Exploring the Seasonality of Birth Defects in the New York State Congenital Malformations Registry

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BACKGROUND: Examining seasonal patterns of birth defects may help to identify environmental risk factors. Because the teratogenic window for most birth defects is during gestational weeks 3 to 8, investigating exposures closer to the timing of conception is important. However, studies are usually based on month of birth, which is not the biologically relevant exposure period and does not account for differences in gestational length. We aimed to determine whether the occurrence of birth defects varied by month of conception using the population-based New York State Congenital Malformations Registry (CMR). **METHODS:** We merged live birth certificates (n = 2,044,091) with CMR records for mothers residing in New York State, excluding New York City, for the years 1992 through 2006. We categorized birth defects according to the National Birth Defects Prevention Network guidelines and performed Cochran-Armitage trend, Hewitt-Rogerson, and Walter-Elwood tests on month of conception and chi-square tests on season of conception. We graphed seasonal distributions and seasonality test results. We performed stratified analyses by maternal and infant characteristics. **RESULTS:** Of 42 groups examined in the 15-year period, 24 (57%) had at least one statistically significant test result, suggesting a trend or seasonal variation: Cochran-Armitage (18), Hewitt-Rogerson (17), Walter-Elwood (4), and chi-square (5). Ventricular septal defect showed the most consistent results: Cochran-Armitage ($p = 0.0006$), Hewitt-Rogerson (December to May; $p = 0.0130$), Walter-Elwood (March 14; $p = 0.0027$), and chi-square (winter; $p = 0.0046$). Congenital cataract, pulmonary valve atresia/stenosis, coarctation of aorta, biliary atresia, and renal agenesis or hypoplasia had at least three significant tests. **DISCUSSION:** These results may help to generate hypotheses about environmental factors that vary by season for further studies. *Birth Defects Research (Part A) 00:000–000, 2012.* © 2012 Wiley Periodicals, Inc.

Key words: birth defects; epidemiology; registry; seasonality; surveillance

INTRODUCTION

Although major birth defects occur in approximately 3% of births (Centers for Disease Control and Prevention, 2008), the causes of most birth defects are unknown (Nelson and Holmes, 1989). Examining seasonal patterns using routinely collected birth defects surveillance data may help us generate hypothesis about environmental risk factors that can be tested in analytic studies. Results of seasonality studies in the literature have been inconsistent by geography and time period and are often based on month of birth, which is not the biologically relevant exposure period and does not account for differences in length of gestation (Bound et al., 1989; Castilla et al., 1990; Siffel et al., 2005). For most birth defects, the critical period of exposure is in the 3rd to 8th weeks after conception during organogenesis (Sadler, 2004); therefore, it is important to examine environmental factors closer to the timing of conception and early pregnancy. Our objective was to determine whether the occurrence of birth defects in upstate New York varied by month of conception by using the population-based New York State Congenital Malformations Registry (CMR).

MATERIALS AND METHODS

Appropriate institutional review board approvals were granted to access New York State birth certificate data from vital records and birth defects data from the CMR. We linked live birth certificates (n = 2,044,091) with CMR records for mothers residing in upstate New York (New York State, excluding New York City) at birth for

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the years 1992 to 2006 to construct a 15-year live birth cohort. The CMR is a population-based registry that receives mandated reports on children who were born in New York State and were diagnosed with birth defects, metabolic defects, or chromosomal anomalies up until 2 years of age from hospitals and physicians. Hospital audits are conducted to capture the unreported cases. On-site hospital medical record audits documented that the CMR reports were greater than 90% correct (Wang et al., 2010), which is comparable to that of the Metropolitan Atlanta Congenital Defects Program, an active surveillance system that is regarded as the gold standard (Honein and Paulozzi, 1999). The birth certificate contains data on maternal and infant characteristics, such as maternal age, race or ethnicity, education level, date of last menses, infant date of birth, sex, birth weight, and gestational age. Roohan et al. (2003) assessed the accuracy of the date of last menses recorded on the New York State birth certificate by checking medical records; they found the date to be correct 87% of the time and 93% accurate within 1 week of the actual date.

Using the *International Classification of Disease Clinical Modification*, *Ninth Revision*, diagnosis codes from the CMR records, we grouped birth defects into 45 categories as defined in the guidelines of the National Birth Defects Prevention Network (NBDPN; National Birth Defects Prevention Network, 2010). We excluded three case groups with fewer than 50 cases from our analyses: aniridia (n = 9), common truncus (n = 44), and bladder exstrophy (n = 23). The remaining 42 case groups selected for analyses are listed in Table 1.

We estimated date of conception by adding 14 days to the maternal date of last menses. Based on this reference point, we categorized each birth into 12 months and four seasons of conception: winter (December–February), spring (March–May), summer (June–August), and fall (September–November). Because there is a seasonal variation in live births, it is important to account for that variation in analyses of the distribution of adverse birth outcomes (Darrow et al., 2009). To visualize the distributions across seasons, we plotted birth defects prevalence rates per 10,000 live births (No. of birth defects $\times$ 10,000 $\div$ No. of live births) by month and season of conception. We performed four statistical tests to examine trend and seasonal variation of the birth defects groups based on timing of conception. According to the statistical methods recommended for analyzing the seasonal variation of birth defects proposed and described in detail by Siffel et al. (2005), we conducted the Cochran-Armitage trend test, the Hewitt-Rogerson test, and the Walter-Elwood test using month of conception. Each test accounts for the seasonal variation of live births. The Cochran-Armitage test is used to detect an underlying trend in data with binomial proportions (Cochran, 1954; Armitage, 1955). The Hewitt-Rogerson test is a nonparametric test for seasonality that ranks monthly prevalence rates from lowest to highest, sums all possible sequences of six consecutive months, and identifies the 6-month period with the maximum rank sum (i.e., the Hewitt Score; Hewitt et al., 1971; Rogerson, 1996). The test requires at least 6 months with nonzero frequencies. The Walter-Elwood test is a parametric test for seasonality that uses a simple harmonic curve and allows for a variable population at risk (Walter and Elwood, 1975). The test estimates the amplitude of the seasonal variation, the date at which the maximum occurs, and the goodness of fit. The test requires at least 50 cases. Because New York has four distinct seasons, we also performed a chi-square test using season of conception. The chi-square test is used to test for the relationship between two discrete variables by comparing observed versus expected values (Cochran, 1954). It is recommended that no more than one fifth of cells have expected values less than 5. To perform the Hewitt-Rogerson and Walter-Elwood tests, we used the Statistical Analysis Battery for Epidemiologic Research (SABER) version 1.96, developed by LM James and downloaded from the Centers for Disease Control and Prevention (Atlanta, GA; http://www.cdc.gov/ncbddd/birthdefects/research-tools.html). Other analyses were performed in SAS version 9.1 (SAS Institute, Cary, NC).

Because seasonal patterns of births varied by maternal sociodemographics in a study in metropolitan Atlanta (Darrow et al., 2009), and because some studies have reported sex differences in seasonality of birth defects (Heikkilä, 1984; Puri and Singh, 1995; Fraser and Gwyn, 1998; Krost and Schubert, 2006; Liu et al., 2011), we also examined seasonality within strata of maternal age (<20, 20–34, ≥35 years), race or ethnicity (non-Hispanic white, non-Hispanic black, Hispanic), education level (<12, 12–15, ≥16 years), and infant sex (male, female). The Walter-Elwood test was limited to case groups with at least 50 subjects, and the Hewitt-Rogerson and chi-square tests were limited to case groups with at least 20 subjects.

