

PROSTATE CANCER

CHAPTER 1

Epidemiology, Etiology
Chemoprevention

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Abbreviations and Acronyms

+ve	= Positive
-ve	= Negative
5-ARIs	=5- α Reductase Inhibitors
AD	=Autosomal Dominant
AR	=Androgen Receptor
AUA	= American Urological Association
ASCO	= American Society of Clinical Oncology
CCS	= Canadian Cancer Society
CDC	= Center for Disease Control
CUA	= Canadian Urological Association
HG	= High Grade
HPC1	= Hereditary Prostate Cancer 1
Hx	= History
IGF1	=Insulin-Like Growth Factor 1
LN	=Lymph node
NCI	= National Cancer Institute
PCa	= Prostate Cancer
PCPT	=Prostate Cancer Prevention Trial
Pts	= Patients
REDUCE	= Reduction by Dutasteride of Prostate Cancer Events
SEER	= The Surveillance Epidemiology and End Results Program
SELECT	= Selenium and Vitamin E Cancer Prevention Trial

Section 1

Epidemiology and Etiology

Prostate cancer is the most common noncutaneous cancer in men and accounted for over a quarter (27%) of new cancer cases in men during 2012^{1,2}. In fact, 1 out of 6-7 men gets prostate cancer during his life^{1, 3}. Prostate cancer also contributes significantly in cancer specific death rate. Statistics show that prostate cancer is the 2nd and 3rd leading cause of cancer-related deaths in US and Canada^{1, 2}. The median age at diagnosis of prostate cancer is 67 and the median age of death due to it is 80³.

A decrease in mortality rate of prostate cancer is currently seen in many countries including US and Canada^{1, 2}. Prostate cancer incidence and mortality differs in different races and ethnicities and is more common in African Americans than any other groups³. Current SEER (The Surveillance Epidemiology and End Results program) data shows that nearly 81% of prostate cancer cases are diagnosed when they are still localized and have 5 year survival of nearly 100%³.

On January 1, 2009, in the United States there were approximately 2,496,784 men alive who had a history of prostate cancer³. 241,740 and 26,500 men estimated to be diagnosed with prostate cancer in US and Canada in 2012 alone and 28,170 and 4,000 estimated to die because of it in these countries respectively^{1, 4}.

Prostate cancer can also affect younger people. 1154 patients with the age of 35-44 were diagnosed with prostate cancer and 27 people in the same age group died due to prostate cancer during 2009 in United States³. Furthermore, 18,266 patients were between 45 and 54 at the time of diagnosis and 410 patient who died because of prostate cancer were in the same age group³. Prostate cancer epidemiology highlights have been summarized in table-1.

