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# Prostate Cancer Trends and the USPSTF Recommended PSA 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 recently 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 fifty 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 of changes in screening recommendations. Illinois saw a steadily decreasing trend of prostate cancer mortality on 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 rate from 2009 to 2013. Declining rates of early stage prostate cancer incidence coincide with screening changes recommended 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. After that, the rates returned to what they were in 1986.<sup>1</sup>

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 over diagnosis and overtreatment.<sup>2,3</sup> Revised guidelines recommended against routine screening while advising providers to support informed decision making. In 2008 the United States Preventative Services Task Force (USPSTF) recommended against screening men older than 75.<sup>4</sup> Results of two major screening trials were published in 2009. One found a modest survival benefit with PSA screening and the other no benefit.<sup>5,6</sup> 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 recommendation.<sup>7</sup>

Three studies have examined the temporal associations between changes in PSA screening recommendations and prostate cancer incidence.<sup>8-10</sup> All three papers utilized samples of incident cancers for their analysis, 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,<sup>9,10</sup> 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.<sup>11</sup> 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, has attained the North American Association of Central Cancer Registries Gold certification for the past 18 years (1996-2013) and is a 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.<sup>12</sup>

Trends in prostate cancer were examined 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.<sup>13</sup> 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.<sup>14</sup>

## **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 over 70 years of age, the incidence of localized/regional disease was unchanged, in large part, 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 where 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 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 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 and above, 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 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 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 and above 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 declined significantly over the entire time period. A similar declining trend was seen in men 70 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 of age and older saw a significantly declining prostate cancer mortality over the entire time period. Black males aged 50 to 69, as well as those aged 70 and above 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, 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 where concerns around overtreatment and overdiagnosis of prostate cancers in men precipitated changes in screening recommendations from professional associations as well as the USPTF. 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 displayed 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. It is unclear as to 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. A reduction in screening will reduce the incidence of prostate cancer and the risk of over diagnosis, however there is concern that lack of screening will increase the rate of late stage disease. A study by Weiner et al reported a significant increase in the number of late stage prostate cases in a hospital sample. In this study, utilizing a population based data set and examining age adjusted rates versus counts of cases, there was no observed significant rise in the age adjusted incidence of late stage prostate cancer or a concomitant rise in the rate of prostate cancer mortality.

This study has important limitations as it only studied an association between screening recommendations and incidence of prostate cancer at the population level and the screening history of individual men diagnosed with prostate cancer is unknown. Also, while mortality data is included in this analysis, longer follow up time is 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 recommended 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:

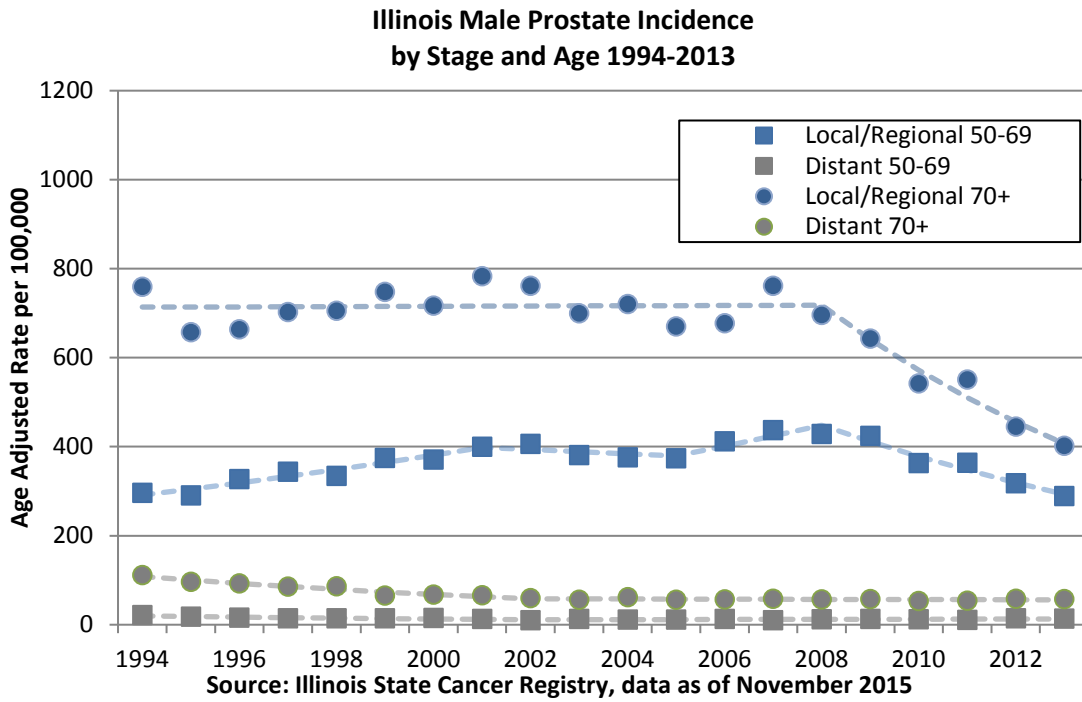


Figure 2:

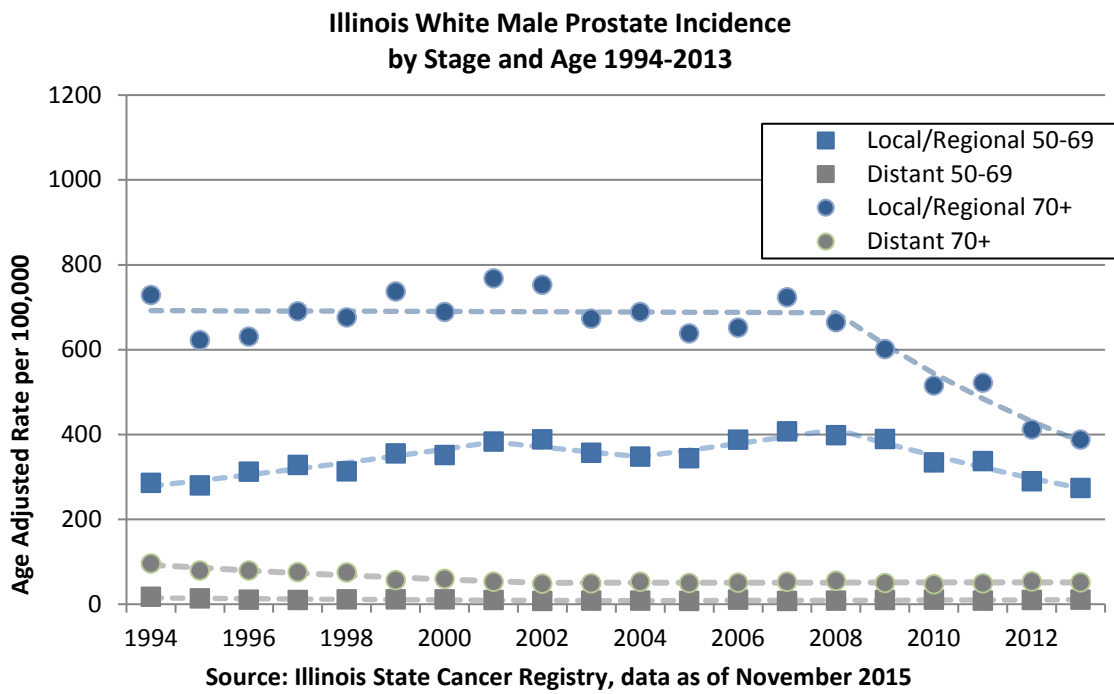
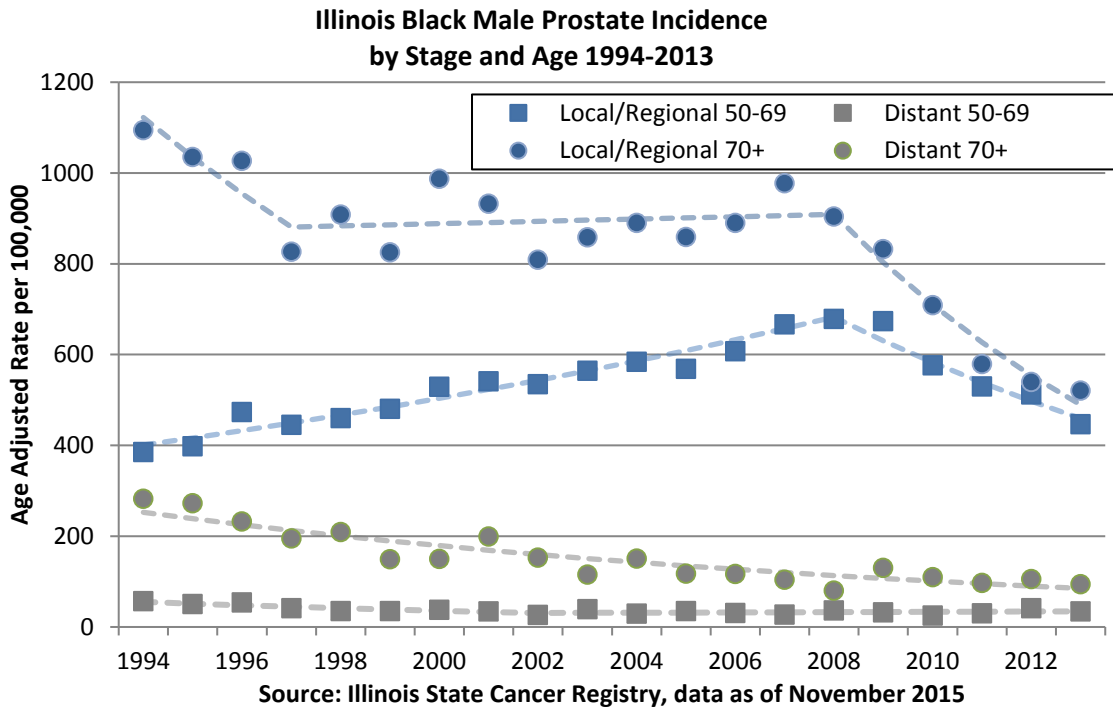




Figure 3:



**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

**Table 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+	1	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