Illinois Morbidity and Mortality Bulletin

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Message from Director Shah

Welcome to the fourth issue of the Illinois Morbidity and Mortality Bulletin (IMMB), a Department-wide publication that we created last year to present topics of interest to public health communities in Illinois through scientific analysis and interpretation of data.

In this issue, Jane Fornoff, Theresa Sandidge, Dejan Jovanov, and Ginger Mullin present the most recent knowledge about Zika virus and establish baseline data in Illinois for disease that may be associated with Zika virus infection using data from the Adverse Pregnancy Outcomes Reporting System, Hospital Discharge Data, and the Early Hearing Detection and Intervention Program.

In the second article, Kyle Garner and Tiefu Shen use data from the Illinois State Cancer Registry to examine trends in prostate cancer incidence and mortality in Illinois during the time when guidelines for prostate cancer screenings were changing.

We also encourage contributions from public health professionals at the state and local levels. Please send your manuscripts to the bulletin's editor, Dr. Tiefu Shen at Tiefu.Shen@illinois.gov (217.785.1873)

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Health Outcomes Associated with Zika Virus Infections: An Illinois Perspective

Recent outbreaks of Zika virus (ZIKV) in the Pacific, South America, and the Caribbean have been linked with birth defects, poor pregnancy outcomes and an increase in the occurrence of associated Guillain-Barré syndrome (GBS). This article presents the most recent knowledge about ZIKV and establishes baseline data in Illinois for diseases that may be associated with ZIKV infection. Data from three IDPH programs, the Adverse Pregnancy Outcomes Reporting System (APORS), Hospital Discharge Data (HDD), and the Early Hearing Detection and Intervention (EHDI) Program were used to calculate prevalence and hospitalization rates for congenital conditions potentially associated with ZIKV infection, including brain, eye, and ear/hearing anomalies. HDD was used to calculate hospitalization rates……. Read more

Temporal Trends in Prostate Cancer Incidence and Mortality in Illinois during Years of Recommended Screening Changes

After the introduction of Prostate Specific Antigen (PSA) screening in the late 1980s, prostate cancer incidence rates increased substantially. Concerns about overdiagnosis and overscreening have led the United States Preventative Services Task Force (USPSTF) and other professional groups to recommend against routine PSA screening. Trends in prostate cancer incidence and mortality in Illinois were examined …. Read more

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Health Outcomes Associated with Zika Virus Infections: An Illinois Perspective

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Abstract

Recent outbreaks of Zika virus (ZIKV) in the Pacific, South America, and the Caribbean have been linked with birth defects, poor pregnancy outcomes, and an increase in the occurrence of associated Guillain-Barré syndrome (GBS). This article presents the most recent knowledge about ZIKV and establishes baseline data in Illinois for diseases that may be associated with ZIKV infection. Data from three IDPH programs, the Adverse Pregnancy Outcomes Reporting System (APORS), Hospital Discharge Data (HDD), and the Early Hearing Detection and Intervention (EHDI) Program were used to calculate prevalence and hospitalization rates for congenital conditions potentially associated with ZIKV infection, including brain, eye, and ear/hearing anomalies. HDD was used to calculate hospitalization rates for GBS. GBS hospitalizations rates in Illinois were found to increase dramatically with age and were slightly more common in men than women. For several child-associated conditions, differences by sex were seen, with microcephaly more commonly reported among females, while other specific brain conditions, microtia, and hearing loss were reported more often in males. Racial disparities were observed in the prevalence of brain, eye, and ear conditions, with black and Hispanic babies exhibiting higher rates of disease compared to white babies. Very premature babies exhibited the highest prevalence and hospitalization rates for nearly all conditions examined. These findings provide a foundation in Illinois for future studies of the impact of diseases potentially associated with ZIKV infection.

Introduction

Origins

Zika virus (ZIKV) is an arthropod-borne flavivirus transmitted by the *Aedes* species of mosquito. ZIKV was first identified in 1947, in a rhesus monkey from the Zika forest in Uganda during research being conducted about yellow fever and other arboviruses.[1,2] The first evidence of human infection came from Uganda and areas close by, with only occasional cases reported in Africa and South-east Asia until 2007, when an outbreak occurred on the Yap Island of Micronesia.[2] In 2013-2014, major epidemics occurred in areas of the South Pacific including French Polynesia, New Caledonia and other islands.[3] It was during the outbreak in French Polynesia that the first cases of perinatal (mother to child) transmissions were confirmed in two patients.[2]

In 2015, dramatic increases in ZIKV infection were reported in the Americas, with Brazil being the most affected country.[3] In the fall of 2015, the Brazilian Ministry of Health reported an increase in cases of neonatal microcephaly (a condition where a baby's head is much smaller than expected) among women who had been infected with ZIKV.[2] In December 2015, the World Health Organization issued an alert along with

recommendations for prevention, surveillance, and control of the disease.[2] Currently, local transmission of ZIKV in the U.S. is limited to parts of southeastern Florida, southern Texas, and U.S. territories, including Puerto Rico .[4]

Transmission and Diseases

While the primary mode of transmission of ZIKV infections is through the bite of an infected mosquito, ZIKV may also be transmitted through sex with an infected person and may be passed from a woman to her child during pregnancy or delivery. It is also possible that ZIKV may be transmitted through a blood transfusion, although that risk is low at this time in the U.S.[5,6] Nevertheless, the U.S. Department of Health and Human Services is recommending that all blood donations are screened for ZIKV.