RESULTS

Of the 2,044,091 live births within the 1992 to 2006 study period, 1,967,654 (96.3%) infants with dates of last menstrual period were included in the analyses. Live birth prevalence rates per 10,000 live births and results of the four statistical tests for the selected birth defects groups are displayed in Table 1. Twenty-four (57%) of the 42 groups examined had at least one statistically significant test result, suggesting a trend or seasonal variation. The Cochran-Armitage trend test was significant and suggested heterogeneity of monthly distributions for nine groups of congenital heart defects (i.e., tetralogy of Fallot, ventricular septal defect, atrial septal defect, endocardial cushion defect, pulmonary valve atresia or stenosis, Ebstein anomaly, aortic valve stenosis, patent ductus arteriosus, and coarctation of the aorta) and nine other birth defects groups: hydrocephalus without spina bifida, anophthalmia or microphthalmia, congenital cataract, biliary atresia, renal agenesis/hypoplasia, lower limb reduction, Down syndrome, trisomy 18, and fetal alcohol syndrome. The Hewitt-Rogerson test was significant for certain 6-month intervals in 17 birth defect groups: pulmonary valve atresia or stenosis, coarctation of the aorta, and amniotic bands (January–June); biliary atresia, lower limb reduction, and trisomy 18 (March–August); congenital megacolon (April–September); congenital cataract and renal agenesis or hypoplasia (June–November); endocardial cushion defect (July–December); hydrocephalus without spina bifida and transposition of the great arteries (August–January); upper limb reduction (September–February); anotia or microtia (October–March); and encephalocele, ventricular septal defect, and fetal alcohol syndrome (December–May). The Walter-Elwood test was significant for ventricular septal defect (peak, March 14), pulmonary valve atresia/stenosis (peak, October 14),

Table 1
Summary of Trend and Seasonality Tests for Selected Birth Defects in Upstate New York, 1992–2006

			Cochrane-Armitage	Hewitt-Rogerson			Walter-Elwood			Chi-square	
Group	Live births	Rate per 10,000 live births	*p* value, 2-sided	Hewitt score	Peak 6-month period	*p* value	Peak	*p* value, center of gravity	*p* value, goodness of fit	Peak season	*p* value
Live Births	1,967,654										
Central Nervous System											
Anencephalus	92	0.47	0.129	48	Oct–Mar	0.090	Feb 1	0.571	0.809	Winter	0.834
Spina bifida without anencephalus	359	1.82	0.438	44	Mar–Aug	0.242	Mar 2	0.976	0.461	Spring	0.968
Hydrocephalus without spina bifida	989	5.03	0.048[a]	51	Aug–Jan	0.033[a]	Nov 3	0.651	0.872	Winter	0.812
Encephalocele	97	0.49	0.068	51	Dec–May	0.033[a]	Feb 19	0.427	0.561	Winter	0.270
Microcephalus	634	3.22	0.154	48	Nov–Apr	0.090	Dec 19	0.773	0.938	Fall	0.799
Eye											
Anophthalmia, microphthalmia	99	0.50	0.013[a]	48	Dec–May	0.090	Mar 6	0.308	0.358	Spring	0.101
Congenital cataract	236	1.20	0.007[a]	53	Jun–Nov	0.013[a]	Mar 20	0.231	0.012	Summer	0.027[a]
Ear											
Anotia, microtia	105	0.53	0.136	52	Oct–Mar	0.021[a]	Dec 10	0.668	0.678	Fall	0.927
Cardiovascular											
Transposition of great arteries	234	1.19	0.152	52	Aug–Jan	0.021[a]	Nov 7	0.199	0.986	Fall	0.645
Tetralogy of Fallot	386	1.96	0.020[a]	46	Jul–Dec	0.155	Nov 1	0.681	0.166	Fall	0.055
Ventricular septal defect	4923	25.02	0.001[a]	53	Dec–May	0.013[a]	Mar 14	0.003[a]	0.168	Winter	0.005[a]
Atrial septal defect	2645	13.44	0.027[a]	48	Jan–Jun	0.090	Mar 27	0.196	0.044	Spring	0.090
Endocardial cushion defect	156	0.79	0.013[a]	56	Jul–Dec	0.002[a]	Mar 28	0.060	0.001	Fall	0.327
Pulmonary valve atresia or stenosis	1408	7.16	0.010[a]	53	Jan–Jun	0.013[a]	Oct 14	0.018[a]	0.003	Spring	0.034[a]
Tricuspid atresia or stenosis	140	0.71	0.117	48	Sep–Feb	0.090	Jan 7	0.741	0.346	Winter	0.413
Ebstein anomaly	96	0.49	0.049[a]	46	Oct–Mar	0.155	Nov 24	0.179	0.337	Fall	0.772
Aortic valve stenosis	269	1.37	0.042[a]	47	Jan–Jun	0.120	Oct 26	0.503	0.049	Winter	0.307
Hypoplastic left heart syndrome	284	1.44	0.184	48	May–Oct	0.090	Feb 5	0.614	0.353	Fall	0.620
Patent ductus arteriosus (≥2500 gm)	1789	9.09	0.024[a]	49	Feb–Jul	0.066	Nov 23	0.125	0.059	Summer	0.564
Coarctation of aorta	706	3.59	0.008[a]	56	Jan–Jun	0.002[a]	Oct 6	0.044[a]	0.005	Winter	0.048[a]
Orofacial											
Cleft palate without cleft lip	1087	5.52	0.075	47	Nov–Apr	0.120	Feb 2	0.490	0.423	Winter	0.781
Cleft lip with and without cleft palate	1509	7.67	0.139	46	Mar–Aug	0.155	Dec 17	0.780	0.074	Summer	0.614
Choanal atresia	312	1.59	0.085	48	Mar–Aug	0.090	Dec 18	0.777	0.162	Summer	0.450
Gastrointestinal											
Esophageal atresia, tracheoesophageal fistula	363	1.84	0.130	47	May–Oct	0.120	Dec 1	0.788	0.580	Winter	0.726
Rectal and large intestinal atresia or stenosis	555	2.82	0.112	44	May–Oct	0.242	Feb 4	0.641	0.226	Summer	0.763
Pyloric stenosis	4026	10.46	0.105	45	Jun–Nov	0.197	NC			Summer	0.226
Hirschsprung disease (congenital megacolon)	394	2.00	0.147	50	Apr–Sep	0.047[a]	Jan 2	0.411	0.475	Summer	0.711
Biliary atresia	152	0.77	0.014[a]	56	Mar–Aug	0.002[a]	Dec 6	0.027[a]	0.001	Summer	0.056
Genitourinary											
Renal agenesis or hypoplasia	567	2.88	0.001[a]	51	Jun–Nov	0.033[a]	Mar 16	0.142	<0.001	Summer	0.010[a]
Obstructive genitourinary defect	5091	25.87	0.203	47	Jun–Nov	0.120	Mar 18	0.926	0.156	Fall	0.610
Hypospadias, epispadias	7623	75.68	0.273	42	Jan–Jun	0.350	NC			Summer	0.561
Musculoskeletal											
Upper limb reduction deformity	381	1.94	0.057	50	Sep–Feb	0.047[a]	Jan 3	0.124	0.866	Winter	0.124
Lower limb reduction deformity	243	1.23	0.029[a]	51	Mar–Aug	0.033[a]	Nov 11	0.246	0.105	Spring	0.114
Gastroschisis	344	1.75	0.102	44	Mar–Aug	0.243	Feb 9	0.925	0.518	Summer	0.908
Omphalocele	246	1.25	0.327	45	Nov–Apr	0.197	Nov 22	0.861	0.709	Fall	0.875
Congenital hip dislocation	2467	12.54	0.101	49	Mar–Aug	0.066	Dec 19	0.305	0.317	Spring	0.191

Table 1
Summary of Trend and Seasonality Tests for Selected Birth Defects in Upstate New York, 1992–2006 (Continued)

Group	Live births	Rate per 10,000 live births	Cochrane-Armitage: *p* value, 2-sided	Hewitt-Rogerson: Hewitt score	Hewitt-Rogerson: Peak 6-month period	Hewitt-Rogerson: *p* value	Walter-Elwood: Peak	Walter-Elwood: *p* value, center of gravity	Walter-Elwood: *p* value, goodness of fit	Chi-square: Peak season	Chi-square: *p* value
Diaphragmatic hernia	346	1.76	0.173	45	Jun–Nov	0.197	Feb 16	0.888	0.690	Summer	0.462
Chromosomal											
Trisomy 13	136	0.69	0.191	48	Feb–Jul	0.090	Nov 19	0.880	0.892	Winter	0.854
Down syndrome (trisomy 21)	2254	11.46	0.046[a]	45	Dec–May	0.195	Mar 19	0.401	0.243	Winter	0.114
Trisomy 18	202	1.03	0.009[a]	51	Mar–Aug	0.033[a]	Nov 16	0.361	0.080	Summer	0.108
Other											
Fetal alcohol syndrome	231	1.17	0.029[a]	50	Dec–May	0.047[a]	Feb 14	0.071	0.202	Winter	0.089
Amniotic bands	79	0.40	0.115	50	Jan–Jun	0.047[a]	Feb 7	0.562	0.809	Winter	0.709

[a]Statistically significant trend or seasonality test ($p \leq 0.05$).
NC, not computed.

coarctation of the aorta (peak, October 6), and biliary atresia (peak, December 6); however, only the peak for ventricular septal defect fell within the time periods indicated by the Hewitt-Rogerson and chi-square tests. The chi-square test for season of conception was significant for congenital cataract (summer peak), ventricular septal defect (winter peak), pulmonary valve atresia/stenosis (spring peak), coarctation of the aorta (winter peak), and renal agenesis/hypoplasia (summer peak).

