\hat{p}_1 - \hat{p}_2) - 0}{\sqrt{\hat{p}(1 - \hat{p}) \left(\frac{1}{n_1} + \frac{1}{n_2} \right)}}$$

Where \hat{p} is the proportion of cases in the two periods combined.

$$\hat{p} = \frac{Y_1 + Y_2}{n_1 + n_2}$$

p_1 = the proportion of the case in the pre period (07/01/2012 – 12/31/2013) ;
 p_2 = the proportion of the case in the post period (07/01/2014 – 12/31/2015).

Method 2

Estimate Standardized Incidence Ratio (SIR) Relative to Expected Counts Based on Michigan Rates

- In this CDC approach, we estimated expected outcome for each quarter of the year (2010-2015) for the city of Flint by using data from the rest of the State of Michigan, after excluding the Flint data.
- The expected outcomes for Flint were estimated for White Non-Hispanic and Black Non-Hispanic populations separately, multiplying the race/ethnicity-specific Michigan rate by the appropriate Flint live birth count.
- The expected total number of outcomes in Flint was then estimated by summing the race/ethnicity-specific expected counts.
- The expected outcome counts in Flint were then used as an offset term in a Poisson regression model to fit these data using SAS Proc Genmod.
- Flint-specific standardized incidence ratios (SIR) relative to the rest of the State both before and after the exposure period were estimated, and the ratio of SIRs was estimated by including a time period variable (07/01/2014 – 12/31/2015 vs. 01/01/2010 – 06/30/2014) in the model.

Method 3

- We used a Bayesian modeling approach to specifically evaluate the likelihood that the SIRs for infant mortality in Flint were elevated after 07/01/2014. The observed infant mortality counts for Flint were assumed to be a random sample from a Poisson distribution such that

$$Infant_Deaths_i^{Flint} \sim Poisson(\mu_i)$$

where

$$\mu_i = Exp_Infant_Deaths_i^{Flint} * e^{\beta_0 + \beta_1 * t_i} \quad [1]$$

- In equation [1], the variable t_i takes the value of 1 if the time variable is greater than or equal to 07/01/2014 and is set to 0 for all time points before 07/01/2014. Using this model, the estimated SIR for time periods before 07/01/2014 is given by e^{β_0} while the SIR after 07/01/2014 is estimated using $e^{\beta_0 + \beta_1}$. Therefore, the estimated change in the infant mortality risk in Flint after July 2014 is given by e^{β_1} .
- The Bayesian modelling approach enabled not only estimation of the SIRs for infant mortality in Flint, but also the probability that the risk of infant mortality increased after 07/01/2014.
- We also compared SIRs between Flint and Saginaw, Detroit, Grand Rapids, and Lansing for both time periods.
- The above method was also applied to estimate the SIRs for preterm birth and low birthweight.

Method 3 (Continued)

- We used a Bayesian modeling approach to specifically evaluate the likelihood that the SIRs for stillbirth in Flint were elevated after 07/01/2014. Due to the numerous quarters in which no stillbirths were reported in Flint, we assumed that the observed stillbirth counts for Flint were observations from a Zero-inflated Poisson (ZIP) distribution with mean given by

$$\text{Stillbirth}_i^{\text{Flint}} \sim p * 0 + (1 - p) * \text{Poisson}(\mu_i)$$

Where p is a Bernoulli random variable representing the probability that the observed stillbirth counts takes a value of 0 and μ_i is the mean value of the non-zero observed stillbirth counts defined as

$$\mu_i = \text{Exp_Stillbirth}_i^{\text{Flint}} * e^{\beta_0 + \beta_1 * t_i} \quad [2]$$

- In equation [2], the variable t_i takes the value of 1 if the time variable is greater to or equal to 07/01/2014 and is set to 0 for all time points before 07/01/2014. Using this model, the estimated SIR for time periods before 07/01/2014 is given by e^{β_0} , while the SIR after 07/01/2014 is estimated using $e^{\beta_0 + \beta_1}$. Therefore, the estimated change in the stillbirth risk in Flint after 07/01/2014 is given by e^{β_1} .
- The Bayesian modelling approach enabled not only estimation of the SIRs for stillbirth in Flint, but also the probability that the risk of stillbirth increased after 07/01/2014.
- We also compare SIRs between Flint and Saginaw, Detroit, Grand Rapids, and Lansing for both time periods.