In adults, ZIKV infection presents much like that of dengue and chikungunya, and is usually self-limiting, with those infected experiencing either no symptoms or only mild symptoms. The most common symptoms include fever, maculopapular rash, joint pain, and conjunctivitis, lasting from several days to a week .[1,3,7] Past ZIKV infection is thought to provide protection from future infections. While ZIKV infection is generally not a cause for hospitalization and rarely a cause of death, complications may occur in some people.

Guillain-Barré Syndrome (GBS), a neurological manifestation causing muscle weakness and possible paralysis, has been reported among patients with ZIKV infection in both French Polynesia and Brazil .[2,3] While the link between ZIKV and GBS has been confirmed, it remains an uncommon complication and one that CDC continues to investigate.[8]

Infection with ZIKV during pregnancy has been associated with a spectrum of adverse out comes ranging from pregnancy loss, to impaired growth and serious birth defects in infants. As the full scope of disease continues to be studied, the pattern of congenital anomalies seen in conjunction with ZIKV infection is being referred to as Congenital Zika Syndrome, which includes, but is not limited to, microcephaly, intracranial calcifications and other brain anomalies, and eye anomalies.[9,10,11]

Microcephaly, a serious birth defect which can be indicative of poor brain development, has generally been linked to a range of other conditions including developmental delays, intellectual disability, feeding issues, seizures, hearing and vision problems, among others.[12]

Specific brain anomalies that have been found in children infected with ZIKV include; intracranial calcifications; ventriculomegaly and extra axial fluid; polymicrogyria; decreased brain parenchymal volume; cortical atrophy; hypoplasia of the cerebellum, brain stem, and cerebellar vermis; delayed myelination; and hypoplasia or thinning of the corpus callosum.[11] Eye anomalies that have been documented include chorioretinal anomalies of the macula, optic nerve anomalies, iris coloboma, and lens subluxation.[2]

Other findings have included club foot and contractures of single or multiple joints (arthrogryposis), which are likely a result of damage to the central nervous system .[11]

Placental insufficiencies and intrauterine growth restriction also have been frequently described in association with infection during pregnancy.[9]

Zika Virus and Illinois

Illinois is likely at low-risk of wide-spread, year-long, local transmission of ZIKV as the *Aedes aegypti* mosquito, the primary vector for ZIKV transmission, is rarely found in Illinois. The *Aedes albopictus* mosquito, a potential secondary ZIKV vector, is found primarily throughout the southern two-thirds of the state, so some local transmission may be possible. [4]

The principal ZIKV infection risk to Illinois residents is from travel to areas with active ZIKV transmission or from unprotected sex with someone who traveled to an area with active ZIKV transmission. In 2014, more than 15 percent of Illinois births were to couples where at least one parent was born in a country with active ZIKV transmission. It is likely that these parents, and many more who were born in the U.S., have high rates of travel to countries with active ZIKV transmission.

At this time, all but one confirmed cases of ZIKV infections in Illinois have been linked to travel. One case became infected through sexual transmission from someone who traveled to an area with active ZIKV transmission. The Illinois Department of Public Health (IDPH) has developed a Zika Virus Action Plan which outlines how offices at IDPH will work with other partners throughout the state and at the federal level to address and prevent further spread of disease in Illinois in the event of a local transmission. This plan is dynamic and continually adapted as circumstances change and research is updated. It can be found on the IDPH website at http://www.dph.illinois.gov/topics-services/diseases-and-conditions/zikavirus.

IDPH is also currently engaged in a variety of ongoing activities in an effort to monitor and address ZIKV in Illinois. IDPH's strong vector surveillance program is supporting active mosquito surveillance and abatement activities throughout the state. IDPH is conducting human surveillance for ZIKV and is participating in CDC's Zika Pregnancy Registry, which gathers information about pregnancy and infant outcomes after laboratory evidence of ZIKV infection has been found during pregnancy. [10] The IDPH laboratory is working with local health departments to provide testing for ZIKV infection. IDPH's Division of Infectious Disease provides counts of confirmed or inconclusive cases of ZIKV infection to the CDC on a weekly basis. The Division of Communications and Office of Women's Health and Family Services are providing educational information and messaging to the public, pregnant women, travelers, and health care providers throughout the state using a variety of means. Weekly information sharing meetings are held among the various offices throughout IDPH to communicate the latest ZIKV related activities.

The purpose of this article is to document the current understanding of ZIKV, and to establish baseline data in Illinois for diseases thought to be associated with infections.

Methods

Three IDPH programs collect data about conditions potentially associated with ZIKV: the Adverse Pregnancy Outcomes Reporting System (APORS), Hospital Discharge Data (HDD) and the Early Hearing Detection and Intervention (EHDI) Program. APORS and HDD use the International Classification of Diseases (ICD) to document conditions. Some newborn conditions linked to ZIKV infection, such as brain calcifications, polymicrogyria or, hypoplasia of the corpus callosum, do not have specific ICD codes, but rather fall under general groups. The newborn brain anomalies in this report that have their own specific ICD-9 codes are anencephaly (740.0, 740.1), encephalocele (742.0), microcephaly (742.1), hydrocephaly (742.3), anopthalmia (743.0-743.12) and microtia (744.23). Other brain anomalies that do not have a specific code were grouped together: reduction deformities of the brain (742.2) and other specified anomalies of brain (742.4). Eye anomalies (other than anopthalmia) were also grouped and included cataracts (743.30-743.34), and other anomalies of the posterior segment of the eye (743.51-743.59). HDD also has information about GBS (357.0). The EHDI Program contributed information about congenital hearing loss and will be able to provide information on congenital, late-onset and progressive hearing loss for infants and toddlers in the years to come.

