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Response to United States Preventative Services Task Force draft PSA Screening recommendation:

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Cancer Incidence Statistics, 2011

Estimated New Cases*

			Males	Females			
Prostate	240,890	29%			Breast	230,480	30%
Lung & bronchus	115,060	14%			Lung & bronchus	106,070	14%
Colon & rectum	71,850	9%			Colon & rectum	69,360	9%
Urinary bladder	52,020	6%			Uterine corpus	46,470	6%
Melanoma of the skin	40,010	5%			Thyroid	36,550	5%
Kidney & renal pelvis	37,120	5%			Non-Hodgkin lymphoma	30,300	4%
Non-Hodgkin lymphoma	36,060	4%			Melanoma of the skin	30,220	4%
Oral cavity & pharynx	27,710	3%			Kidney & renal pelvis	23,800	3%
Leukemia	25,320	3%			Ovary	21,990	3%
Pancreas	22,050	3%			Pancreas	21,980	3%
All Sites	822,300	100%	All Sites	774,370	100%		

Estimated Deaths

			Males	Females			
Lung & bronchus	85,600	28%			Lung & bronchus	71,340	26%
Prostate	33,720	11%			Breast	39,520	15%
Colon & rectum	25,250	8%			Colon & rectum	24,130	9%
Pancreas	19,360	6%			Pancreas	18,300	7%
Liver & intrahepatic bile duct	13,260	4%			Ovary	15,460	6%
Leukemia	12,740	4%			Non-Hodgkin lymphoma	9,570	4%
Esophagus	11,910	4%			Leukemia	9,040	3%
Urinary bladder	10,670	4%			Uterine Corpus	8,120	3%
Non-Hodgkin lymphoma	9,750	3%			Liver & intrahepatic bile duct	6,330	2%
Kidney & renal pelvis	8,270	3%			Brain & other nervous system	5,670	2%
All Sites	300,430	100%	All Sites	271,520	100%		

Response to United States Preventative Services Task Force draft PSA Screening recommendation:

- Their Basic Study Method:
- Evaluation of published randomized comparative studies:
 - PSA Screen vs. No PSA Screen
 - 5 studies



Response to United States Preventative Services Task Force draft PSA Screening recommendation:

- What they found:
- “The mortality benefits of PSA-based prostate cancer screening through 10 years are small to none, while the harms are moderate to substantial. Therefore, the USPSTF concludes with moderate certainty that PSA-based screening for prostate cancer, as currently utilized and studied in randomized, controlled trials, has no net benefit.”



Response to United States Preventative Services Task Force draft PSA Screening recommendation:

- What they found (continued):
- The USPSTF concludes that there is moderate certainty that harms of PSA-based screening for prostate cancer outweigh the benefits.
- This is a “D” Recommendation
- Significance: Medicare only has to pay for USPSTF “A” and “B” recommendations.
- Many private insurers follow suit



Response to United States Preventative Services Task Force draft PSA Screening recommendation:

- What they found (continued):
- The Task Force did not evaluate the use of the PSA test as part of a diagnostic strategy in men with symptoms that are highly suspicious for prostate cancer. This recommendation also does not consider the use of the PSA test for surveillance after diagnosis and/or treatment of prostate cancer.



Response to United States Preventative Services Task Force draft PSA Screening recommendation:

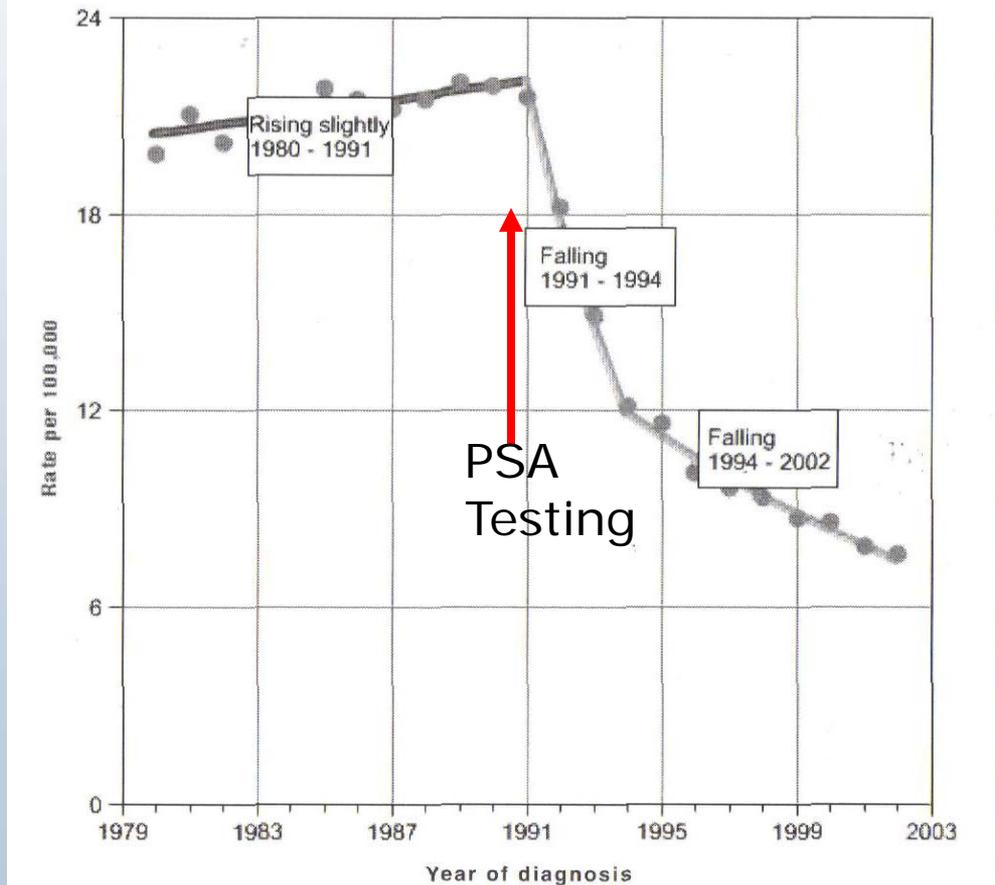
- What they missed:
- The National Cancer Institute SEER (*Surveillance Epidemiology and End Results*) database shows a 75% decrease in metastatic disease at diagnosis during the PSA era
- Concept: Freedom from Castration (i.e. - How many untreated men are still “alive” thanks to Androgen Ablation – an original “male disaster”)



Response to United States Preventative Services Task Force draft PSA Screening recommendation:

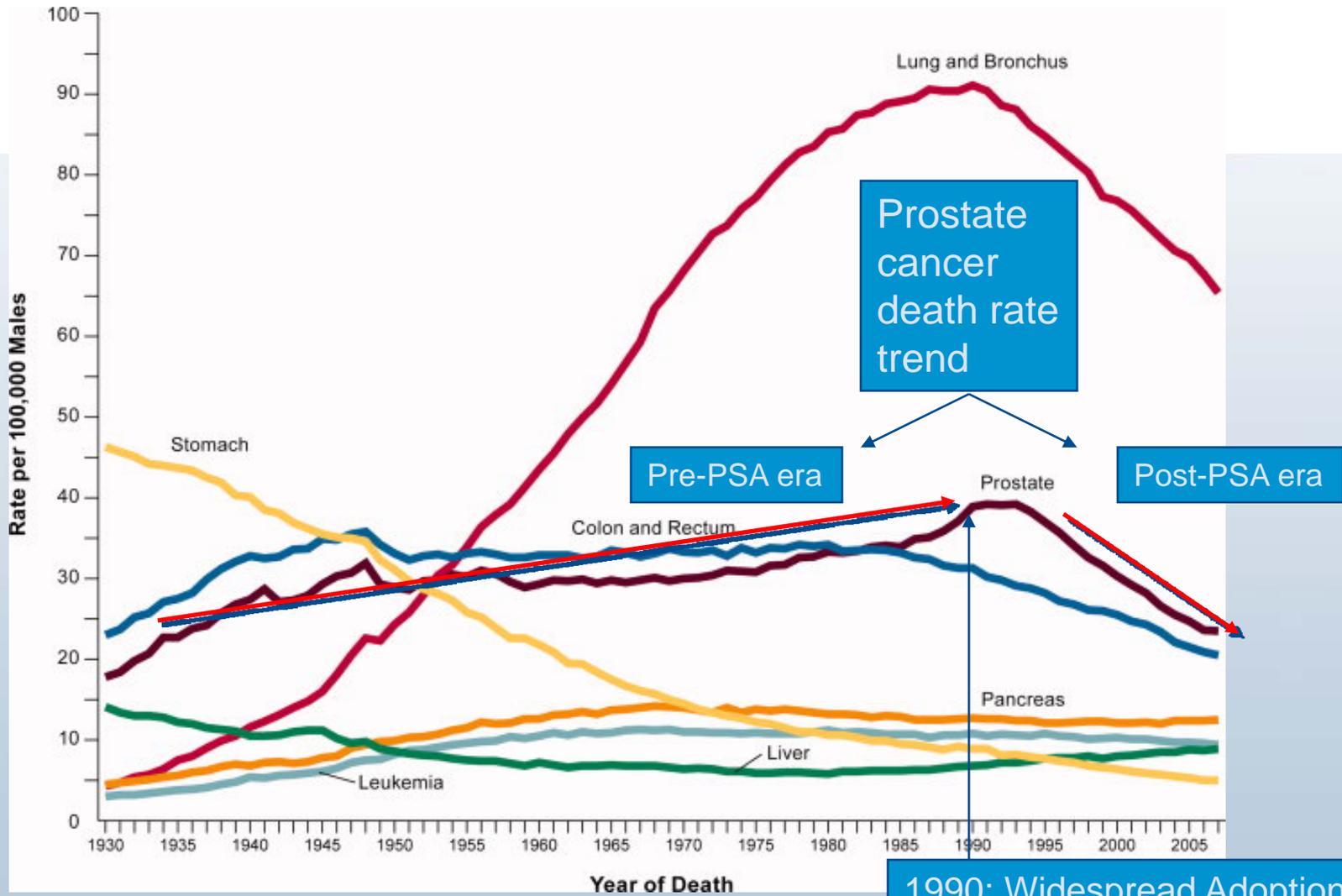
- What they missed (Continued):
- SEER data: 40% decrease in the prostate cancer death rate since 1992
- While the U.S. prostate cancer mortality rate has dropped by nearly half since the advent of PSA screening, this is not discussed or even contemplated in this report . . . Not one word!
 - What is the “Alternate Hypothesis” for this?