PROSTATE CANCER

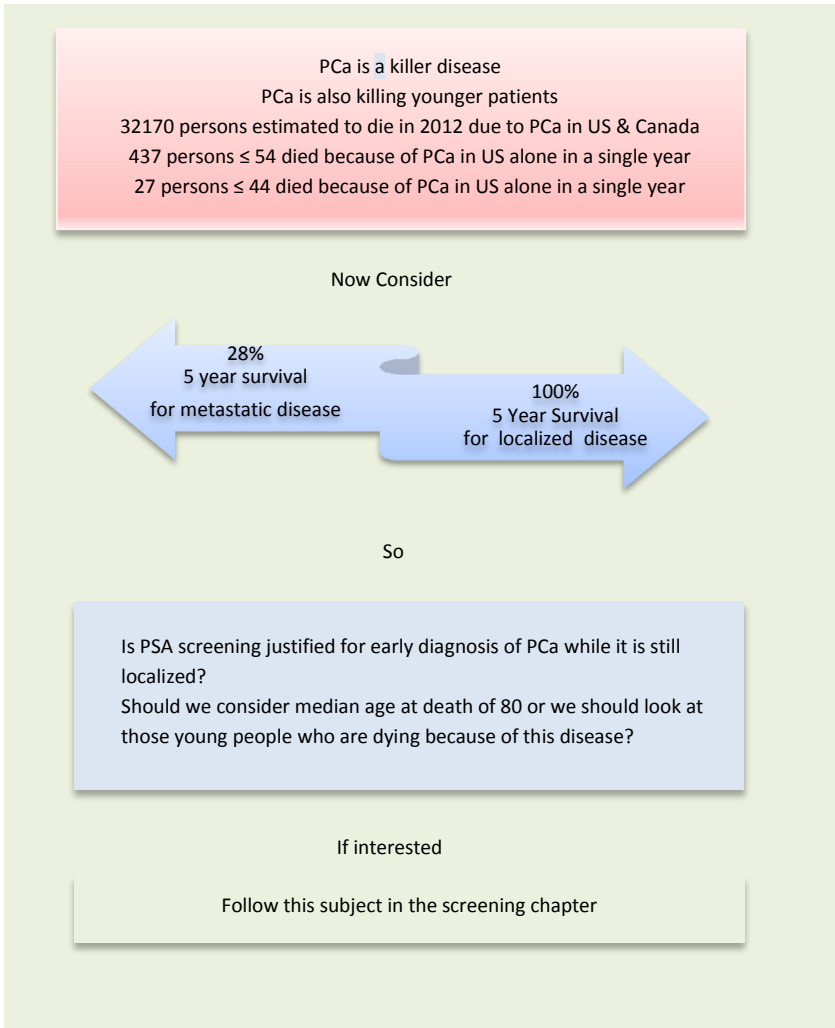
Table 1-Prostate cancer epidemiology highlights

Parameter	Location	Statistics	Remarks	Source
Incidence rank	Ca	1 st	Excluding non-	CCS
	US	1st	melanoma skin cancer	CDC
Death rank	Ca	3 rd	Between all cancers	CCS
	US	2 nd		CDC
Life time risk	Ca	1 in 7	2012	CCS
	US	1 in 6	2012	SEER
New cases	Ca	26,500	2012	CCS
	US	241,740	2012	NCI
Death	Ca	4000	2012	CCS
	US	28,170	2012	NCI
Percentage of all estimated new cancer cases in men	Ca	27%	2012	CCS
Incidence trend	Ca	Increasing	1980-2012	CCS
	US	Decreasing	2000-2009	SEER
Mortality trend	Ca	Decreasing	Mid 1990s-2012	CCS
	US	Decreasing	1991-2009	CDC
Stage at diagnosis	US	Localized N +ve M +ve	81% 12% 4% Regional LN	SEER
5 year survival	US	Localized N +ve M +ve	100% 100% 27.8%	2002-2008 SEER
Disease diagnosed In young patients	US	35-44 yr	1154	2009 SEER
		45-54 yr	18,266	
No. of deaths due to PCa in young pts	US	35-44yr	27	2009 SEER
		45-54yr	410	
Median age at diagnosis	US	67	2005-2009	SEER
Median age at death	US	80	2005-2009	SEER

Incident rate by race	US	Black	236	Per 100,000 men	SEER
		White	146.9		
		Hispanic	125.9		
		Asian	84.4		
		Aboriginal	78.4		
Death rate by race	US	Black	53.1	Per 100,000 men	SEER
		White	21.7		
		Hispanic	17.8		
		Asian	10		
		Aboriginal	19.7		
Diagnosis age	US	35-44yr	0.6 %	2005-2009	SEER
		45-54yr	9.5 %		
		55-64yr	31.6%		
		65-74yr	35.5%		
		75-84yr	18.6%		
		>85yr	4.1%		
Death age	US	35-44yr	0.1 %	2005-2009	SEER
		45-54yr	1.5 %		
		55-64yr	8%		
		65-74yr	19.8 %		
		75-84yr	38.6 %		
		>85yr	32 %		