APORS has been collecting information reported by hospitals about adverse pregnancy outcomes in Illinois since 1989. Reported outcomes, including those infants diagnosed with microcephaly, other brain anomalies, and eye anomalies, were coded using ICD-9-CM codes prior to 2013 and with ICD-10-CM codes from 2013 onwards. Program staff review medical records of children reported with selected birth defects to confirm, add, or remove birth defect diagnoses made in the first two years of life. To provide baseline data for this report, the most recently reviewed five years of data (2009-2013) were selected. Some of the conditions considered here are confirmed through medical chart review, others are not; there is less confidence about the numbers based on hospital reported cases.

Hospital Discharge Data (HDD) collects patient level discharge data from all Illinois acute care hospitals, specialty hospitals, and ambulatory surgical treatment centers. HDD contains coded hospital inpatient discharge information derived from hospital billing systems. Information includes billing data, ICD-9/10 diagnoses codes, CPT procedure codes, patient demographics, other patient identification information and charges by revenue codes. The diagnostic codes were coded using ICD-9 until October 2015 when hospitals started using ICD-10. Data from 2009 to 2013 are included here for newborn conditions. The data represent hospital visits, so a child may be counted more than once. GBS syndrome data from 2013 to 2015 are included and represent unique individuals. Personal identifiers have been included in discharge data collection since the fourth quarter of 2012, allowing unique patients to be identified with the HDD.

Since 2003, the Illinois EHDI Program has worked with parents and providers to ensure all babies are screened for hearing loss no later than one month of age. Infants who do not pass their hearing screen receive diagnostic evaluations no later than three months of age. Infants with hearing loss are enrolled in early intervention and parent support services no later than six months of age. The program collects data to document these activities. Beginning with the 2017 birth cohort, the Illinois EHDI program will collect information on children birth through six years of age.

GBS rates were calculated overall and by sex, race and age using census data as the denominator. The rates of each newborn condition identified in children less than two years of age were calculated overall, and by sex, race, gestational age, delivery weight and maternal age, using the number of live births as the denominator. Since the purpose of the study is to establish baseline data for future surveillance and the data sources used by this study capture all cases (i.e., complete enumeration), statistical significant tests and confidence intervals based on sampling were not applied.

Results

Guillain–Barré Syndrome 2013-2015

The overall hospitalization rate for GBS was 3.2 per 100,000 of the population. Rates increased as age increased, with those older than70 years hospitalized at a rate of 9.9, compared to those younger than 50 years hospitalized at a rate of 1.6. Hospitalizations rates were slightly higher for men when compared with women (3.4 versus 3.0). By race, whites and blacks were hospitalized at nearly the same rate (2.7 and 3.0 respectively), with Hispanics being hospitalized less often (2.1).

Brain Anomalies 2009-2013

With APORS data, brain reduction defects were the most commonly reported among selected brain anomalies at a rate of 7.3 per 10,000 live births (2.9 from HDD). "Other" brain anomalies and hydrocephaly were the second and third most reported defects (6.3 and 5.4 calculated using APORS data and 4.0 and 4.2 from HDD respectively). With HDD, microcephaly was the highest reported condition (4.3 per 10,000 live births). From both data sources, females had a higher rate of anencephaly and microcephaly when compared with males, while the category of "other" brain anomalies was reported slightly more in males when compared with females (Table 2).

Both data sources indicate that Hispanic babies had a higher rate of anencephaly and encephalocele when compared with white and black babies. For the remaining brain anomalies, black children exhibited higher rates of brain defects when compared with white and Hispanic babies (Table 2).

For all brain defects and both data sources, reported prevalence rates were highest in the most premature babies and decreased as gestational age increased (Table 3). Anencephaly rates appeared to decrease as maternal age increased, with a rate of 2.1 among babies of women younger than 20 years, compared with a

rate of 0.8 among babies of women 35 years and older. Rates for the remaining brain anomalies tended to follow a U-shaped pattern with the higher rates being seen in the youngest (younger than 20 years) and oldest (35 years and older) maternal age groups.

Eye Anomalies 2009-2013

Overall, anophthalmia/microphthalmia was identified by APORS data at twice the rate of other eye abnormalities (1.5 versus 0.7), while HDD identified more hospital visits for other eye abnormalities. HDD identified more males than females with anophthalmia/microphthalmia, while APORS data showed similar rates of reported disease for both sexes and conditions. HDD showed that black children had the highest rates of hospitalization (0.8) for anophthalmia/ microphthalmia, with Hispanic children close behind (0.7), while APORS data identified Hispanic children as having a higher rate of anophthalmia than white or black children. Both data sources showed black children as having a higher rate of other eye abnormalities compared with other races (Table 2).

The most premature babies had the highest rates of eye anomalies, and rates decreased as gestational age increased (Table 3). Children of women age 35 years and older exhibited a higher rate (2.9) of anophthalmia/microphthalmia compared with all other maternal age groups (range 1.0 to 1.3).

Ear/Hearing anomalies

Microtia was reported at a rate of 1.1 per 10,000 live births by both data sources. Slightly more microtia was reported in males than females (Table 3). Both data sources indicated that Hispanic babies had a much higher rate of microtia reported when compared with white and black babies. Babies with a gestational age of 32-36 weeks exhibited a higher rate of microtia compared with those with a shorter or longer gestational age. When examining maternal age, there is some evidence of a trend with the youngest mothers having babies with the lowest rate of microtia and babies of women age 35 years and older having the highest rate (Table 3).

The overall prevalence rate for congenital deafness was 16.8 with a higher rate reported in males (17.2) compared with females (15.4).