Figure 1 displays the results of the four statistical tests graphically for the 17 birth defect groups with at least one statistically significant seasonality test during 1992 to 2006. Each panel in the figure provides a visual summary of the results for one birth defect group. The bars represent the rates by season of conception, with darker gray shading indicating a statistically significant chi-square test. The line shows the rates by month of conception, with solid black indicating statistical significance of the Cochran-Armitage test for trend. The boxes on the x-axis mark the peak 6-month period of conception with the solid black indicating a statistically significant Hewitt-Rogerson test. Finally, the triangle near the top of the plot marks the peak month of conception with the solid black indicating statistical significance of the Walter-Elwood test.

In stratified analyses of maternal characteristics and infant sex, each of the 25 birth defect groups that did not exhibit a seasonal pattern in the total live birth cohort displayed a positive seasonality test within at least one stratum. Among infants of mothers younger than 20 years (7.5% of live births), seasonal patterns were detected for tetralogy of Fallot, omphalocele, congenital hip dislocation, diaphragmatic hernia, and Down syndrome (Table 2). Infants of mothers 20 to 34 years old (75.2% of live births) displayed seasonal patterns for microcephalus, atrial septal defect, Ebstein anomaly, and patent ductus arteriosus. Seasonal variation in infants of mothers 35 years and older (17.3% of live births) was apparent for spina bifida, hypoplastic left heart syndrome, esophageal atresia–tracheoesophageal fistula, pyloric stenosis, obstructive genitourinary defect, hypospadias or epispadias, congenital hip dislocation, and fetal alcohol syndrome.

Infants of non-Hispanic white mothers (76.4% of live births) demonstrated seasonality for microcephalus, atrial septal defect, hypoplastic left heart syndrome, patent ductus arteriosus, rectal and large intestinal atresia or stenosis, biliary atresia, renal agenesis or hypoplasia, omphalocele, and congenital hip dislocation (Table 3). Infants of non-Hispanic black mothers (10.4% of live births) displayed seasonality for omphalocele, congenital hip dislocation, and diaphragmatic hernia. Infants of Hispanic mothers (9.7% of live births) showed seasonal patterns for microcephalus, atrial septal defect, aortic valve stenosis, cleft palate, choanal atresia, rectal and large intestinal atresia/stenosis, pyloric stenosis, and hypospadias or epispadias.

Infants of those with less than a high school education (14.2% of live births) displayed seasonality for tetralogy of Fallot, esophageal atresia–tracheoesophageal fistula, rectal and large intestinal atresia or stenosis, pyloric stenosis, biliary atresia, congenital hip dislocation, and Down syndrome (Table 4). Tetralogy of Fallot, patent ductus arteriosus, gastroschisis, omphalocele, trisomy 13, and Down syndrome exhibited seasonal patterns in

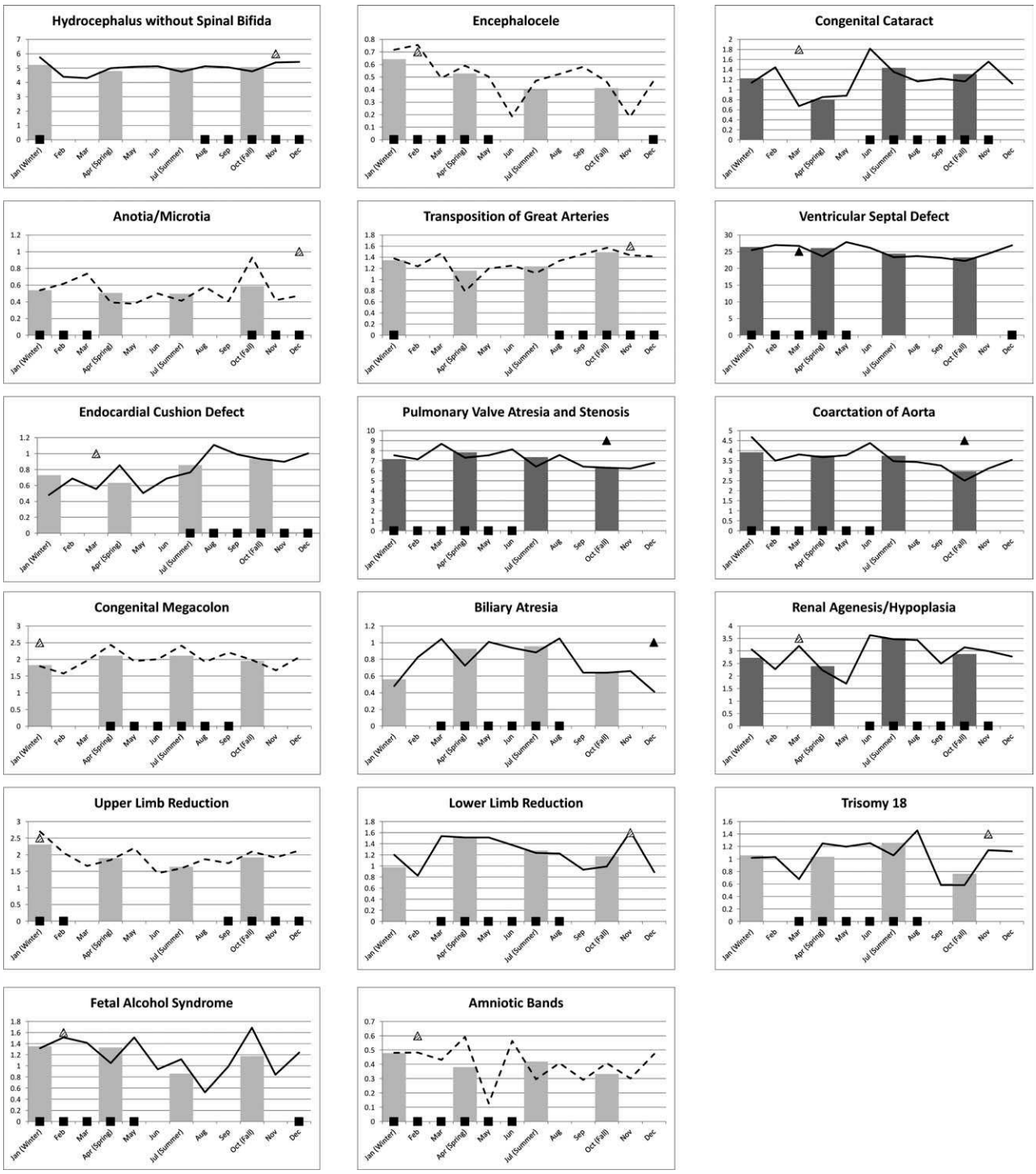

Figure 1. Graphical summaries of trend and seasonality tests for birth defects groups with at least one statistically significant seasonality test. The *line* shows the live birth prevalence rates by month of conception, with solid black indicating statistical significance ($p \leq 0.05$) of the Cochrane-Armitage test for trend. The *boxes* on the x-axis mark the peak 6-month period of conception, with solid black indicating a statistically significant ($p \leq 0.05$) Hewitt-Rogerson test. The *triangle* near the top of the plot marks the peak month of conception, with solid black indicating statistical significance ($p \leq 0.05$) of the Walter-Elwood test. The *bars* represent the rates by season of conception with darker gray shading indicating a statistically significant ($p \leq 0.05$) chi-square test.

infants of mothers with high school or some college education (55.3% of live births). Infants of women with a college degree (30.5% of live births) demonstrated seasonality for microcephalus, anophthalmia or microphthalmia, tetralogy of Fallot, atrial septal defect, tricuspid atresia or stenosis, Ebstein anomaly, hypoplastic left heart