Method --- Outcomes

- **Infant mortality** is defined as a death of a baby before his or her first birthday.
- **Stillbirth** is defined as a death of a fetus that has completed at least 20 weeks of gestation or weighs at least 400 grams.
- **Preterm birth** is defined as a birth of a baby less than 37 completed weeks of estimated gestation.
- **Low birthweight** is defined as a birthweight of a baby less than 2,500 grams.
- **Small for gestational age** baby is defined as a baby who is smaller in size than normal for the gestational age, most commonly defined as a weight below the 10th percentile for the gestational age.
- **Stillbirth and neonatal death** is defined as a sum of a death of a fetus that has completed at least 20 weeks of gestation or weighs at least 400 grams, and a death during the first 28 days of life (0-27 days).

Results --- Infant Mortality

Method 1: There was not enough evidence to indicate that the estimated infant mortality rates were significantly different over the two time periods.

Table 3: Infant Mortality Rate per 1,000 Live Birth in Flint, 2012-2015

	# Live Births	# Infant Mortality	Infant Mortality Rate per 1,000 Live Births	95% C. I.
07/01/2012 --- 12/31/2013	2348	29	12.35	(7.88, 16.82)
07/01/2014 --- 12/31/2015	2121	25	11.79	(7.19, 16.38)
p-value	0.86			

Results --- Infant Mortality

Method 2: There was not enough evidence to indicate that the estimated standardized incidence ratios for infant mortality were significantly different over the two time periods.

Table 1: Standardized Incidence Ratios of Infant Mortality in Flint, 2010-2015

	Infant Mortality		
	N	SIR	95% C. I.
Overall			
2010 Q1 - 2014 Q2	85	1.17	[0.95, 1.45]
2014 Q3 - 2015 Q4	25	1.18	[0.80, 1.74]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.01	[0.64, 1.57]
White Non-Hispanic			
2010 Q1 - 2014 Q2	19	1.47	[0.94, 2.31]
2014 Q3 - 2015 Q4	3	0.85	[0.27, 2.63]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		0.58	[0.17, 1.95]
Black Non-Hispanic			
2010 Q1 - 2014 Q2	65	1.14	[0.90, 1.46]
2014 Q3 - 2015 Q4	21	1.24	[0.81, 1.91]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.09	[0.67, 1.78]

Results --- Infant Mortality

Method 3: There was not enough evidence to indicate that the estimated standardized incidence ratios for infant mortality were significantly different over the two time periods.

	Infant Mortality	
	SIR	95% C. I.
Flint		
2010 Q1 - 2014 Q2	1.17	[0.94, 1.43]
2014 Q3 - 2015 Q4	1.18	[0.77, 1.68]
Probability (2014 Q3 - 2015 Q4 > 2010 Q1 - 2014 Q2)	0.49	
2010 Q1 - 2014 Q2		
Flint	1.17	[0.94, 1.43]
Saginaw	1.25	[0.92, 1.65]
Probability (SIR Flint > SIR Saginaw)	0.36	
2014 Q3 - 2015 Q4		
Flint	1.17	[0.75, 1.68]
Saginaw	1.61	[0.95, 2.43]
Probability (SIR Flint > SIR Saginaw)	0.16	
2010 Q1 - 2014 Q2		
Flint	1.17	[0.94, 1.43]
Detroit	1.21	[1.12, 1.31]
Probability (SIR Flint > SIR Detroit)	0.37	
2014 Q3 - 2015 Q4		
Flint	1.18	[0.76, 1.68]
Detroit	1.31	[1.14, 1.50]
Probability (SIR Flint > SIR Detroit)	0.28	