Discussion

Each data source used in this analysis has apparent and unique strengths and limitations. While the ICD-9/10 system provides standardization in disease coding, not all selected disease conditions have unique codes, thus requiring the use of broader groupings and limiting the identification of precise disease. While APORS is the most complete source of adverse birth outcomes in Illinois, its passive nature of surveillance may underestimate adverse outcome rates. More confidence lies in APORS data confirmed by medical chart reviews. Because of the lack of a unique personal identifier in the hospital discharge dataset until the fourth quarter of 2012, there was not a mechanism for identifying readmissions of an individual for the same condition. For anencephaly, this is unlikely to have made a difference since all babies born with this condition

die soon after delivery. However, for a condition such as hydrocephaly, a baby is likely to have multiple admissions, leading to higher hospitalization rates. GBS hospitalizations rates in Illinois increased dramatically with age and were slightly more common in men than women. This type of pattern is not unexpected, given current literature on GBS prevalence.[13, 14]

Generally, the number of children younger than two years identified by APORS was higher than those identified by HDD, even though HDD counts hospitalizations and not unique children. This is primarily a result of the different purposes for which the data are collected. For some conditions, such as anencephaly and some other brain anomalies, many pregnancies end in miscarriage. These cases are included in APORS data, but not in the HDD data.

For a few child-associated conditions, differences by sex were noted. Microcephaly was more commonly reported among females versus males, while certain other brain conditions were reported slightly more often among males. Microtia and hearing loss were reported at higher rates for male versus female children. Racial disparities were observed in the APORS prevalences of brain, eye, and ear conditions with black and Hispanic babies exhibiting higher rates of disease compared to white babies. This is in line with what is already known.[15]

The most premature babies exhibited the highest prevalence and hospitalization rates for nearly all conditions, which is to be expected. However, for microtia, infants of 32-36 weeks gestation exhibited higher disease and hospitalization rates than younger and older babies.

It should be noted that infections such as ZIKV were probably the cause of very few of these cases. Most will be understood as sequalae of conditions with a known cause such as genetic syndromes (e.g. Trisomy 13, 18 or 21) or intraventricular hemorrhage, while many will remain unexplained.

These baseline data provide a reference point for Illinois when examining future potential impacts of disease associated with ZIKV infection. IDPH's Division of Infectious Diseases, HDD, EHDI, and APORS programs will continue to improve surveillance of associated conditions over the next few years, placing IDPH in a strong position to understand and address the impact of ZIKV on the citizens of Illinois.

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Table 1. Number and Rates of Guillain-Barré Syndrome 2013-2015

Total		Sex		Age				Race		
N	Rate[1]	Male	Female	<50	50-60	60-70	70+	White	Black	Hispanic
1,224	3.2	3.4	3.0	1.6	4.3	6.0	9.9	2.7	2.9	2.1

Source: Hospital Discharge Data as of September 2016.
[1] Rates per 100,000 population

Table 2. Number and Rates[2] of Congenital Conditions Potentially Associated with the Zika Virus, 2009-2013, by sex and race

Condition	Data Source	Total		Sex		Race			Fetal/Infant Death Rate
		N	Rate[2]	M	F	WNH	BNH	H	
Brain Anomalies									
Anencephaly	APORS Review	122	1.5	1.3	1.6	1.3	1.1	2.5	100.0
	Live Births	59	0.7	0.5	0.9	0.5	0.6	1.4	100.0
	HDD	46	0.6	0.4	0.7	0.5	0.4	0.8	
Encephalocele	APORS Review	65	0.8	0.9	0.7	0.4	1.0	1.5	36.9
	HDD	47	0.6	0.6	0.6	0.3	0.6	0.9	
Microcephaly	APORS Review	427	5.2	4.3	6.2	4.1	8.6	5.9	17.3
	HDD	351	4.3	3.3	5.3	2.6	9.3	2.7	
Brain Reduction Defects	APORS Hosp Rpt	594	7.3	7.4	7.0	6.4	10.3	7.3	23.3
	HDD	234	2.9	2.6	3.1	2.5	3.5	2.3	
Hydrocephaly	APORS Hosp Rpt	439	5.4	5.4	5.3	4.5	8.7	5.0	23.4
	HDD	342	4.2	4.1	4.2	3.5	6.6	2.9	
Other brain anomalies	APORS Hosp Rpt	514	6.3	6.5	6.0	5.7	9.9	5.1	8.5
	HDD	324	4.0	4.5	3.4	2.7	6.1	3.3	
Eye Anomalies									
Anophthalmia	APORS Review	119	1.5	1.5	1.4	1.4	1.3	1.9	33.6
	HDD	54	0.7	0.9	0.4	0.4	0.8	0.7	
Other eye abnormalities	APORS Hosp Rpt	56	0.7	0.8	0.6	0.3	1.7	0.9	17.9
	HDD	77	0.9	0.9	1.0	0.7	1.4	0.8	
Ear/Hearing Anomalies									
Microtia	APORS Review	92	1.1	1.3	0.9	0.8	0.4	2.3	6.5
	HDD	86	1.1	1.1	1.0	0.8	0.3	1.7	
Congenital deafness	(2013-2015) EHDI	794	16.8[1]	17.2	15.4				

M=Male; F=Female; WNH=White Non-Hispanic; BNH=Black Non-Hispanic; H=Hispanic; HDD=Hospital Discharge Data; Hosp Rpt = Hospital Report

Source: APORS, HDD, and EHDI data as of September 2016.
[1] Uses estimated number of births for 2015
[2] Rates per 10,000 live births