Table 2
Summary of Seasonality Tests by Maternal Age for Selected Birth Defects in Upstate New York, 1992–2006

	<20 years				20–34 years				≥35 years			
Group	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live Births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Live Births	147,914				1,479,284				339,805			
Central Nervous System												
Anencephalus	10	NC	NC	NC	65	Jan–Jun	Jan 10	Winter	17	NC	NC	NC
Spina bifida without anencephalus	31	Jun 1–Dec 1	NC	Fall	269	Mar–Aug	Dec 28	Summer	59	Sep–Feb[a]	Dec 18[a]	Winter[a]
Hydrocephalus without spina bifida	108	Oct–Mar	Nov 21	Winter	728	Aug–Jan[a]	Oct 16	Winter	152	Dec–May	Apr 1	Spring
Encephalocele	8	NC	NC	NC	71	Dec–May	Feb 6	Winter	18	NC	NC	NC
Microcephalus	61	Nov–Apr	Jan 27	Spring	466	Sep–Feb[a]	Dec 30	Fall	107	Jul–Dec	Feb 26	Summer
Eye												
Anophthalmia, microphthalmia	5	NC	NC	NC	75	Dec–May	Feb 21	Spring	19	NC	NC	NC
Congenital cataract	21	Nov 1–May 1	NC	Summer	178	Jun–Nov[a]	Mar 10	Summer[a]	37	Aug–Jan	NC	Winter
Ear												
Anotia, microtia	10	NC	NC	NC	73	May–Oct[a]	Jan 14	Spring	22	Nov–Apr[a]	NC	Winter
Cardiovascular												
Transposition of great arteries	20	Jul–Dec[a]	NC	Fall	169	Oct–Mar	Jan 2	Fall	45	Aug–Jan[a]	NC	Winter
Tetralogy of Fallot	29	Jun 15–Dec 16	NC	Fall[a]	288	Dec–May	Dec 1	Spring	69	Feb–Jul	Mar 23	Fall
Ventricular septal defect	347	Dec–May[a]	Mar 14	Winter	3629	Jan–Jun	Mar 14[a]	Winter[a]	946	Feb–Jul	Oct 19	Spring
Atrial septal defect	212	Aug–Jan	Jan 4	Spring	1920	Jan–Jun[a]	Mar 11	Spring	511	Mar–Aug		Spring
Endocardial cushion defect	7	NC	NC	NC	122	Aug–Jan[a]	Oct 12	Fall	27	May–Oct	NC	Fall
Pulmonary valve atresia or stenosis	130	May–Oct[a]	Feb 6	Summer	1019	Jan–Jun[a]	Oct 17[a]	Spring[a]	258	Dec–May	Feb 24	Spring
Tricuspid atresia or stenosis	13	NC	NC	NC	102	Sep–Feb	Mar 16	Winter	25	Nov–Apr	NC	Winter
Ebstein anomaly	6	NC	NC	NC	76	Dec–May[a]	Dec 11	Winter	14	NC	NC	NC
Aortic valve stenosis	15	NC	NC	NC	210	Jan–Jun	Oct 15	Winter	44	Feb–Jul	NC	Summer
Hypoplastic left heart syndrome	18	NC	NC	NC	230	Sep–Feb	Feb 10	Fall	36	Apr–Sep[a]	NC	Spring
Patent ductus arteriosus (≥2500 gm)	123	May–Oct	Jan 26	Fall	1313	Feb–Jul[a]	Nov 16	Summer	353	Nov–Apr	Oct 8	Spring
Coarctation of aorta	47	Jan–Jun[a]	NC	Winter	524	Dec–May	Oct 7	Winter[a]	134	Jan–Jun	Nov 23	Summer
Orofacial												
Cleft palate without cleft lip	83	May–Oct	Dec 10	Winter	800	Jun–Nov	Jan 14	Winter	203	Sep–Feb	Mar 8	Fall
Cleft lip with and without cleft palate	143	Jun–Nov	Oct 17	Fall	1134	Mar–Aug	Nov 26	Spring	231	Jun–Nov	NC	Fall
Choanal atresia	19	NC	NC	NC	214	Aug–Jan	Mar 25	Spring	79	Mar–Aug	Nov 1	Spring
Gastrointestinal												
Esophageal atresia, tracheoesophageal fistula	24	Jul–Dec	NC	Winter	256	Dec–May	Mar 1	Winter	83	May–Oct[a]	Jan 7	Summer
Rectal and large intestinal atresia or stenosis	46	Aug–Jan	NC	Spring	408	Jul–Dec	Feb 17	Summer	101	May–Oct	Jan 10	Spring
Pyloric stenosis	399	Nov–Apr	Feb 17	Spring	3052	Jun–Nov	NC	Winter	573	Jun–Nov[a]	Mar 14	Summer
Hirschsprung disease (congenital megacolon)	39	Nov–Apr	NC	Spring	289	Apr–Sep[a]	Jan 6[a]	Summer	66	Nov–Apr	Dec 8	Winter
Biliary atresia	22	Feb 1–Aug 1	NC	Spring	108	Mar–Aug[a]	Dec 11[a]	Summer[a]	22	Jan–Jun	NC	Winter
Genitourinary												
Renal agenesis or hypoplasia	53	Jul–Dec[a]	Mar 17	Summer	424	Jun–Nov	Mar 26	Summer	90	Jun–Nov[a]	Mar 10	Fall
Obstructive genitourinary defect	341	Sep–Feb	Mar 29	Fall	3721	Apr–Sep	NC	Summer	1029	Sep–Feb[a]	Oct 24	Fall
Hypospadias, epispadias	555	Jan–Jun	Nov 1	Summer	5720	Oct–Mar	Jan 12	Summer	1352	Apr–Sep[a]	Jan 6	Summer
Musculoskeletal												
Upper limb reduction deformity	31	Jan 1–Jul 1	NC	Winter[a]	292	Oct–Mar	Jan 7	Winter	58	Aug–Jan	Oct 6	Fall
Lower limb reduction deformity	20	Mar 1–Sep 1[a]	NC	Spring	193	Mar–Aug[a]	Nov 16	Spring	30	May–Oct	NC	Spring
Gastroschisis	116	Mar–Aug	Nov 7	Summer	222	Jun–Nov	Dec 1	Fall	5	NC	NC	NC

Table 2
Summary of Seasonality Tests by Maternal Age for Selected Birth Defects in Upstate New York, 1992–2006 (Continued)

Group	<20 years				20–34 years				≥35 years			
	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live Births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Omphalocele	26	Nov–Apr[a]	NC	Spring	173	Sep–Feb	Mar 15	Summer	47	Mar–Aug	NC	Summer
Congenital hip dislocation	155	Feb–Jul[a]	Dec 1	Summer	1899	Jun–Nov	Feb 7	Fall	413	Jan–Jun[a]	Oct 15	Spring
Diaphragmatic hernia	24	Nov 1–May 1[a]	NC	Summer	264	Aug–Jan	NC	Summer	58	Mar–Oct	Jan 17	Summer
Chromosomal												
Trisomy 13	9	NC	NC	NC	89	Feb–Jul	Oct 23	Winter	38	Jul–Dec	NC	Summer
Down syndrome (trisomy 21)	105	Sep–Feb[a]	Jan 9	Winter	1148	Nov–Apr	Mar 5	Winter	1001	Apr–Sep	NC	Winter
Trisomy 18	9	NC	NC	NC	110	Sep–Feb	Jan 20	Summer	83	Mar–Aug	Jan 9	Summer
Other												
Fetal alcohol syndrome	13	NC	NC	NC	163	Sep–Feb	Jan 20	Winter	54	Dec–May[a]	Feb 23[a]	Spring[a]
Amniotic bands	8	NC	NC	NC	61	Jan–Jun	Feb 13	Winter	10	NC	NC	NC

[a]Statistically significant trend or seasonality test ($p \leq 0.05$).
NC, not computed.

syndrome, patent ductus arteriosus, hypospadias or epispadias, and omphalocele.

