Prostate Cancer in Africa - Dilemmas in Screening & Prevention

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ESMO Cape Town 2017
Disclosures

- Adcock Ingram
- Allergan
- Astellas
- Astra-Zeneca
- Bayer
- Eli Lilly
- Ferring
- Janssen
- Pfizer
- Sanofi
Prevalence of cancer in males

Percentage incidence of cancer in males.
What’s driving this?

- Higher T-stage and Mortality stage for stage
- Socioeconomic Status
- Choice of Rx
Risk/Protective factors for PCa

- Cooked Tomatoes? Melons!
- Androgen Level, Receptors? CAG repeats!
- Infections? Prostatitis? STIs!
- Sex? Marriage?
- Other causes of Inflammation? Genotype!
  - Oxygen Radicals - Cytochrome P450
  - Single Nucleotide Polymorphism
  - COX-2
The Metabolic Syndrome
Views on the Future of Cancer Care from Bert Vogelstein - 2013

• Vogelstein is a pioneer in cancer genomics and the world’s most cited scientist.

• He is skeptical of scientists who talk about cures. “What we really should first be thinking about is detecting and preventing cancer at a stage when it can be cured by conventional means”.

• “I think 50 years from now, three-quarters of cancer deaths will be gone. That’s a realistic estimate, and I think most of that decrease will come from better prevention and early diagnosis, and the rest will come from better therapies.”
Absorption of PSA into bloodstream and prostatic ducts

- Intermediate segment
- Prostatic gland lumen
- Prostatic epithelium
- Basal cell layer
- Capillary
- Basement membrane

Free PSA
Complexed PSA
α-MG
ACT
PSA testing saves few lives and leads to risky and unnecessary treatments for large numbers of men.

Urology group stops recommending routine PSA test.

Healthy men don’t need PSA testing for prostate cancer, panel says.
Early Diagnosis and Treatment

• **PSA Testing** – does it save lives and what should we be saying?

• **Comparison of screening trials** - PLCO versus ERSPC.
In medicine there are **always** two things that we should **never** say – always and never!

- Does PSA testing save lives? **Yes and no.**
- Can PSA testing do more harm than good? **Yes and no.**
- What is the difference? The viewpoint:
  - **Public Heath** - where the word *PSA screening* refers to populations.
  - **Patient Care** - where the word *PSA testing* refers to individuals.
Economics of PCa Screening in RSA

- History and clinical examination (USD50)
- USS- (USD60)
- PSA- (USD12)
- GDP Health~9% = USD 45 billion
- If screen~ same as for hypertension~ 7,5% of total health budget = USD 3.6 billion!
In medicine there are **always** two things that we should **never** say – always and never!

- Does PSA testing save lives?  
  Yes
The Prostate Cancer Conundrum Revisited

Treatment Changes and Prostate Cancer Mortality Declines

Cancer 2012

Ruth Etzioni, PhD; Roman Gulati, MS; Alex Tsodikov, PhD; Elisabeth M. Wever, MS; David F. Penson, MD; Eveline A. M. Heijnsdijk, PhD; Jeffrey Katcher, BS; Gerrit Draisma, PhD; Eric J. Feuer, PhD; Harry J. de Koning, PhD; and Angela B. Mariotto, PhD
# Impact of PSA Testing on Clinical Stage at Diagnosis

<table>
<thead>
<tr>
<th>Stage</th>
<th>1990</th>
<th>2009</th>
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<tbody>
<tr>
<td>Localized disease</td>
<td>68%</td>
<td>91%</td>
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<tr>
<td>Metastases to bone</td>
<td>21%</td>
<td>4%</td>
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Age-adjusted death rate in US Men

Age-adjusted death rate in US Men

Lung
Nerve-sparing radical prostatectomy
PSA Testing

In medicine there are always two things that we should never say – always and never!

• Does PSA testing save lives?
  Yes and no.
In randomized trials PSA screening has minimal/no effect

- **PLCO** (severely flawed for many reasons) – no effect
- **ERSPC** – 20% reduction in death from prostate cancer but to achieve this positive effect 1000 men must be screened to reduce one death.

- What’s the problem? Both studies are based on mortality at 10 years.
Most men with curable disease who are untreated do not die within 10 years

- Observational study of 223 men with early, low risk prostate cancer –
  - 47% non-palpable,
  - 66% Grade 1 and 15% Grade 2

- Followed expectantly for 30 years without initial treatment. Hormonal therapy administered at progression.
Most men with curable disease who are untreated do not die within 10 years.
Most men with curable disease who are untreated do not die within 10 years. If prostate cancer mortality is used as the end-point, the follow-up must be ≥ 20 years.
• The problem with using mortality as the endpoint.
• How do we balance the possibility of a later life with advanced prostate cancer marked by bone pain, pathologic fractures, and urinary obstruction against the more immediate symptoms of incontinence and impotence that often follow curative treatments.
• In the PLCO and ERSPC, there is no mention nor consideration of the side effects from hormonal therapy, metastases, nor the weakness and inanition that precede death – the only side effects considered were incontinence, impotence and rectal injury.
My approach to PSA testing

• Who should be tested – men with a 10-15 year lifespan who do not want to die from prostate cancer.

• What can we can do to improve screening? (Carlsson et al. J Clin Oncol 2012; 30:2581-84)
  – Avoid screening in men with a limited lifespan
  – Avoid treatment in men who do not need it.
  – Refer men who need treatment to high-volume centers so that the risk of treatment-related complications is reduced.
The Panel does not recommend routine screening in men between ages 40 to 54 years at average risk EXCEPT for men younger than age 55 years at higher risk (e.g. positive family history or African American race)
There is no information for or against testing at this age and for men in their forties, a single baseline PSA measurement is useful in risk stratification.

AUA Guideline - 2013

• The Panel does not recommend routine PSA screening in men over age 70 years or any man with less than a 10 to 15 year life expectancy. Some men over age 70 years who are in excellent health may benefit.

• **The cutoff at age 70 needs to be revisited.**
  
  – 50% of deaths from prostate cancer occur in men who are diagnosed after age 75 (Scosyev et al Cancer 2012;118:3062)

  – 9 years after stopping PSA testing the incidence of potentially lethal cancers equals that of nonscreened men. (Bergdahl et al. Eur Urol 2013; Epub May 8, 2013)
Diagnostic tools for detecting prostate cancer
Full Panel members
- Urologist
- Medical Oncologist
- Radiologist
- Radiotherapist

Additional:
- Neurosurgeon
- General Surgeon
- Thoracic Surgeon
- Pathologist