Table 3. Rates of Congenital Conditions Potentially Associated with the Zika Virus, 2009-2013, by Prematurity and Maternal Age

Condition		Prematurity (weeks)			Maternal Age (years)				
		< 32	32-36	37+	<20	20-24	25-29	30-34	35+
Brain Anomalies									
Anencephaly	APORS Review	45.3	4.1	0.4	2.1	1.4	1.4	1.1	0.8
	Live Births	12.4	2.9	0.3	1.2	0.7	0.8	0.7	0.5
	HDD	6.9	1.5	0.4					
Encephalocele	APORS Review	8.2	2.8	0.5	1.3	0.6	0.7	0.5	1.3
	HDD	2.7	1.2	0.5					
Microcephaly	APORS Review	29.5	16.2	3.7	8.3	7.0	4.9	2.7	6.1
	HDD	30.9	10.1	3.2					
Brain Reduction Defects	APORS Hosp Rpt	122.2	18.2	4.0	9.9	7.6	5.1	6.2	7.7
	HDD	15.1	4.7	2.5					
Hydrocephaly	APORS Review	115.4	13.8	2.4	8.0	5.5	3.7	4.6	5.8
	HDD	74.2	8.4	2.4					
Other brain anomalies	APORS Hosp Rpt	120.9	13.7	3.3	7.2	6.4	5.5	5.4	7.1
	HDD	86.5	7.1	2.0					
Eye Anomalies									
Anophthalmia	APORS Review	7.6	5.0	1.0	1.3	1.2	1.2	1.0	2.9
	HDD	6.2	1.9	0.4					
Other eye abnormalities	APORS Hosp Rpt	8.9	2.4	0.4	0.6	0.9	0.7	0.3	0.8
	HDD	8.9	2.4	0.7					
Ear/Hearing Anomalies									
Microtia	APORS Review	1.4	2.5	1.0	0.7	1.0	1.2	1.1	1.5
	HDD	0.7	1.6	1.0					

HDD=Hospital Discharge Data; Hosp Rpt = Hospital Report

Source: APORS and HDD data as of September 2016.

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Temporal Trends in Prostate Cancer Incidence and Mortality in Illinois during Years of Recommended Screening Changes

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Abstract

After the introduction of Prostate Specific Antigen (PSA) screening in the late 1980's, prostate cancer incidence rates increased substantially. Concerns about overdiagnosis and overscreening have led the United States Preventative Services Task Force (USPSTF) and other professional groups to recommend against routine PSA screening. Trends in prostate cancer incidence and mortality in Illinois were examined over the time period encompassing these guideline changes, 1994 through 2013. Data were from the Illinois State Cancer Registry. Age adjusted cancer incidence and mortality rates were examined for men 50 years of age or older with a malignant cancer of the prostate (ICD-O3 code C1619) by race (All Race, White, Black), age group (50-69, 70+), and by cancer stage (local/regional and distant). Joinpoint regression analysis was used to quantify trends in the annual percent changes (APC). Illinois started seeing the beginnings of downward trends in localized/regional prostate cancer incidence among both white and black men in 2008. Changes in distant stage prostate cancer incidence in younger Illinois men and older white men appear to level off during the period when screening recommendations were changing. There was a steadily decreasing trend of prostate cancer mortality among older men of both races as well as younger black men. Younger white men, however, displayed a decreasing trend until 2009 and assumed a seemingly flat trend from 2009 to 2013. Declining rates of early stage prostate cancer incidence coincide with screening changes recommend by the USPSTF. Increasing late stage prostate cancer incidence in younger white men was observed, however, this increase was not statistically significant. Prostate cancer mortality rates appeared to have leveled off prior to the implementation of prostate cancer screening changes with no subsequent increase in the trend.

Introduction

The Prostate Specific Antigen (PSA) test was first approved for use as a screening method for prostate cancer in 1986. In the early 1990's the American Urological Association (AUA) and the American Cancer Society (ACS) began recommending routine annual PSA testing. The impact of these events was an increase in the incidence rate of prostate cancer in Illinois men, which rose from 103.1 per 100,000 in 1986 to a high of 190 per 100,000 in 1992. After 1992, the rate slowly declined, but tracked back up to 178.4 per 100,000 in 2002. After 2002, the rates declined until 2013 when the rates returned to what they were in 1986. [1]

Beginning in 2000, the ACS and the AUA guidelines were changed and began advising against the use of PSA screening due to potential harms of overdiagnosis and overtreatment.[2,3] Revised guidelines recommended against routine screening while advising providers to support informed decision making. In 2008 the USPSTF

recommended against screening men older than 75 years.[4] Results of two major screening trials were published in 2009. One found a modest survival benefit with PSA screening and the other no benefit.[5,6] The ACS and AUA, in 2010 and 2013 respectively, issued recommendations affirming the importance of informed decision making. Lastly, in 2011 the USPSTF released draft guidelines advising against the use of PSA-based screening for prostate cancer. These were approved in 2012 with the publication of the final recommedation.[7]

Three studies have examined the temporal associations between changes in PSA screening recommendations and prostate cancer incidence.[8-10] All three papers utilized samples of incident cancers for their analysis, Surveillance, Epidemology, and End Results (SEER) 18 and the National Cancer Database. Increasing trends in late stage disease were observed for men younger than 70 years of age in two of the analyses,[9,10] which raise concerns due to the decreased survival of prostate cases diagnosed at a distant stage compared to those diagnosed at a local or regional stage.[11] This study aims to examine trends in prostate cancer incidence and mortality by race, age, and stage for Illinois men between 1994 and 2013.