Male infants (51.2% of live births) displayed seasonal patterns for anencephalus, anophthalmia or microphthalmia, Ebstein anomaly, hypoplastic left heart syndrome, cleft lip with and without cleft palate, omphalocele, congenital hip dislocation, diaphragmatic hernia, trisomy 13, and Down syndrome (Table 5). Female infants (48.8% of live births) demonstrated seasonality for spina bifida, patent ductus arteriosus, cleft lip with and without cleft palate, pyloric stenosis, and trisomy 13.

DISCUSSION

To generate hypotheses about environmental causes of birth defects, we used a large, population-based birth defects registry to examine the seasonality of specific birth defects in geographically diverse upstate New York. A trend or seasonal pattern was detected in 24 (57%) of the 42 NBDPN surveillance birth defect groups examined in the 15-year birth cohort. Eighteen birth defects groups had a statistically significant Cochran-Armitage test for trend, 17 groups had a significant Hewitt-Rogerson test, four groups had a significant Walter-Elwood test, and five groups had a significant chi-square test. Ventricular septal defect showed the most consistent results with four statistically significant tests: Cochran-Armitage ($p = 0.0006$), Hewitt-Rogerson (December–May; $p = 0.0130$), Walter-Elwood (March 14; $p = 0.0027$), and chi-square (winter; $p = 0.0046$). Pulmonary valve atresia or stenosis and coarctation of the aorta tested positive in all four tests; however, the peaks in the Walter-Elwood tests (October 14 and October 6, respectively) fell outside the periods identified by the Hewitt-Rogerson (January–June peaks for both) and chi-square tests (spring and winter, respectively). Both congenital cataract and renal agenesis or hypoplasia showed a 6-month peak in June to November conceptions with the Hewitt-Rogerson test and a summer peak with the chi-square test. Biliary atresia had a significant Hewitt-Rogerson test (March–August peak) but a conflicting December 6 peak in the Walter-Elwood test.

In the total live birth cohort for the study period, we detected some evidence of seasonality in upstate New York for 17 groups of birth defects. These findings are consistent with other seasonality analyses of ventricular septal defect, endocardial cushion defect, and renal defect (Bound et al., 1989). There have been mixed results of seasonality reported in the literature for encephalocele (Castilla et al., 1990; Roux et al., 2009), anotia and microtia (Castilla et al., 1990; Liu et al., 2011), pulmonary valve atresia or stenosis (Bound et al., 1989; Bosshardt et al., 2005; Siffel et al., 2005), biliary atresia (Caton et al., 2004; The et al., 2004; Wada et al., 2007; Yoon et al., 1997; Livesey et al., 2009), and trisomy 18 (Gadow et al., 2006; Tonelli et al., 2006). In contrast, there have been only negative reports of hydrocephalus (Sandahl, 1977b; Castilla et al., 1990), congenital cataract (Haargaard et al., 2005), transposition of the great arteries (Bound et al., 1989), coarctation of the aorta (Bound et al., 1989; Tikkanen and Heinonen, 1993), and limb reduction (Bound et al., 1989). No literature on the seasonality of congenital megacolon, fetal alcohol syndrome, and amnionic bands was identified.

Table 3
Summary of Seasonality Tests by Maternal Race/Ethnicity for Selected Birth Defects in Upstate New York, 1992–2006

	Non-Hispanic White				Non-Hispanic Black				Hispanic			
Group	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Live Births	1,498,498				203,081				189,512			
Central Nervous System												
Anencephalus	69	Dec–May	Feb 18	Winter	8	NC	NC	NC	12	NC	NC	NC
Spina bifida without anencephalus	275	May–Oct	Feb 21	Spring	30	May–Oct	NC	Winter	41	Feb–Jul	NC	Spring
Hydrocephalus without spina bifida	671	Jun–Nov[a]	Mar 15	Summer	163	Nov–Apr[a]	Feb 25	Spring	129	Sep–Feb	Dec 8	Winter
Encephalocele	70	Dec–May	Mar 6	Winter	14	NC	NC	NC	12	NC	NC	NC
Microcephalus	411	Nov–Apr[a]	Jan 27	Winter	143	Sep–Feb	Dec 14	Winter	70	Jun–Nov[a]	Feb 8[a]	Summer[a]
Eye												
Anophthalmia, microphthalmia	74	Feb–Jul	Oct 22	Spring	10	NC	NC	NC	10	NC	NC	NC
Congenital cataract	181	Jun–Nov	Oct 7	Summer[a]	32	Jun–Nov	NC	Fall[a]	15	NC	NC	NC
Ear												
Anotia, microtia	68	Oct–Mar	Oct 1	Winter	4	NC	NC	NC	26	Oct–Mar	NC	Fall
Cardiovascular												
Transposition of great arteries	188	Oct–Mar[a]	Dec 1	Winter	20	Jul 1—Jan 1	NC	Winter	19	NC	NC	NC
Tetralogy of Fallot	286	Jul–Dec	Dec 20	Spring	46	Apr–Sep	NC	Fall	36	Oct–Mar	NC	Spring
Ventricular septal defect	3763	Dec–May[a]	Mar 21[a]	Winter[a]	506	Feb–Jul	Mar 13	Spring	480	Jun–Nov	NC	Fall
Atrial septal defect	1891	Jan–Jun[a]	Mar 15	Spring	370	Nov–Apr	Dec 27	Summer	281	Apr–Sep[a]	Dec 29	Spring
Endocardial cushion defect	118	Jul–Dec[a]	Mar 3	Summer	17	NC	NC	NC	16	NC	NC	NC
Pulmonary valve atresia or stenosis	967	Mar–Aug[a]	Oct 29[a]	Spring[a]	260	Jan–Jun	Mar 13	Winter	130	Jan–Jun	Jan 30	Winter
Tricuspid atresia or stenosis	98	Sep–Feb	Dec 11	Winter	20	Jan 1–Jul 1	NC	Winter	19	NC	NC	NC
Ebstein anomaly	70	Oct–Mar	Nov 17	Fall	5	NC	NC	NC	15	NC	NC	NC
Aortic valve stenosis	227	Feb–Jul	Nov 16	Winter	13	NC	NC	NC	20	Jan–Jun[a]	NC	Winter
Hypoplastic left heart syndrome	210	Apr–Sep[a]	Jan 18	Fall	38	Aug–Jan	NC	Winter	29	Jan–Jun	NC	Fall
Patent ductus arteriosus (≥2500 gm)	1172	Jan–Jun[a]	Nov 2	Summer	332	Jun–Nov[a]	Feb 9	Fall[a]	186	Mar–Aug	Dec 6	Summer
Coarctation of aorta	572	Jan–Jun[a]	Oct 4[a]	Winter	61	Aug–Jan	Oct 29	Winter	52	Mar–Aug[a]	Nov 5	Spring
Orofacial												
Cleft palate without cleft lip	883	Nov–Apr	Feb 8	Fall	61	Jan–Jun	Feb 9	Winter	95	Feb–Jul[a]	Feb 20	Summer
Cleft lip with and without cleft palate	1220	Mar–Aug	Jan 3	Spring	105	Sep–Feb	Nov 17	Fall	131	Mar–Aug	Dec 9	Summer
Choanal atresia	256	Mar–Aug	Nov 14	Summer	23	Apr–Sep	NC	Spring	26	Apr–Sep[a]	NC	Summer
Gastrointestinal												
Esophageal atresia, tracheoesophageal fistula	303	May–Oct	Dec 2	Winter	26	May–Oct	NC	Fall	26	Mar–Aug	NC	Summer
Rectal and large intestinal atresia or stenosis	427	Jul–Dec[a]	Feb 20	Fall	49	May–Oct	Oct 11	Fall	51	Jan–Jun[a]	Mar 29[a]	Spring
Pyloric stenosis	3364	Apr–Sep	Jan 26	Summer	220	Jun–Nov	Oct 24	Summer	371	Oct–Mar[a]	Jan 20	Winter
Hirschsprung disease (congenital megacolon)	286	Apr–Sep[a]	Jan 19	Summer	62	Oct–Mar[a]	Jan 24	Winter	29	Mar–Aug[a]	NC	Spring
Biliary atresia	101	Mar–Aug[a]	Dec 1	Summer	29	Feb–Jul	NC	Spring	14	NC	NC	NC
Genitourinary												
Renal agenesis or hypoplasia	433	Jun–Nov	Apr 1	Summer[a]	70	Jun–Nov[a]	Feb 11	Summer	44	Jun–Nov	NC	Fall
Obstructive genitourinary defect	3904	Feb–Jul	NC	Fall	440	Aug–Jan	Mar 28	Fall	552	Sep–Feb	Oct 20	Winter
Hypospadias, epispadias	6256	Jun–Nov	Jan 25	Summer	714	Feb–Jul	Dec 18	Fall	455	Jan–Jun[a]	Nov 3[a]	Summer
Musculoskeletal												
Upper limb reduction deformity	306	Aug–Jan	Dec 15	Winter	34	Dec 1–Jun 1[a]	NC	Winter[a]	28	Sep 1–Mar 1	NC	Winter
Lower limb reduction deformity	187	Mar–Aug[a]	Dec 1	Spring	23	Jan 31–Jul 31	NC	Spring	23	Feb–Jul	NC	Fall
Gastroschisis	272	Mar–Aug	Feb 11	Summer	31	Jun–Nov	NC	Fall	34	Apr–Sep	NC	Summer
Omphalocele	186	Nov–Apr[a]	Feb 15	Winter	38	Jun–Nov[a]	NC	Fall	16	NC	NC	NC