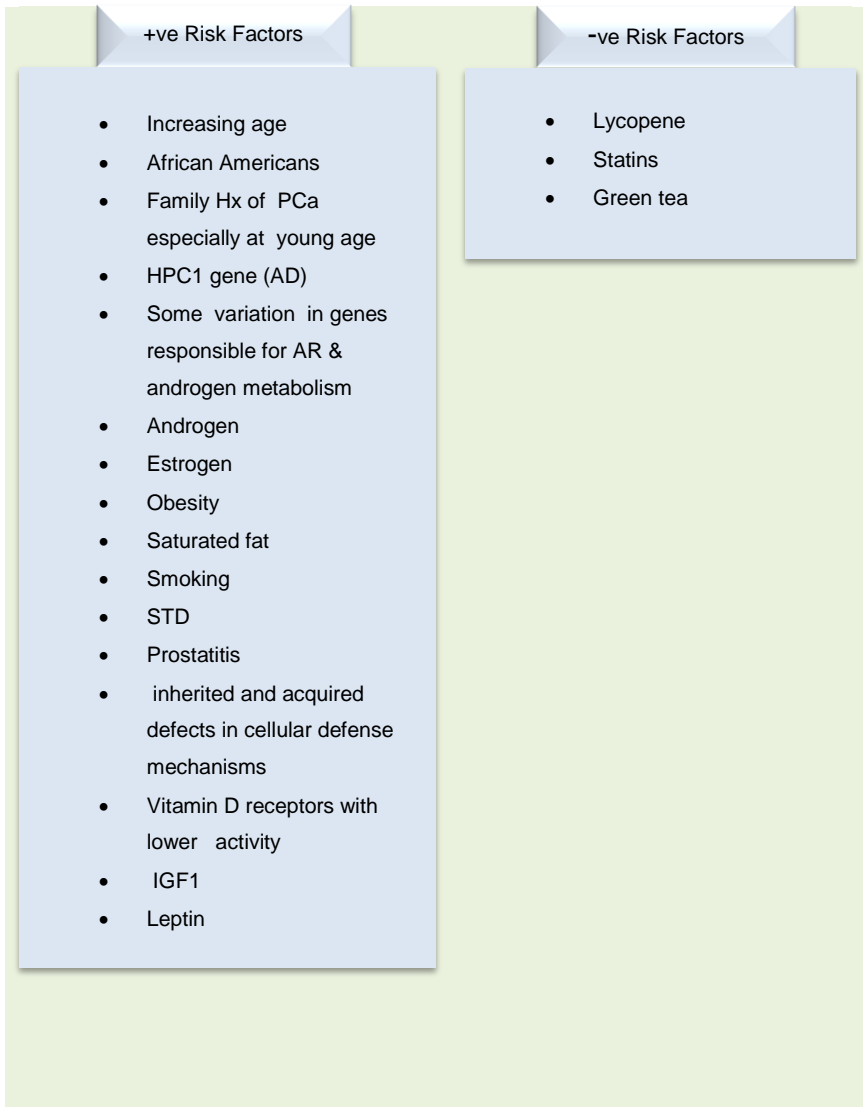
There has been continuing debate regarding the role of PSA testing in the screening and diagnosis of prostate cancer. In fact, different authors and institutes have quite different and even opposing viewpoints on this issue. Reviewing prostate cancer epidemiology would help us to better judge about this subject. Some highlights of prostate cancer screening in this regard have been shown in figure 1.

Figure1 – Prostate cancer statistics, mortality and screening policy



Many factors have been proposed as positive or negative risk factors for prostate cancer^{5, 6}. A summary of some of suggested factors is shown in the figure 2.

Figure2 – Suggested positive and negative risk factors for prostate cancer or high grade tumors or advanced disease



Section 2 Chemoprevention

The high incidence of PCa, its associated high death rate, the complications of its treatment and a partial insight to its biologic basis have led to an interest in chemoprevention strategies. Most studies have been done on 5-alpha reductase (5-AR) inhibitors. SELECT (testing selenium and vitamin E), PCPT (testing finasteride) and REDUCE (testing dutasteride) are 3 landmark trials in this regard⁷⁻²⁶.