Rates of New Cases: Late Stage Prostate Cancer 1988-2002



Catalona: Ramon Guiterez Lecture: AUA 2011

Cancer Death Statistics, 2011

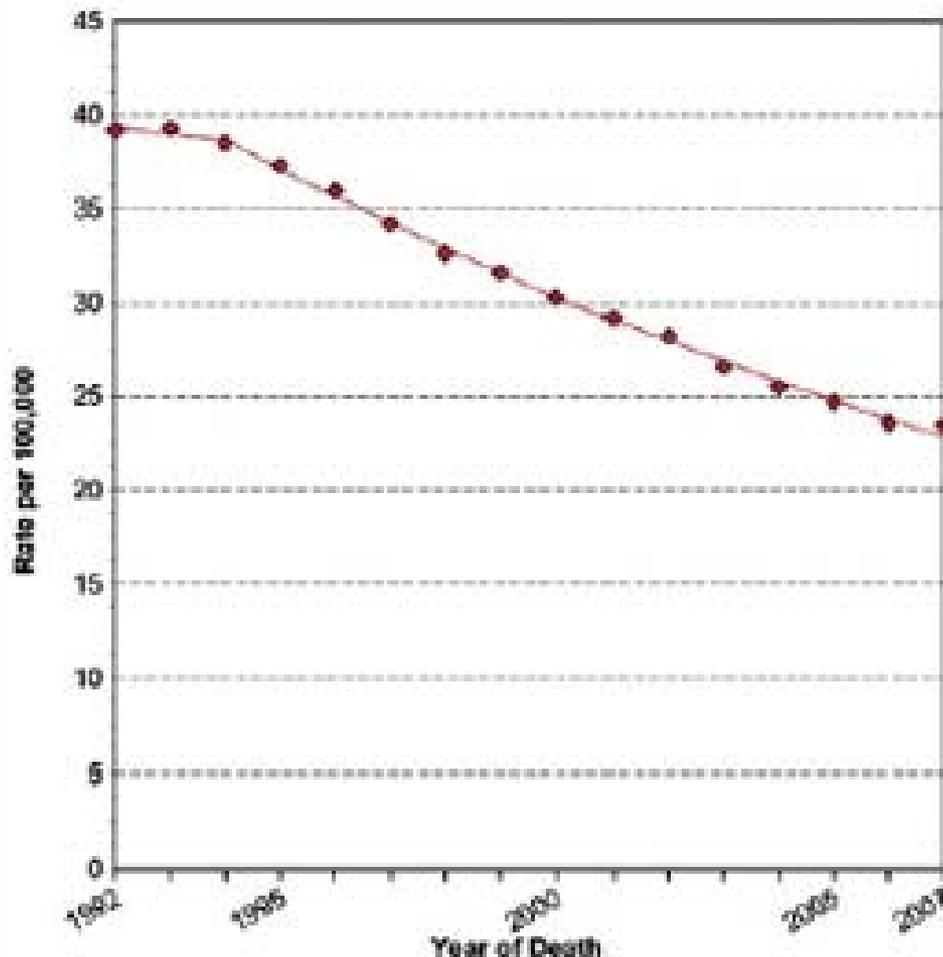


CA: A Cancer Journal for Clinicians
Volume 61, Issue 4, pages 212-236, 17 JUN 2011

1990: Widespread Adoption of PSA-screening

Age-Adjusted US Mortality Rates

17,000 fewer men per year died of prostate cancer in 2007 than in 1992.



- Prostate cancer death rate has decreased by 40% in the PSA era
- Although both surgery and radiotherapy have been refined, no therapeutic breakthrough occurred during this time period
- There is no credible alternative explanation to earlier diagnosis, for the prostate cancer mortality reduction trend that has occurred since 1992



PLCO

(Prostate, Lung, Colorectal, and Ovary Screening Trial)

- 79,693 men/10 centers
- Annual PSA for 6 years, DRE for 4 years
- PSA cutoff = 4 ng/ml
- **No difference in mortality rates**

- Flaws:
 - Short follow-up (7-10 yrs)
 - **50% of controls have PSA done – Contaminated Data base!!**

ERSPC

(European Randomized Screening for Prostate Cancer)

- 182,000 men 50-74yo
- Screening PSA every 4 years PSA cutoff=3ng/ml
- 9 year f/u
- **Screening did reduced cancer deaths by 20%**
 - **Marginal Statistical Survival Benefit**
- Flaws:
 - Short follow-up
 - **20% of controls have PSA done**

N Engl J Med. 2009 Mar 26;360(13):1320-8

GÖTEBORG randomized prostate-cancer screening trial

- 20,000 men 50-64 (median 56=younger)
- PSA every 2 years
- PSA cutoff =3.4 (2.5 ng/ml after 2004)
- 3% PSA in control group
- Sextant biopsies
- F/u= 14 years

- **Strongest Level 1 evidence**
- **44% reduction in Cancer death**
- **THIS study has the smallest screening crossover and the longest median f/u (i.e. – Cleanest study)**