Table 3
Summary of Seasonality Tests by Maternal Race/Ethnicity for Selected Birth Defects in Upstate New York, 1992–2006 (Continued)

Group	Non-Hispanic White				Non-Hispanic Black				Hispanic			
	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Congenital hip dislocation	2058	Mar–Aug[a]	Dec 17	Spring	101	Oct–Mar[a]	Dec 25	Winter	219	May–Oct	Dec 25	Summer
Diaphragmatic hernia	259	Jun–Nov	Apr 1	Summer	38	Apr–Sep[a]	NC	Summer	30	Nov 1–May 1	NC	Fall
Chromosomal												
Trisomy 13	94	May–Oct	Dec 8	Winter	19	NC	NC	NC	16	NC	NC	NC
Down syndrome (trisomy 21)	1758	Dec–May	Mar 21	Winter	198	Jan–Jun	Mar 27	Winter	227	Apr–Sep	Jan 23	Summer
Trisomy 18	145	Apr–Sep	Dec 19	Summer	32	Nov–Apr[a]	NC	Winter	22	Jan 14–Jul 14[a]	NC	Spring
Other												
Fetal alcohol syndrome	78	Oct–Mar[a]	Jan 8	Winter	138	Dec–May	Feb 23	Winter	9	NC	NC	NC
Amniotic bands	59	Jan–Jun	Jan 23	Summer	15	NC	NC	NC	3	NC	NC	NC

[a]Statistically significant trend or seasonality test ($p \leq 0.05$).
NC, not computed.

We found no evidence of seasonality for the other twenty-five NBDPN birth defects groups in the entire live birth cohort. These findings are in agreement with other negative seasonality findings for esophageal atresia (Kyyrönene et al., 1988; Bound et al., 1989; Castilla et al., 1990), rectal atresia or stenosis (Kyyrönene and Hemminki, 1988; Bound et al., 1989; Castilla et al., 1990), obstructive genitourinary defects (Bound et al., 1989), hypospadias (Castilla et al., 1990; Skriver et al., 2004), omphalocele (Bound et al., 1989), and diaphragmatic hernia (Bound et al., 1989; Castilla et al., 1990; Torfs et al., 1992). Mixed results have been published for anencephaly (Sandahl, 1977a; Jorde et al., 1984; Fraser et al., 1986; Bound et al., 1989; Castilla et al., 1990; Siffel et al., 2005), spina bifida (Sandahl, 1977a; Jorde et al., 1984; Fraser et al., 1986; Bound et al., 1989; Castilla et al., 1990; Siffel et al., 2005; Beyer et al., 2011), aortic valve stenosis (Bound et al., 1989; Bosshardt et al., 2005; Siffel et al., 2005), hypoplastic left heart syndrome (Tikkanen and Heinonen, 1994; Siffel et al., 2005; Eghtesady et al., 2011), oral clefts (Sandahl, 1977b; Coupland and Coupland, 1988; Bound et al., 1989; Castilla et al., 1990; Amidei et al., 1994; Fraser and Gwyn, 1998; Cooper et al., 2000; Siffel et al., 2005; Krost and Schubert, 2006; Elliott et al., 2008; Gregg et al., 2008; de la Vega and Lopez-Cepero, 2009; Chung et al., 2011), esophageal atresia (Kyyrönene et al., 1988; Bound et al., 1989; Castilla et al., 1990), rectal atresia or stenosis (Kyyrönene and Hemminki, 1988; Bound et al., 1989; Castilla et al., 1990), obstructive genitourinary defects (Bound et al., 1989), hypospadias (Castilla et al., 1990; Skriver et al., 2004), gastroschisis (de la Vega and Lopez-Cepero, 2009; Waller et al., 2010), omphalocele (Bound et al., 1989), congenital hip dislocation (Chen et al., 1970; Heikkilä, 1984; Bound et al., 1989; Siffel et al., 2005; Anand et al., 1992), diaphragmatic hernia (Bound et al., 1989; Castilla et al., 1990; Torfs et al., 1992), trisomy 13 (Gadow et al., 2006; Tonelli et al., 2006), and Down syndrome (Videbech and Nielsen, 1984; Bound et al., 1989; Castilla et al., 1990; Puri and Singh, 1995; Stolwijk et al., 1997; Morris et al., 1998; Gadow et al., 2006; Tonelli et al., 2006). Our findings differ from other reports of positive seasonality tests for atrial septal defect (Bound et al., 1989), tricuspid atresia and stenosis (Bosshardt et al., 2005), and patent ductus arteriosus (Bound et al., 1989). No seasonality studies of microcephalus, anophthalmia, microphthalmia, tetralogy of Fallot, Ebstein anomaly, choanal atresia, and pyloric stenosis were detected.

Because some studies have reported sex differences in seasonality of birth defects, we performed stratified analyses by infant sex. Our findings of sex differences in seasonal patterns agree with earlier findings in cleft lip and palate (Fraser and Gwyn, 1998; Krost and Schubert, 2006) and microtia (Liu et al., 2011). Whereas births in females with congenital hip dislocation (Heikkilä, 1984) and Down syndrome (Puri and Singh, 1995) displayed seasonal variation in prior studies, we found positive Hewitt-Rogerson tests in males for both groups. Because Darrow et al. (2009) showed that seasonal patterns of births in metropolitan Atlanta varied by maternal sociodemographics, we also performed stratified analyses by maternal age, race/ or ethnicity, and education level. Our stratified analyses revealed additional seasonal patterns among strata for the 25 birth defects groups that did not demonstrate seasonality in the total live birth cohort. These findings suggest that inconsistencies in seasonality

Table 4
Summary of Seasonality Tests by Maternal Education for Selected Birth Defects in Upstate New York, 1992–2006