Table 2: Standardized Incidence Ratios of Infant Mortality in Flint, 2010-2015

	Infant Mortality	
	SIR	95% C. I.
2010 Q1 - 2014 Q2		
Flint	1.17	[0.94, 1.43]
Grand Rapids	1.10	[0.91, 1.31]
Probability (SIR Flint > SIR Grand Rapids)	0.67	
2014 Q3 - 2015 Q4		
Flint	1.18	[0.76, 1.69]
Grand Rapids	0.90	[0.61, 1.24]
Probability (SIR Flint > SIR Grand Rapids)	0.84	
2010 Q1 - 2014 Q2		
Flint	1.17	[0.94, 1.43]
Lansing	0.99	[0.76, 1.25]
Probability (SIR Flint > SIR Lansing)	0.85	
2014 Q3 - 2015 Q4		
Flint	1.18	[0.76, 1.68]
Lansing	1.09	[0.69, 1.57]
Probability (SIR Flint > SIR Lansing)	0.60	

Results --- Stillbirth

Method 1: There was not enough evidence to indicate that the estimated stillbirth rates were significantly different over the two time periods.

Table 6: Stillbirth Rate per 1,000 Live Birth in Flint, 2012-2015

	# Live Births	# Stillbirth	Stillbirth Rate per 1,000 Live Births	95% C. I.
07/01/2012 --- 12/31/2013	2348	25	10.65	(6.50, 14.80)
07/01/2014 --- 12/31/2015	2121	24	11.32	(6.81, 15.82)
P-value	0.83			

Results --- Stillbirth

Method 2: There was not enough evidence to indicate that the estimated standardized incidence ratios for stillbirth were significantly different over the two time periods.

Table 4: Standardized Incidence Ratios of Stillbirth in Flint, 2010-2015

	Stillbirth		
	N	SIR	95% C. I.
Overall			
2010 Q1 - 2014 Q2	78	1.48	[1.18, 1.84]
2014 Q3 - 2015 Q4	24	1.84	[1.24, 2.75]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.25	[0.79, 1.97]
White Non-Hispanic			
2010 Q1 - 2014 Q2	26	2.46	[1.68, 3.62]
2014 Q3 - 2015 Q4	4	1.32	[0.50, 3.52]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		0.54	[0.19, 1.54]
Black Non-Hispanic			
2010 Q1 - 2014 Q2	44	1.11	[0.82, 1.49]
2014 Q3 - 2015 Q4	15	1.60	[0.96, 2.65]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.44	[0.80, 2.59]

Results --- Stillbirth

Method 3: There was not enough evidence to indicate that the estimated standardized incidence ratios for stillbirth were significantly different over the two time periods.