Lancet Oncol. 2010 Aug;11(8):725-32

Conclusion: Screening

- The USPSTF recommendation is based on seriously flawed studies, misinterpreted data, inadequate follow-up and incomplete analysis
- Specific USPSTF Analytical Deficiencies:
 - Contamination of the “control arms” with a high incidence of patient self-selected PSA screening – dilutes any differences – Especially the PLCO trial
 - Short follow-up interval in the majority of their cited studies relative to natural history of prostate cancer (Which is likely 20+ years in the current population)
 - Failure to appropriately recognize the fact that several of their analyzed studies do show a survival benefit to screening, particularly the most rigorous study with the longest follow-up (GÖTEBORG Randomized prostate-cancer Screening Trial)
 - Failure to contemplate or provide any alternate explanation of the reason for the dramatic decline in US prostate cancer deaths during the “PSA era”
 - Although the prostate cancer treatment methods have improved, there has been no “breakthrough” treatment to explain a 40% drop in prostate cancer mortality
 - Failure to contemplate the benefit of reduced metastases and castration – Survival as a sole endpoint completely misses destroyed quality of life due to cancer



Conclusion: Screening

- PSA definitely has a significant false positive rate; often identifying non-malignant conditions such as Benign Prostatic Hypertrophy (BPH) or prostatitis
- However, ALL “screening” tests have a high false (+) rate – The nature of the beast . .
 - CXR
 - EKG
 - Mammogram
 - CT Thorax
- This issue is NOT unique to PSA
- Our basic job, as doctors, regardless of the entity we are screening for, is to sift out the false positives from the true positives as efficiently and as painlessly as possible
- As with all diagnostic tests, proper interpretation will minimize adverse outcomes



Conclusion: Screening

- Several current guidelines, including ACS and AUA, suggest that men with a ≥ 10 -year life expectancy should have an informed discussion of the benefits and risks of PSA screening. If they decide to be screened, a baseline PSA and DRE (**Digital Rectal Exam**) should be performed at age 40 to assess their individual risk.
- If the risk is high, as defined by having a positive family history of prostate cancer, being of African-American race, having a baseline PSA of more than 1.0 ng/mL at age 40, annual screening is indicated (NCCN).
- If the risk is average, repeat screening is recommended at age 45 and then, if the individual risk still appears to be average, annual screening should begin at age 50 (NCCN).

Screening Detected Cancer

- What do we do when screening does detect a prostate cancer?
- Initial decision point: Active Surveillance versus Definitive Treatment
- Active surveillance (AS): May be appropriate for selected low-risk patients (Stage \leq T1c, Gleason score \leq 6, limited biopsy involvement; low PSA and low PSA density).
 - AS management may also be contemplated on a case-by-case basis for moderately more advanced prostate cancer patients, if they have significant other comorbidities. Their risk of clinical disease progression will be higher but this may be partially or completely offset by competing mortality risk.

Screening Detected Cancer

- AS Protocol: AS is a different strategy than “Watchful Waiting”
- AS means detailed initial evaluation of the tumor to rule out the presence of an initially undetected more dangerous lesion, with structured ongoing follow-up to detect progression of the cancer at an early enough point to still effectively treat it, before it passes through the “window of curability.”
- Genesis Healthcare Partners (GHP) has a formal AS protocol for appropriate prostate cancer patients.

Screening Detected Cancer

- Definitive treatment: Is still indicated for patients whose cancer is too advanced for AS protocol - the exception being patients that have active comorbidities or limited additional life expectancy
- Patients DO still die from prostate cancer – This IS preventable
- The precision of our treatments has improved greatly - We can usually prevent this with a reasonable quality of life trade-off

PSA-based Screening and directed treatment: Final Conclusion

- The USPSTF recommendation threatens to return us to the era of advanced and fatal prostate cancer – a change that will take 20 years to evolve, just as it has taken 20 years to decline. Those of us that trained before the “PSA Era” still remember these scores of suffering souls, vividly
 - Hematuria . . Paralysis . . PAIN . . Catheters . . Slow wasting . . Castration
 - USPSTF definition of “benefit” is limited to survival benefit
 - Any reduction in P Ca “suffering and misery” does not meet their definition
- PSA Abandonment = Throwing out the baby with the bath water
- It is best to have an educated and actively engaged patient, rather than to have that individual “managed” by a potentially flawed, group-imposed approach. Use PSA wisely.

PSA-based Screening and directed treatment: Final Conclusion

- Thank You