	Less than high school (<12 years)				High school or some college (12–15 years)				College degree (≥16 years)			
Group	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Live Births	274,479				1,069,926				589,111			
Central Nervous System												
Anencephalus	23	Feb–Jul	NC	Spring	40	Nov–Apr	NC	Winter	22	Aug 1–Feb 1	NC	Fall
Spina bifida without anencephalus	50	Mar–Aug	Nov 1	Summer	217	Oct–Mar	Dec 21	Winter	84	Oct–Mar	Mar 18	Spring
Hydrocephalus without spina bifida	211	May–Oct	Feb 17	Summer	545	Aug–Jan[a]	Oct 14	Fall	208	Nov–Apr	Feb 23	Spring
Encephalocele	20	Dec 1–Jun 1[a]	NC	Winter	58	Jan–Jun	Mar 12	Winter	17	NC	NC	NC
Microcephalus	145	Dec–May	Mar 11	Spring	367	Nov–Apr	Jan 15	Winter	108	Jun–Nov[a]	Mar 21	Fall
Eye												
Anophthalmia, microphthalmia	12	NC	NC	NC	48	May–Oct	NC	Fall	35	Dec–May[a]	NC	Spring[a]
Congenital cataract	36	Jun–Nov[a]	NC	Summer	122	Sep–Feb	Dec 30	Winter	66	Jun–Nov[a]	Mar 7	Summer
Ear												
Anotia, microtia	31	Jul–Dec[a]	NC	Fall	46	Mar–Aug	NC	Summer	27	Jan–Jun[a]	NC	Winter
Cardiovascular												
Transposition of great arteries	38	Jan–Jun	NC	Spring	133	Aug–Jan[a]	Oct 10	Summer	58	Aug–Jan[a]	Nov 26	Fall
Tetralogy of Fallot	65	Jul–Dec	Nov 25	Fall[a]	204	Jul–Dec[a]	Oct 16	Fall	110	Mar–Aug	Oct 26	Spring[a]
Ventricular septal defect	680	Dec–May	Jan 26	Winter	2,673	Jan–Jun[a]	Oct 8	Spring	1484	Dec–May[a]	Mar 3	Winter[a]
Atrial septal defect	401	Apr–Sep	Dec 19	Spring	1454	Jan–Jun	Oct 13	Spring	735	Dec–May[a]	Feb 23	Winter
Endocardial cushion defect	32	Jun–Nov[a]	NC	Fall[a]	79	Jul–Dec	Nov 9	Fall	37	Apr–Sep	NC	Summer
Pulmonary valve atresia or stenosis	242	Apr–Sep	Dec 3	Summer	799	Jan–Jun[a]	Oct 11	Winter	337	Mar–Aug[a]	Oct 3	Spring[a]
Tricuspid atresia or stenosis	17	NC	NC	NC	84	May–Oct	Dec 10	Fall	35	Nov–Apr[a]	NC	Winter
Ebstein anomaly	16	NC	NC	NC	47	Mar–Aug	NC	Spring	29	Aug 1–Feb 1[a]	NC	Fall
Aortic valve stenosis	29	Jan 1–Jul 1	NC	Winter	153	Jan–Jun	Oct 20	Winter	80	May–Oct	Jan 9	Summer
Hypoplastic left heart syndrome	39	May–Oct	NC	Fall	163	May–Oct	Feb 15	Summer	66	Jan–Jun[a]	Mar 10	Spring
Patent ductus arteriosus (≥2500 gm)	276	Apr–Sep	Oct 19	Winter	927	Apr–Sep[a]	Jan 3	Summer	555	Feb–Jul[a]	Oct 17	Spring
Coarctation of aorta	93	Oct–Mar	Jan 3	Fall	412	Jan–Jun[a]	Oct 25[a]	Winter[a]	189	Nov–Apr[a]	Mar 3	Spring
Orofacial												
Cleft palate without cleft lip	149	Jan–Jun	Feb 3	Winter	619	Nov–Apr	Mar 13	Fall	296	Dec–May	Jan 22	Winter
Cleft lip with and without cleft palate	250	Dec–May	Mar 13	Spring	861	Mar–Aug	Dec 29	Summer	353	Jul–Dec	Nov 8	Fall
Choanal atresia	34	Feb–Jul	NC	Spring	168	Apr–Sep	Dec 26	Summer	102	Mar–Aug	Oct 10	Spring
Gastrointestinal												
Esophageal atresia, tracheoesophageal fistula	42	Aug–Jan[a]	NC	Fall	196	May–Oct	Dec 5	Spring	122	Mar–Aug	Oct 16	Winter
Rectal and large intestinal atresia or stenosis	84	Aug–Jan[a]	Oct 5	Fall	307	Jun–Nov	Feb 9	Summer	153	Feb–Jul	Oct 23	Spring
Pyloric stenosis	679	Aug–Jan[a]	Dec 17	Winter	2387	Feb–Jul	NC	Summer	909	Jun–Nov	Mar 19	Summer
Hirschsprung disease (congenital megacolon)	66	Apr–Sep	Mar 28	Spring	217	May–Oct[a]	Jan 17	Summer	107	Nov–Apr	NC	Summer
Biliary atresia	35	Feb–Jul[a]	NC	Spring	84	Mar–Aug[a]	Dec 2[a]	Summer	28	Sep–Feb	NC	Winter
Genitourinary												
Renal agenesis, hypoplasia	94	Jul–Dec	Mar 1	Summer	303	Jun–Nov[a]	Mar 5	Summer[a]	143	Aug–Jan	Jan 18	Winter
Obstructive genitourinary defect	668	Sep–Feb	Dec 4	Fall	2610	Jun–Nov	Feb 4	Fall	1722	Apr–Sep	Jan 19	Fall
Hypospadias, epispadias	951	Mar–Aug	Mar 19	Summer	4148	Oct–Mar	NC	Winter	2423	Mar–Aug[a]	Dec 18	Spring
Musculoskeletal												
Upper limb reduction deformity	60	Oct–Mar	Jan 19[a]	Winter[a]	224	Sep–Feb[a]	Dec 9	Fall	91	Apr–Sep	Oct 23	Summer
Lower limb reduction deformity	53	Feb–Jul[a]	Oct 21[a]	Spring[a]	124	Mar–Aug	Oct 30	Spring	58	May–Oct	Feb 3	Fall

Table 4
Summary of Seasonality Tests by Maternal Education for Selected Birth Defects in Upstate New York, 1992–2006 (Continued)

Group	Less than high school (<12 years)				High school or some college (12–15 years)				College degree (≥16 years)			
	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Gastroschisis	106	Jun–Nov	Feb 17	Summer	202	Nov–Apr[a]	Feb 16	Spring	29	May–Oct	NC	Summer
Omphalocele	36	Jul 1–Jan 1	NC	Summer	145	Jun–Nov[a]	Oct 12	Fall	55	Jan–Jun[a]	Oct 27[a]	Spring[a]
Congenital hip dislocation	274	Mar–Aug[a]	Nov 28	Spring	1300	Feb–Jul	Dec 4	Spring	846	Jun–Nov	Jan 27	Fall
Diaphragmatic hernia	60	Nov–Apr	Nov 26	Winter	203	Jun–Nov	Jan 20	Summer	74	Apr–Sep	Mar 12	Winter
Chromosomal												
Trisomy 13	20	Feb 15–Aug 17	NC	Summer	69	Mar–Aug[a]	Nov 12	Summer	39	Sep–Feb	NC	Winter
Down syndrome (trisomy 21)	275	Dec–May	Feb 25	Winter[a]	1195	Jan–Jun[a]	Oct 10	Winter	725	Nov–Apr	Dec 24	Winter
Trisomy 18	26	Dec–May	NC	Spring	118	Mar–Aug[a]	Nov 13	Summer	50	Jun–Nov[a]	Mar 24	Summer[a]
Other												
Fetal alcohol syndrome	91	Sep–Feb	Dec 28	Fall	115	Dec–May[a]	Mar 8[a]	Winter	7	NC	NC	NC
Amniotic bands	8	NC	NC	NC	47	Jun–Nov	NC	Summer	21	Nov 1–May 1[a]	NC	Winter

[a]Statistically significant seasonality test ($p \leq 0.05$).
NC, not computed.

across studies can be partly attributed to sociodemographic differences in the live birth populations.

There are a number of strengths and limitations to this type of analysis. The strengths are that we used a large, population-based birth defects registry with NBDPN birth defects surveillance definitions and examined seasonality based on timing of conception. Using NBDPN definitions permits the analysis of birth defects groups that are more etiologically homogeneous than body system classifications and allows other birth defects surveillance systems to perform comparable analyses. Analyzing seasonal variation of month of conception controls for differences in length of gestation and is closer to the relevant biologic period of exposure for most birth defects than month of birth. Nevertheless, it is important to note that the biologically relevant exposure period for some birth defects can occur before conception (e.g., chromosomal anomalies) or after the first trimester (e.g., amniotic bands, fetal alcohol syndrome). The limitations are that we examined seasonality among live births only, we estimated the date of conception using the last menstrual period as recorded on the birth certificate, seasonal patterns may vary by the selected time-frame, and chance findings could result from multiple testing. Because our analyses were limited to live births, we were unable to detect patterns among birth defects that could result in induced termination, miscarriage, or stillbirth. Strand et al. (2011) reviewed four studies of stillbirths and described geographic variations in seasonal peaks. Our pragmatic use of last menstrual period plus 14 days to estimate the date of conception may be inaccurate because of recording errors or poor recall of the date of last menses and the assumption of a 28-day menstrual cycle with ovulation on day 14 (Lynch and Zhang, 2007). In our birth certificate data, 3.7% of live births and 4.8% of birth defects cases with missing dates for last menstrual period were identified. However, we expect both the misclassification and missing data to be nondifferentially distributed across seasons. In an analysis of data from the Metropolitan Atlanta Congenital Defects Program (Siffel et al., 2005) and in Flyde of Lancashire (Bound et al., 1989), variations in the seasonality findings across selected time frames were noted.