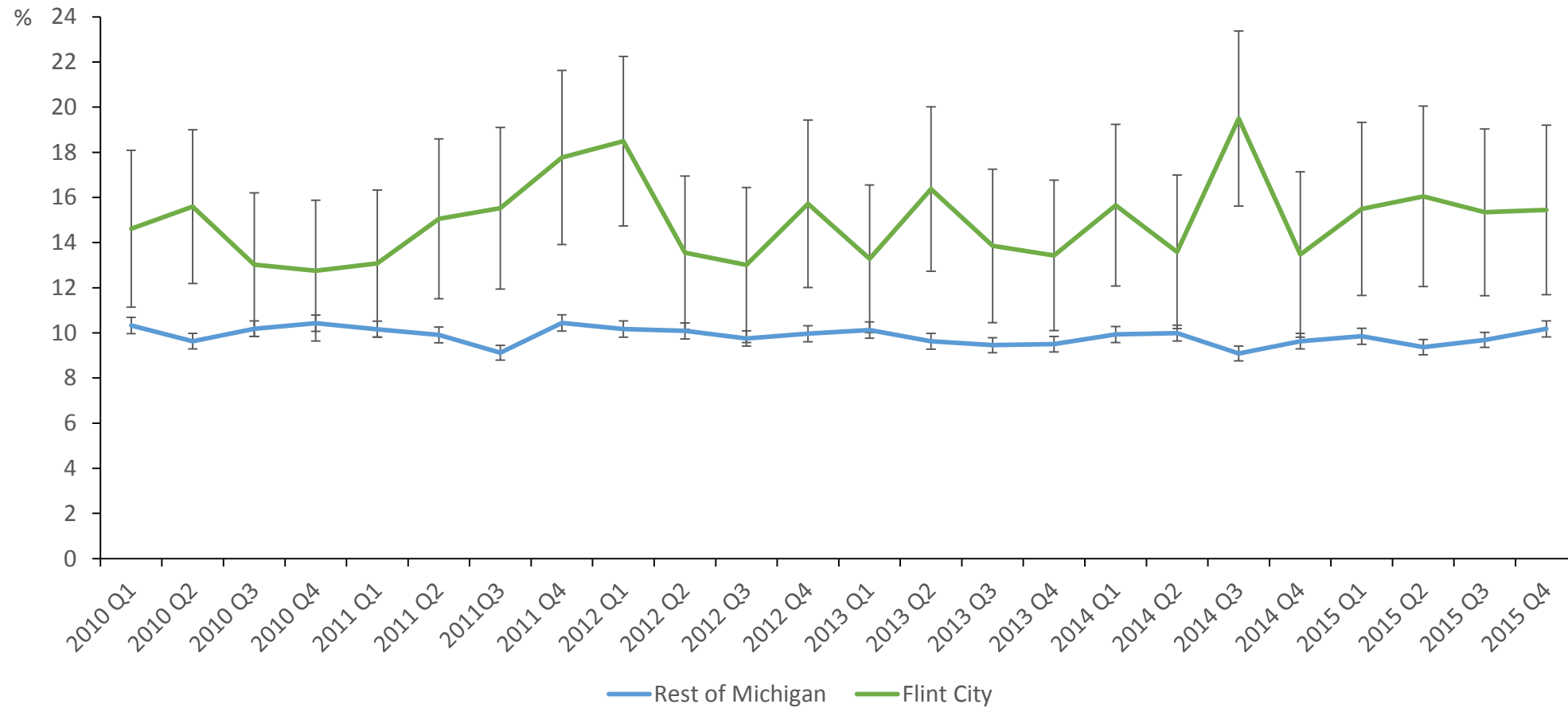
	Stillbirth	
	SIR	95% C. I.
Flint		
2010 Q1 - 2014 Q2	1.47	[1.16, 1.81]
2014 Q3 - 2015 Q4	1.83	[1.18, 2.65]
Probability (2014 Q3 - 2015 Q4 > 2010 Q1 - 2014 Q2)	0.81	
2010 Q1 - 2014 Q2		
Flint	1.47	[1.16, 1.81]
Saginaw	1.13	[0.76, 1.57]
Probability (SIR Flint > SIR Saginaw)	0.90	
2014 Q3 - 2015 Q4		
Flint	1.83	[1.18, 2.65]
Saginaw	1.29	[0.58, 2.25]
Probability (SIR Flint > SIR Saginaw)	0.83	
2010 Q1 - 2014 Q2		
Flint	1.47	[1.16, 1.81]
Detroit	1.03	[0.93, 1.14]
Probability (SIR Flint > SIR Detroit)	0.99	
2014 Q3 - 2015 Q4		
Flint	1.83	[1.18, 2.65]
Detroit	0.70	[0.56, 0.87]
Probability (SIR Flint > SIR Detroit)	1.00	

Table 5: Standardized Incidence Ratios of Stillbirth in Flint, 2010-2015

	Stillbirth	
	SIR	95% C. I.
2010 Q1 - 2014 Q2		
Flint	1.47	[1.16, 1.81]
Grand Rapids	1.19	[0.96, 1.44]
Probability (SIR Flint > SIR Grand Rapids)	0.92	
2014 Q3 - 2015 Q4		
Flint	1.83	[1.18, 2.65]
Grand Rapids	1.17	[0.78, 1.64]
Probability (SIR Flint > SIR Grand Rapids)	0.94	
2010 Q1 - 2014 Q2		
Flint	1.47	[1.16, 1.81]
Lansing	1.04	[0.77, 1.34]
Probability (SIR Flint > SIR Lansing)	0.98	
2014 Q3 - 2015 Q4		
Flint	1.83	[1.18, 2.65]
Lansing	1.54	[0.97, 2.23]
Probability (SIR Flint > SIR Lansing)	0.72	

Results --- Preterm Birth

Incidence of Preterm Birth in Flint City and the Rest of Michigan, 2010-2015



Results --- Preterm Birth

Method 1: There was not enough evidence to indicate that the estimated incidences of preterm birth were significantly different over the two time periods.