SELECT study did show that Vitamin E and Selenium do not prevent prostate cancer.

PCPT and REDUCE trials showed that 5-AR inhibitors were associated with decreased chance of prostate cancer diagnosis. However, high grade prostate cancer rate (Gleason 8–10) increased about 0.5 and 1 percent in REDUCE & PCPT studies respectively. This increase in high grade disease has caused a great deal of controversies in this regard. Some institutes and urologists are pointing to some items that may have biased the studies towards finding more HG-PCa in the 5ARI arms and therefore they consider 5-AR inhibitors for chemoprevention in appropriate candidates. On the other hand, some other organizations have dismissed this approach. To better understand the results of these trials and attitudes of different organizations in this regard, we have summarized them in figures 3-10.

Figure 3- SELECT study main results

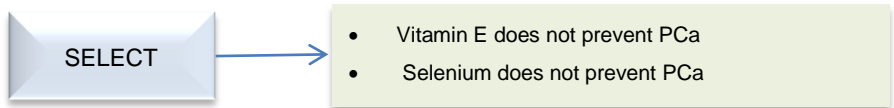


Figure 4- PCPT & REDUCE studies main results

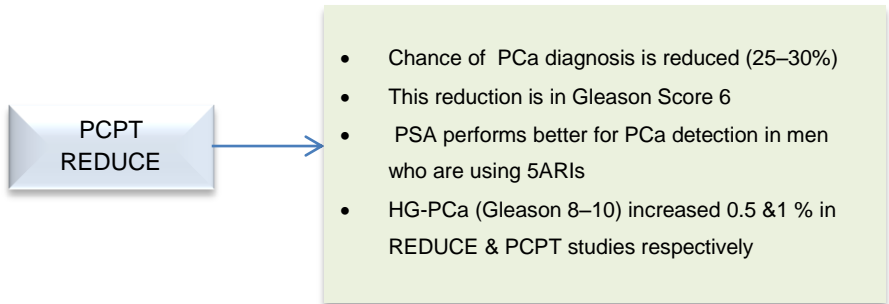
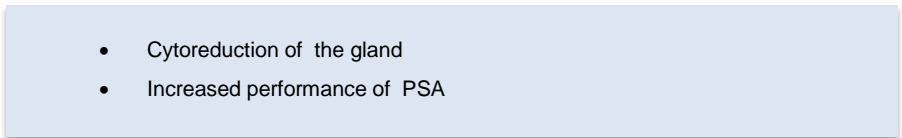


Figure 5 - Items that may have biased the studies towards finding more HG-PCa in the 5ARI arms



It should be emphasized the possibility that, in rare patients, HG-PCa may be induced cannot be dismissed completely.

Figure 6- ASCO-AUA joint recommendation about 5-ARIs position in the prostate cancer chemoprevention (2008)²⁵