Methods

The Illinois State Cancer Registry Cancer (ISCR), which provided data for this study, is a population based surveillance system and has attained the North American Association of Central Cancer Registries Gold certification for the past 18 years (1996-2013) and is a U.S. Centers for Disease Control and Prevention (CDC) - National Program of Cancer Registries "Registry of Excellence." Incidence data were analyzed for all Illinois male residents 50 years of age and older with malignant prostate cancer (ICD-O-3 code C619) diagnosed between 1994 and 2013. Age-adjusted rates were calculated per 100,000 persons in SEER Stat and were standardized to the 2000 U.S. Standard population.[12]

We examined trends in prostate cancer by race (All, White and Black), age group (50-69; 70+) and by stage (local/regional, distant) from 1994 through 2013. SEER Historic A staging was used to ensure comparability over the time period. Joinpoint regression analysis was used to examine the annual percent change (APC) in the resulting model trends.[13] Significance of trends, increasing or decreasing, were noted at the $p<0.05$ level.

Age adjusted mortality rates for deaths due to prostate cancer in Illinois men were also examined by age (50-69; 70+) and race.[14]

Results

Incidence

Age adjusted incidence rates for localized/regional prostate cancer for 50-69 year olds displayed a significant increase from 1994 to 2001. The rate rose slightly from 2005 to 2008 before dropping significantly from 2008 to 2013. The incidence of distant stage disease dropped significantly from 1994 to 2002 before leveling off from 2002 to 2013 (Figure 1, Table 1).

In men older than 70 years of age, the incidence of localized/regional disease was in large part unchanged from 1994 to 2008. After 2008, the rate of localized/regional prostate cancer decreased sharply through 2013. Incidence of distant stage disease dropped significantly from 1994 until 2002 when the trend leveled off and remained flat through 2013.

White Illinois males experienced trends very similar to those of the population as a whole. The local/regional prostate cancer incidence trend in white males aged 50-69 years increased significantly from 1994 through 2001. It then leveled off from 2001 to 2008 and dropped sharply from 2008 to 2013. Distant stage prostate cancer incidence in white men aged 50-69 years declined significantly from 1994 through 2003. From 2003 to 2013, the APC for the trend for this group was not statistically significant.

In older white men, 70 years and older, the prostate cancer incidence trend for local/regional stage disease changed little between 1994 and 2008. After 2008, however, the trend realized a significant decline through 2013. Incidence of distant stage disease in this group of men trended significantly lower from 1994 to 2002. After 2002, the trend flattened through to 2013 (Figure 2, Table 1).

Black Illinois male residents aged 50 to 69 years displayed two significant trends in local/regional prostate cancer incidence during this time period. Between 1994 and 2008 the age-adjusted incidence rate for this group significantly increased. In 2008, the trend began to decrease and was found to be significantly decreasing through 2013. Distant stage disease in black males 50 to 69 years decreased significantly between 1994 and 2002 and subsequently leveled off between 2002 and 2013.

The trend in local/regional prostate cancer incidence in black men aged 70 years and older displayed a significant decrease in the rate between 2008 and 2013. Distant stage disease in this group steadily decreased significantly over the entire time period (Figure 3, Table 1).

Mortality

The age adjusted prostate mortality rate for men 50-69 years declined significantly over the entire time period. A similar declining trend was seen in men 70 years and older. White males 50-69 realized a declining trend from 1994 to 2009. From 2009 to 2013 the trend increased slightly, however, that increase was not statistically significant. White males 70 years and older saw significantly declining prostate cancer mortality over the entire time period. Black males aged 50 to 69 years, as well as those aged 70 years and older saw significant declines in prostate cancer mortality between 1994 and 2013 (Table 2).

Discussion

Using population-based cancer registry data for Illinois from 1994 through 2013, we found that in 2008, Illinois saw the beginnings of downward trends in localized/regional prostate cancer incidence among both white and black men. This coincides with a time when concerns around overtreatment and overdiagnosis of prostate cancers in men precipitated changes in screening recommendations from professional associations as well as

the USPSFT. However, changes in distant stage prostate cancer incidence in younger Illinois men and older white men appear to level off prior to the publication of screening recommendations. Mortality trends displayed steadily decreasing trends of prostate cancer mortality in older men as well as younger black men. Younger white men, however, displayed a decreasing trend until 2009, after which the trend seemed to be attenuated. White and black males in Illinois display similar trends in prostate cancer incidence and mortality despite disparities in the individual annual rates.

The relationship between screening recommendations and population outcomes can be complicated. Why trends in late stage prostate cancer incidence and prostate cancer mortality in younger men leveled off prior to changes observed in early stage prostate cancer incidence is unclear. A reduction in screening will reduce the incidence of prostate cancer and the risk of overdiagnosis, however, there is concern that lack of screening will increase the rate of late stage disease. Weiner et al reported a significant increase in the number of late stage prostate cases in a hospital sample. In our study, utilizing a population based data set and examining age adjusted rates versus counts of cases, we did not observe a significant rise in the age adjusted incidence of late stage prostate cancer or a concomitant rise in the rate of prostate cancer mortality.

Our study has important limitations. We could only study an association between screening recommendations and incidence of prostate cancer at the population level, and we do not know the screening history of individual men diagnosed with prostate cancer. Also, while mortality data is included in this analysis, longer study periods are necessary to gain a clearer picture of the relationship between changing prostate cancer incidence rates and associated rates of prostate cancer mortality.