Table 9: Incidence of Preterm Birth in Flint, 2012-2015

	# Live Births	# Preterm Birth	Incidence of Preterm Birth (%)	95% C. I.
07/01/2012 --- 12/31/2013	2348	335	14.27	(12.85, 15.68)
07/01/2014 --- 12/31/2015	2121	339	15.98	(14.42, 17.54)
P-value	0.11			

Results --- Preterm Birth

Method 2: There was not enough evidence to indicate that the estimated standardized incidence ratios for preterm birth were significantly different over the two time periods.

Table 7: Standardized Incidence Ratios of Preterm Birth in Flint, 2010-2015

	Preterm Birth		
	N	SIR	95% C. I.
Overall			
2010 Q1 - 2014 Q2	1058	1.21	[1.14, 1.29]
2014 Q3 - 2015 Q4	339	1.35	[1.22, 1.50]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.12	[0.99, 1.26]
White Non-Hispanic			
2010 Q1 - 2014 Q2	314	1.43	[1.28, 1.60]
2014 Q3 - 2015 Q4	106	1.75	[1.45, 2.12]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.23	[0.98, 1.53]
Black Non-Hispanic			
2010 Q1 - 2014 Q2	705	1.15	[1.07, 1.24]
2014 Q3 - 2015 Q4	219	1.22	[1.07, 1.39]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.06	[0.91, 1.24]

Results --- Preterm Birth

Method 3: There was not enough evidence to indicate that the estimated standardized incidence ratios for preterm birth were different over the two time periods.

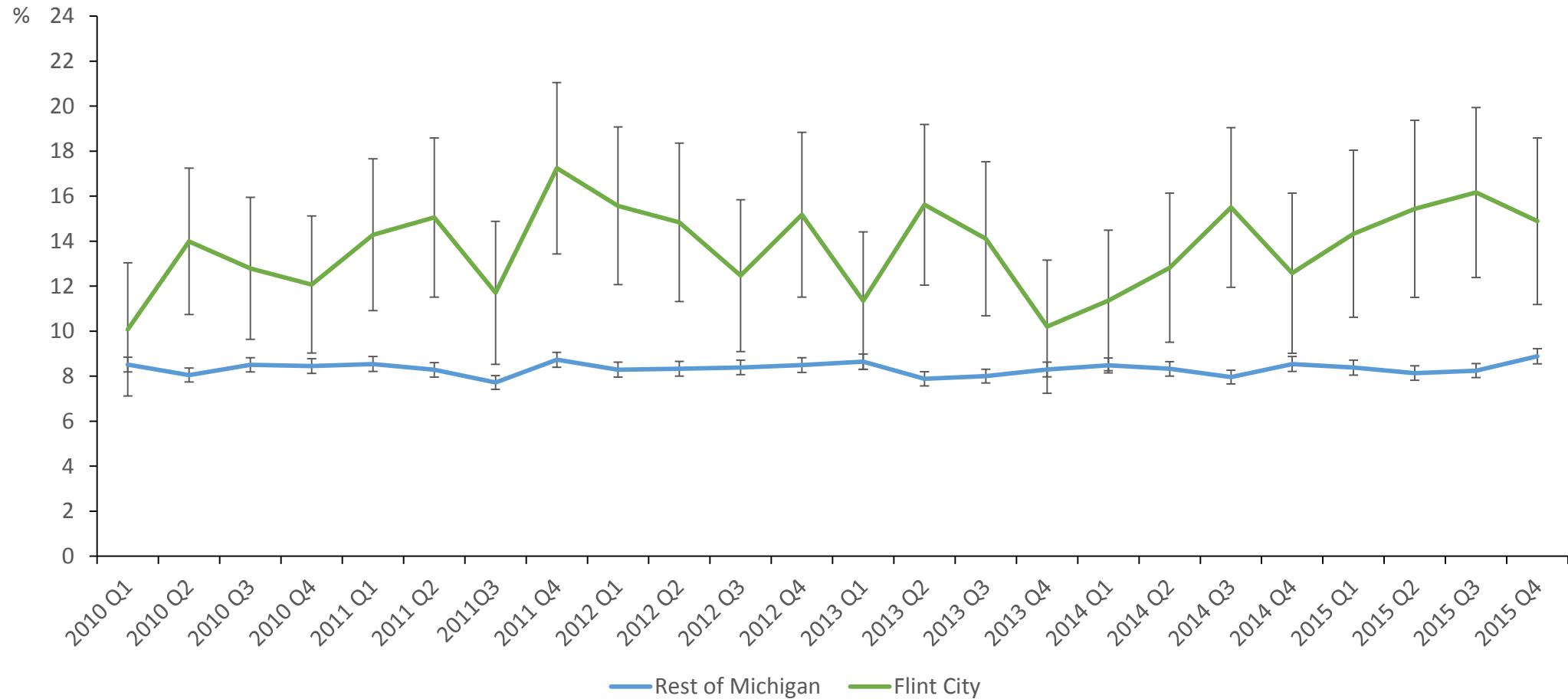
	Preterm Birth	
	SIR	95% C. I.
Flint		
2010 Q1 - 2014 Q2	1.21	[1.14, 1.29]
2014 Q3 - 2015 Q4	1.35	[1.21, 1.50]
Probability (2014 Q3 - 2015 Q4 > 2010 Q1 - 2014 Q2)	0.96	
2010 Q1 - 2014 Q2		
Flint	1.21	[1.14, 1.29]
Saginaw	0.85	[0.77, 0.94]
Probability (SIR Flint > SIR Saginaw)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.35	[1.21, 1.50]
Saginaw	0.91	[0.76, 1.08]
Probability (SIR Flint > SIR Saginaw)	1.00	
2010 Q1 - 2014 Q2		
Flint	1.21	[1.14, 1.29]
Detroit	1.08	[1.06, 1.11]
Probability (SIR Flint > SIR Detroit)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.35	[1.21, 1.50]
Detroit	1.07	[1.02, 1.11]
Probability (SIR Flint > SIR Detroit)	1.00	