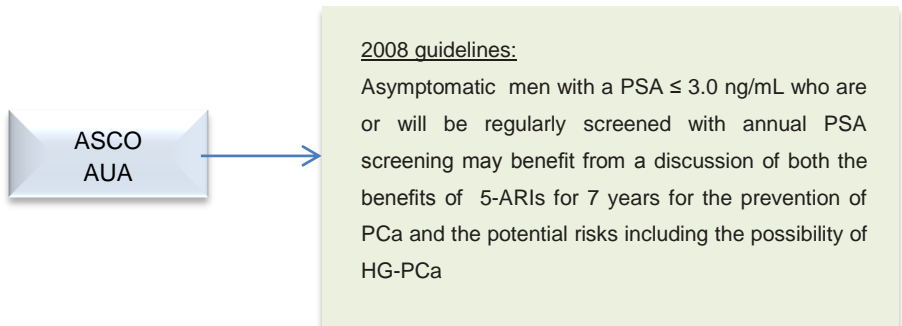


Figure 7– CUA recommendations about 5-ARIs position in chemoprevention²⁶

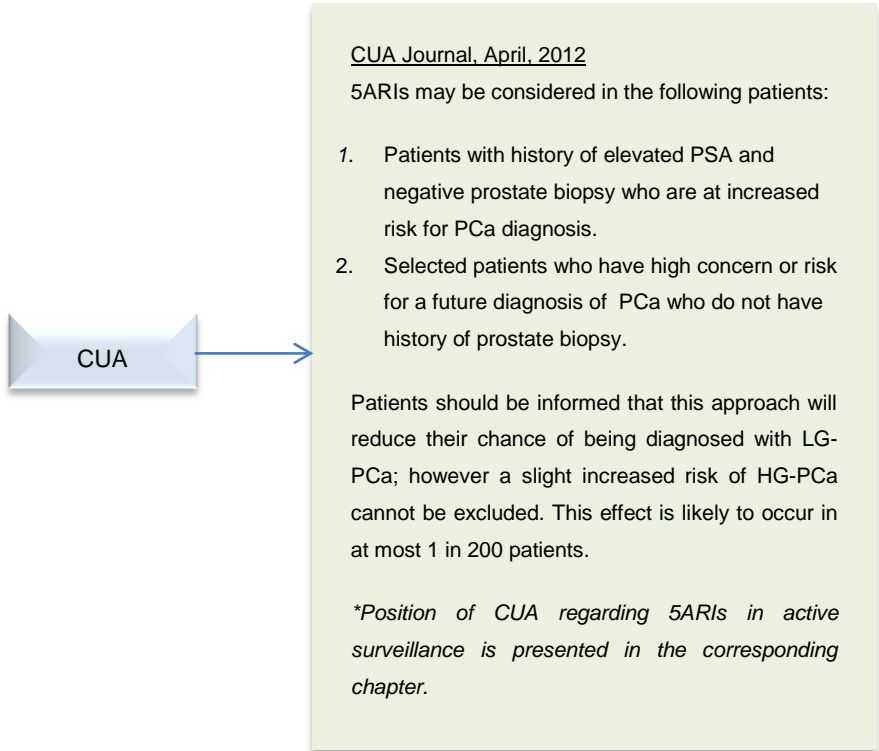


Figure 8 – FDA position regarding 5ARIs in prostate cancer chemoprevention²⁷

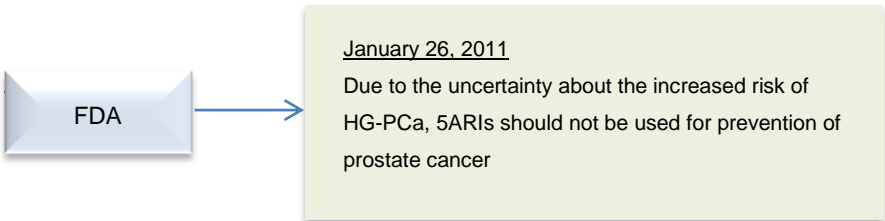


Figure 9- Health Canada position regarding 5ARIs in prostate cancer chemoprevention

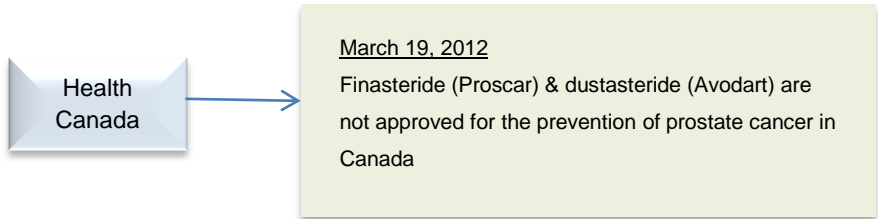


Figure 10- Summary of attitudes of different organizations regarding 5ARIs position in prostate cancer chemoprevention



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