Conclusion

Declining rates of prostate cancer incidence coincide with screening changes recommend by the USPSTF. A change in the trend of late stage prostate cancer incidence in younger white men was observed, however, this increase was not statistically significant. In addition, prostate cancer mortality rates appeared to have leveled off prior to the implementation of screening changes. Additional study in the area of survival is suggested to gain a robust understanding of the impact of changes in incidence and mortality that can be attributed to changes in screening recommendations. Continued observation of prostate incidence, mortality, and survival is necessary to understanding the impact of screening recommendations.

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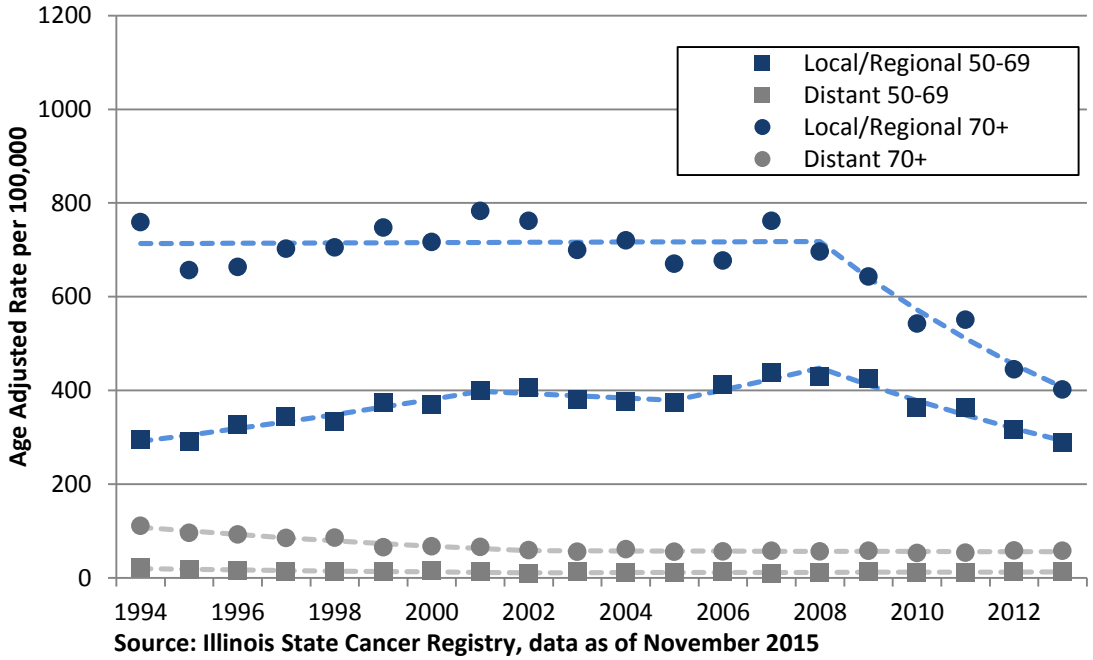
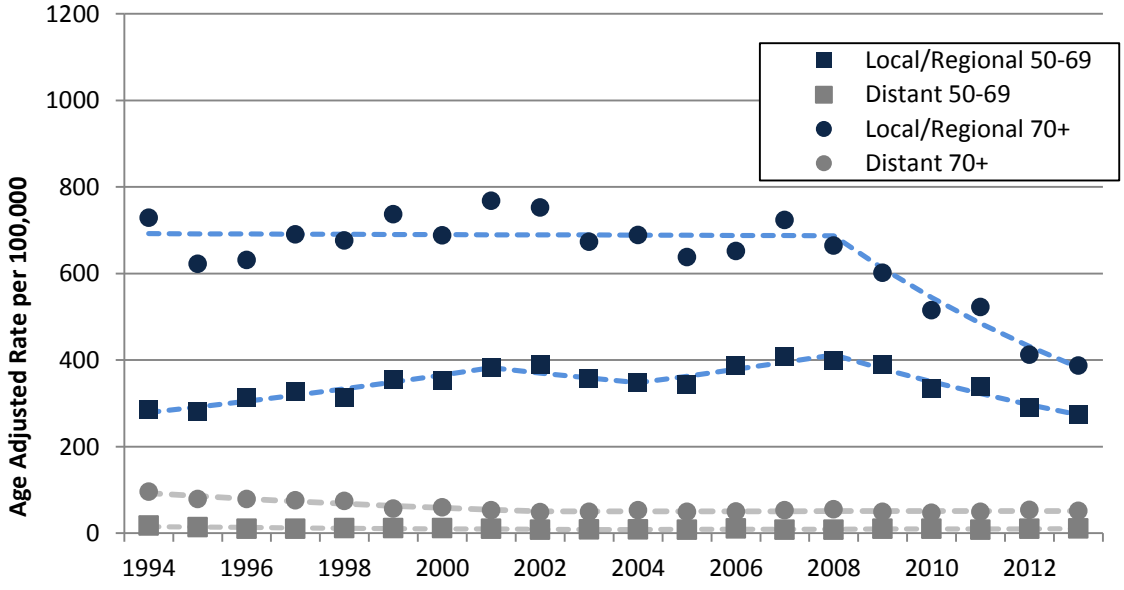
Figure 1. Illinois Male Prostate Incidence by Stage and Age 1994-2013