Table 8: Standardized Incidence Ratios of Preterm Birth in Flint, 2010-2015

	Preterm Birth	
	SIR	95% C. I.
2010 Q1 - 2014 Q2		
Flint	1.21	[1.14, 1.29]
Grand Rapids	1.01	[0.96, 1.07]
Probability (SIR Flint > SIR Grand Rapids)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.35	[1.21, 1.50]
Grand Rapids	1.01	[0.92, 1.11]
Probability (SIR Flint > SIR Grand Rapids)	1.00	
2010 Q1 - 2014 Q2		
Flint	1.21	[1.14, 1.29]
Lansing	0.98	[0.91, 1.05]
Probability (SIR Flint > SIR Lansing)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.35	[1.21, 1.50]
Lansing	1.04	[0.93, 1.16]
Probability (SIR Flint > SIR Lansing)	0.999	

Results --- Low Birthweight

Incidence of Low Birthweight in Flint City and the Rest of Michigan, 2010-2015



Results --- Low Birthweight

Method 1: There was not enough evidence to indicate that the estimated incidences of low birthweight were significantly different over the two time periods.

Table 12: Incidence of Low Birthweight in Flint, 2012-2015

	# Live Births	# Low Birthweight	Incidence of Low Birthweight (%)	95% C. I.
07/01/2012 --- 12/31/2013	2348	308	13.12	(11.75, 14.48)
07/01/2014 --- 12/31/2015	2121	315	14.85	(13.34, 16.36)
P-value	0.09			

Results --- Low Birthweight

Method 2: There was not enough evidence to indicate that the estimated standardized incidence ratios for preterm birth were significantly different over the two time periods.