In this exploratory analysis without prior assumptions of underlying seasonal patterns, we performed multiple statistical tests on 42 groups of birth defects; some statistically significant findings may be the result of chance. We summarized the results of the four statistical tests graphically for each birth defect to allow the reader to visualize the consistency of the results. Siffel et al. (2005) describe the strengths and limitations of the Cochran-Armitage trend, the Hewitt-Rogerson test, and Walter-Elwood tests. The Hewitt-Rogerson test assumes no underlying model for the seasonal pattern and is sensitive, specific, and robust in its detection of a 6-month peak period, whereas the Walter-Elwood test assumes a sinusoidal pattern (i.e., a cyclic variation with one peak in the 12-month period) and measures the goodness-of-fit to that curve. The chi-square test of the four distinctive seasons was a simple test of observed versus expected values in a two-by-four contingency table.

These seasonality tests and graphical summaries can be incorporated into our ongoing birth defects surveillance activities in New York State. Based on our findings, the next steps are to generate hypotheses about potential

Table 5
Summary of Seasonality Tests by Infant Sex for Selected Birth Defects in Upstate New York, 1992–2006

	Male				Female			
Group	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-Square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Live Births	1,007,241				960,374			
Central Nervous System								
Anencephalus	37	Nov–Apr[a]	NC	Winter	55	Dec–May	Mar 8	Spring
Spina bifida without anencephalus	164	Dec–May	Feb 20	Spring	195	May–Oct[a]	Feb 23	Summer
Hydrocephalus without spina bifida	562	Nov–Apr[a]	Jan 27	Winter	427	Aug–Jan[a]	Mar 18	Fall
Encephalocele	49	Dec–May	NC	Winter	48	Dec–May	NC	Winter
Microcephalus	247	Jun–Nov	NC	Fall	387	Nov–Apr	Jan 8	Winter
Eye								
Anophthalmia, microphthalmia	55	Dec–May[a]	Feb 22	Spring [a]	44	Jan–Jun	NC	Spring
Congenital cataract	120	Jun–Nov[a]	Apr 2[a]	Fall[a]	116	Feb–Jul	Dec 9	Summer[a]
Ear								
Anotia, microtia	65	Oct–Mar[a]	Dec 12[a]	Winter	40	Feb–Jul[a]	NC	Summer
Cardiovascular								
Transposition of great arteries	152	Aug–Jan[a]	Nov 13	Winter	82	Oct–Mar	Oct 27	Summer
Tetralogy of Fallot	231	Dec–May	Dec 29	Spring	155	Jul–Dec	Mar 30	Fall
Ventricular septal defect	2316	Dec–May	Mar 9	Winter	2607	Dec–May[a]	Mar 18[a]	Winter [a]
Atrial septal defect	1317	Jan–Jun	Mar 16	Spring	1328	Jan–Jun	Oct 12	Spring
Endocardial cushion defect	77	Aug–Jan[a]	Oct 21	Fall	79	Jul–Dec[a]	Mar 10	Fall
Pulmonary valve atresia or stenosis	669	Dec–May[a]	Apr 1	Spring[a]	739	Jan–Jun[a]	Nov 3	Summer
Tricuspid atresia or stenosis	72	Jan–Jun	Jan 9	Winter	68	May–Oct	Jan 7	Winter
Ebstein anomaly	54	Oct–Mar[a]	Dec 17	Spring	42	Jul–Dec	NC	Fall
Aortic valve stenosis	179	Feb–Jul	Nov 8	Summer	90	Dec–May	Jan 20	Winter
Hypoplastic left heart syndrome	175	May–Oct[a]	Feb 3	Fall	109	Nov–Apr	Feb 7	Winter
Patent ductus arteriosus (≥2500 gm)	880	Nov–Apr	Feb 9	Fall	909	Mar–Aug[a]	Dec 8[a]	Summer[a]
Coarctation of aorta	406	Jan–Jun[a]	Oct 16	Spring	300	Jan–Jun	Mar 22	Winter
Orofacial								
Cleft palate without cleft lip	469	Oct–Mar	Jan 12	Winter	618	Jan–Jun	Feb 12	Winter
Cleft lip with and without cleft palate	972	Jul–Dec[a]	Oct 23	Fall	537	Feb–Jul[a]	Nov 9[a]	Spring[a]
Choanal atresia	152	Jul–Dec	Feb 23	Summer	160	Mar–Aug	Nov 8	Spring
Gastrointestinal								
Esophageal atresia, tracheoesophageal fistula	196	Apr–Sep	Dec 24	Summer	167	Jan–Jun	Feb 6	Spring
Rectal and large intestinal atresia or stenosis	281	Apr–Sep	Jan 29	Summer	274	Oct–Mar	NC	Spring
Pyloric stenosis	3286	Mar–Aug	Mar 20	Summer	740	Sep–Feb[a]	Oct 16	Fall
Hirschsprung disease (congenital megacolon)	273	Apr–Sep[a]	Jan 6	Spring	121	Feb–Jul	Oct 1	Summer
Biliary atresia	73	Mar–Aug	Jan 6	Summer	79	Feb–Jul[a]	Nov 22[a]	Spring
Genitourinary								
Renal agenesis or hypoplasia	346	Jun–Nov[a]	Mar 21	Summer	221	Jun–Nov[a]	Mar 11	Summer[a]
Obstructive genitourinary defect	3589	Apr–Sep	Jan 9	Fall	1502	Jun–Nov	NC	Fall
Hypospadias, epispadias	7623	Jan–Jun	NC	Summer				
Musculoskeletal								
Upper limb reduction deformity	212	Oct–Mar[a]	Dec 28	Winter	169	Sep–Feb	Jan 4	Winter
Lower limb reduction deformity	145	Nov–Apr	Mar 14	Spring	96	Mar–Aug[a]	Dec 9[a]	Spring[a]
Gastroschisis	177	Mar–Aug	Dec 19	Summer	167	Sep–Feb	Dec 25	Fall
Omphalocele	118	Oct–Mar[a]	Dec 14	Winter	128	Apr–Sep	Dec 20	Summer

Table 5
Summary of Seasonality Tests by Infant Sex for Selected Birth Defects in Upstate New York, 1992–2006 (Continued)

	Male				Female			
Group	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-Square (peak season)	Live births	Hewitt-Rogerson (peak 6-month period)	Walter-Elwood (peak)	Chi-square (peak season)
Congenital hip dislocation	611	Jun–Nov[a]	Feb 13	Summer	1856	Mar–Aug	Nov 25	Spring
Diaphragmatic hernia	203	Jul–Dec[a]	Nov 9	Winter	141	Mar–Aug	Dec 9	Summer
Chromosomal								
Trisomy 13	73	Apr–Sep[a]	Dec 28	Summer	63	Dec–May[a]	Jan 30	Winter
Down syndrome (trisomy 21)	1187	Nov–Apr[a]	Mar 4	Winter	1067	Apr–Sep	NC	Winter
Trisomy 18	73	Mar–Aug[a]	Oct 6	Summer	129	Apr–Sep	Dec 22	Summer
Other								
Fetal alcohol syndrome	127	Dec–May[a]	Feb 16[a]	Spring[a]	104	Feb–Jul	Jan 25	Fall
Amniotic bands	31	Jan–Jun[a]	NC	Winter	48	Jun–Nov	NC	Summer

[a]Statistically significant seasonality test ($p \leq 0.05$).
NC, not computed.

etiologic factors that vary by season in New York, such as meteorological factors, environmental chemicals, and maternal infections. For example, influenza displays a seasonal and regional variation in New York (New York State Department of Health, 2011), and maternal fever has been associated certain birth defects in animals and humans (Edwards, 2006). A time series analysis could be performed to assess the correlation between the seasonal pattern of influenza and the occurrence of birth defects in infants. Alternatively, a case-control study could be performed to examine birth defects in infants of mothers whose first trimesters occurred during influenza season.

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