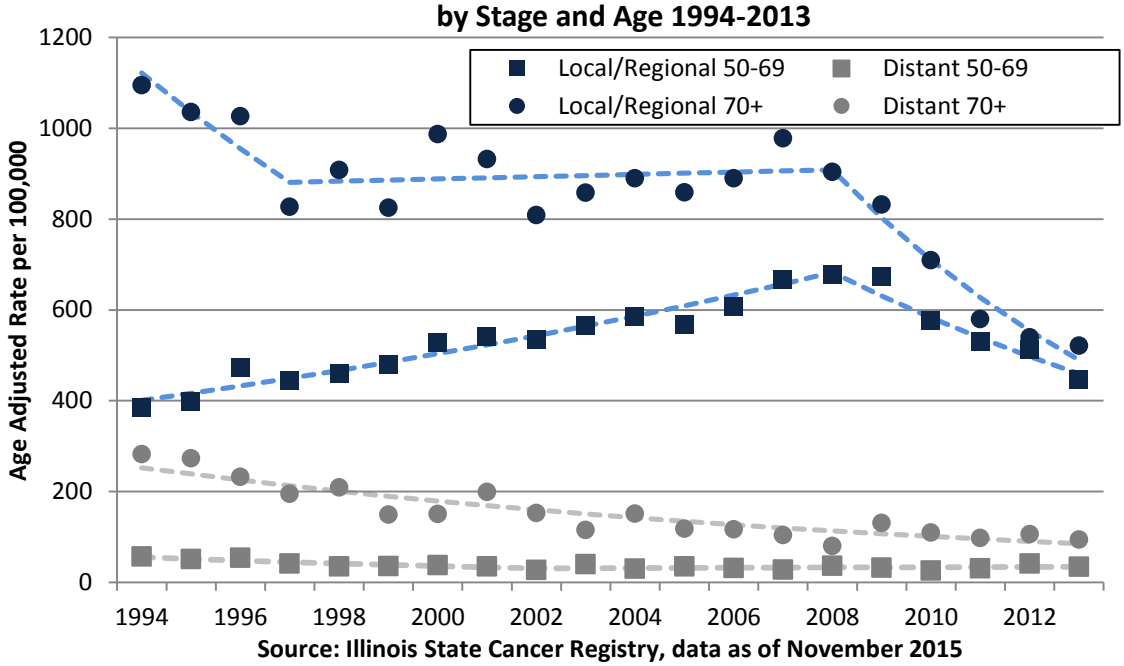
Source: Illinois State Cancer Registry, data as of November 2015

Figure 2. Illinois White Male Prostate Incidence by Stage and Age 1994-2013



Source: Illinois State Cancer Registry, data as of November 2015

Figure 3. Illinois Black Male Prostate Incidence by Stage and Age 1994-2013



Source: Illinois State Cancer Registry, data as of November 2015

Table 1. Trends in Illinois Prostate Cancer Incidence Rates by Stage at Diagnosis, Race and Age, 1994-2013

Race	Age	Stage	Trend	Starting Year	Ending Year	Annual Percent Change	Lower CI	Upper CI
All Races	50-69	LOCAL/ REGIONAL	1	1994	2001	4.6*	2.8	6.4
			2	2001	2005	-1.2	-6.7	4.5
			3	2005	2008	5.7	-4.7	17.3
			4	2008	2013	-8.1*	-10.3	-5.9
	50-69	DISTANT	1	1994	2002	-6.9*	-9.7	-4.0
			2	2002	2013	1.3	-0.6	3.3
	70+	LOCAL/ REGIONAL	1	1994	2008	0.0	-0.8	0.9
			2	2008	2013	-10.7*	-14.6	-6.7
	70+	DISTANT	1	1994	2002	-7.5*	-8.9	-6.0
			2	2002	2013	-0.4	-1.5	0.7
White	50-69	LOCAL/ REGIONAL	1	1994	2001	4.6*	2.7	6.6
			2	2001	2004	-3.1	-14.4	9.6
			3	2004	2008	4.4	-1.6	10.7
			4	2008	2013	-7.9*	-10.3	-5.4
	50-69	DISTANT	1	1994	2003	-6.4*	-9.8	-2.8
			2	2003	2013	2.2	-1.0	5.4
	70+	LOCAL/ REGIONAL	1	1994	2008	0.0	-1.0	0.9
			2	2008	2013	-11.0*	-15.5	-6.3
	70+	DISTANT	1	1994	2002	-7.4*	-9.1	-5.6
			2	2002	2013	0.2	-1.0	1.5
Black	50-69	LOCAL/ REGIONAL	1	1994	2008	3.9*	3.3	4.5
			2	2008	2013	-7.6*	-9.8	-5.4
	50-69	DISTANT	1	1994	2002	-7.1*	-11.1	-2.9
			2	2002	2013	1.0	-1.7	3.8
	70+	LOCAL/ REGIONAL	1	1994	1997	-7.7	-16.5	1.9
			2	1997	2008	0.3	-1.2	1.8
			3	2008	2013	-11.6*	-15.7	-7.4
	70+	DISTANT	1	1994	2013	-5.6*	-6.7	-4.4

Data Source: Illinois State Cancer Registry, data as of November 2015
*Annual Percent Change is statistically different from zero at the p<0.05 level

Figure 2. Trends in Illinois Prostate Cancer Mortality by Age and Race, 1994-2013

Race	Age	Trend	Starting Year	Ending Year	Annual Percent Change	Lower CI	Upper CI
All Races	50-69	1	1994	2013	-3.1*	-3.4	-2.7
	70+	1	1994	2013	-2.8*	-3.0	-2.6
White	50-69	1	1994	2009	-3.8*	-4.5	-3.1
		2	2009	2013	1.8	-4.2	8.3
	70+		1994	2013	-2.9*	-3.1	-2.6
Black	50-69	1	1994	2013	-2.6*	-3.5	-1.7
	70+	1	1994	2013	-3.1*	-3.7	-2.5

Data Source: National Center for Health Statistics

*Annual Percent Change is statistically different from zero at the p<0.05 level