Table 10: Standardized Incidence Ratios of Low Birthweight in Flint, 2010-2015

	Low Birthweight		
	N	SIR	95% C. I.
Overall			
2010 Q1 - 2014 Q2	963	1.19	[1.12, 1.27]
2014 Q3 - 2015 Q4	315	1.28	[1.15, 1.43]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.08	[0.95, 1.22]
White Non-Hispanic			
2010 Q1 - 2014 Q2	258	1.52	[1.35, 1.72]
2014 Q3 - 2015 Q4	87	1.82	[1.47, 2.24]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.19	[0.94, 1.52]
Black Non-Hispanic			
2010 Q1 - 2014 Q2	669	1.11	[1.03, 1.19]
2014 Q3 - 2015 Q4	218	1.16	[1.02, 1.32]
2014 Q3 - 2015 Q4 vs 2010 Q1 - 2014 Q2		1.05	[0.90, 1.22]

Results --- Low Birthweight

Method 3: There was not enough evidence to indicate that the estimated standardized incidence ratios for low birthweight were different over the two time periods.

	Low Birthweight	
	SIR	95% C. I.
Flint		
2010 Q1 - 2014 Q2	1.19	[1.12, 1.27]
2014 Q3 - 2015 Q4	1.29	[1.15, 1.43]
Probability (2014 Q3 - 2015 Q4 > 2010 Q1 - 2014 Q2)	0.87	
2010 Q1 - 2014 Q2		
Flint	1.19	[1.12, 1.27]
Saginaw	0.42	[0.38, 0.46]
Probability (SIR Flint > SIR Saginaw)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.28	[1.15, 1.43]
Saginaw	1.15	[0.97, 1.34]
Probability (SIR Flint > SIR Saginaw)	0.87	
2010 Q1 - 2014 Q2		
Flint	1.19	[1.12, 1.27]
Detroit	1.08	[1.05, 1.11]
Probability (SIR Flint > SIR Detroit)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.28	[1.15, 1.43]
Detroit	1.10	[1.10, 1.15]
Probability (SIR Flint > SIR Detroit)	0.99	

Table 11: Standardized Incidence Ratios of Low Birthweight in Flint, 2010-2015

	Low Birthweight	
	SIR	95% C. I.
2010 Q1 - 2014 Q2		
Flint	1.19	[1.12, 1.27]
Grand Rapids	1.05	[1.00, 1.11]
Probability (SIR Flint > SIR Grand Rapids)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.28	[1.15, 1.43]
Grand Rapids	1.06	[0.96, 1.16]
Probability (SIR Flint > SIR Grand Rapids)	0.995	
2010 Q1 - 2014 Q2		
Flint	1.19	[1.12, 1.27]
Lansing	1.02	[0.95, 1.09]
Probability (SIR Flint > SIR Lansing)	1.00	
2014 Q3 - 2015 Q4		
Flint	1.28	[1.15, 1.43]
Lansing	0.99	[0.87, 1.12]
Probability (SIR Flint > SIR Lansing)	0.999	

Conclusions

- Method 1 indicates that there were no significant increases (at $\alpha=0.05$) in the rates of infant mortality, stillbirth, preterm birth and low birthweight across the two time periods.
- When comparing Flint to the rest of the State (method 2), Flint reported higher rates of stillbirth, preterm birth and low birthweight in both the pre and post water source change time periods.
- There is evidence of an increase in preterm birth within the City of Flint three months after the water source change (2014 Q3), but this rate returned to pre water source change levels for the subsequent quarters.
- Quarterly low birthweight incidence in Flint remained high both before and after the water source change.
- Within Flint, method 2 indicates an increase in the standardized incidence ratios overall and among non-Hispanic Black infants for stillbirth, preterm birth and low birthweight during the post water change period, but none of these increases were statistically significant (at $\alpha=0.05$).
- Method 3 shows similar results to that of method 2. In addition, in both periods, the risk of stillbirth, preterm birth and low birthweight in Flint were higher compared to the cities of Detroit, Grand Rapids, Lansing, and Saginaw, respectively.

Next Steps

- Due to study population demographic differences between the pre and post water change time periods, additional analyses that adjust for these differences are needed.
- MDHHS is currently collaborating with the CDC to prepare these analyses for peer review.
- Analyses of additional post water change time periods will be completed as necessary data become available.