Establishing a Cohort of African-American Men to Validate a Method for using Serial PSA Measures to Detect Aggressive Prostate Cancers

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Cancer Control Program, Health Disparities Committee, Chicago, 14 May 2016

Presentation Objective

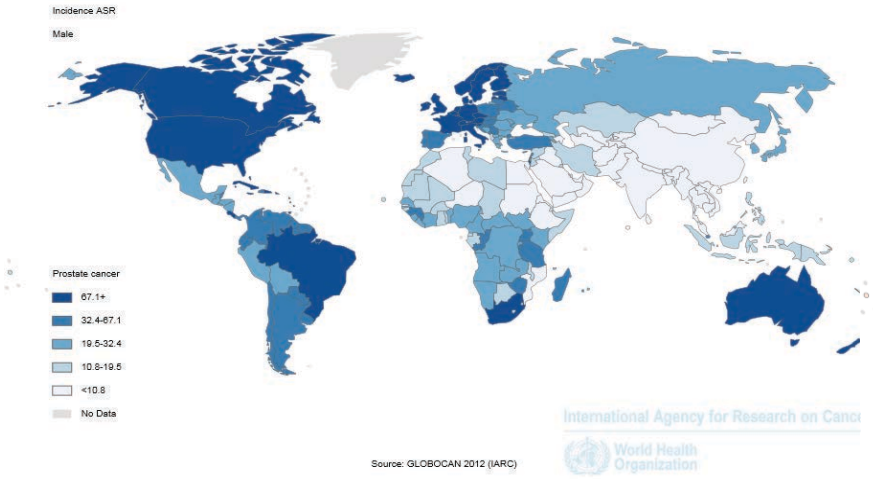
To make the case for establishing this cohort in order to:

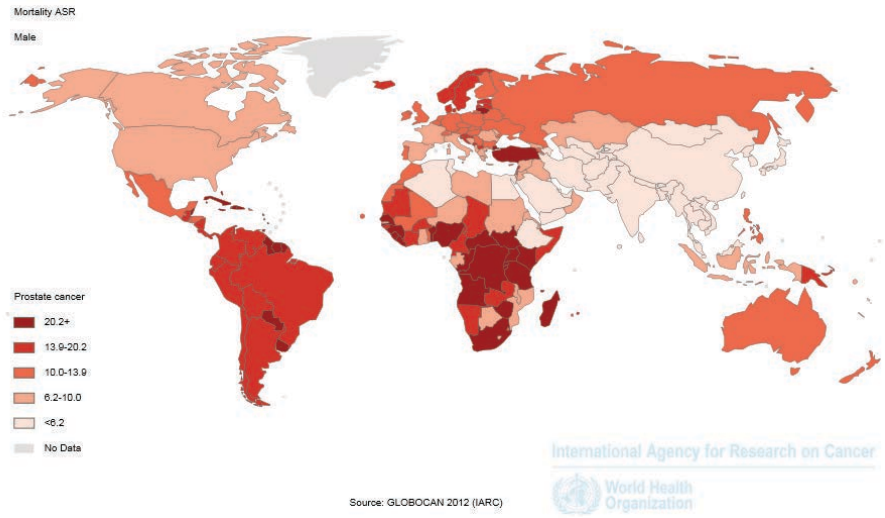
1. **Achieve our Primary Aim and**
2. **Be ready to address other issues relevant to cancer-related health disparities**

Primary Aim

To create a cohort of African-American men who are willing to undergo annual PSA screening with the intention of validating an algorithm that combines multiple PSA measures to detect virulent, high-risk prostate cancer (PrCA).

The discrepancy that we see between the US' highest-world-quintile incidence rates and second-lowest-world-quintile mortality rates …….





….. may be explained, in large part, by the higher incidence of *virulent* disease among African Americans.

PROSTATE CANCER SCREENING AND EARLY DETECTION ISSUES

1. Tension between over-diagnosing indolent cancer and under-diagnosing virulent cancer

- A single PSA greatly limits effectiveness of population-based screening.
- Yet, these data formed the basis on which the US Preventive Services Task Force made its decision to not recommend PSA screening.

PROSTATE CANCER SCREENING AND EARLY DETECTION ISSUES

1. **Over-diagnosing indolent cancer and under-diagnosing virulent cancer**
   - The big Limitation of single PSA based screening.
   - formed the basis on which the US Preventive Services Task Force made its decision to not recommend PSA screening.

2. **Decision-making process is based on evidence derived nearly entirely from European and European-American men**
   - African Americans are much more likely to be diagnosed with later-stage, more virulent disease at younger ages


U.S. Preventive Services TASK FORCE

Prostate Cancer: Screening

Release Date: May 2012

Recommendation Summary

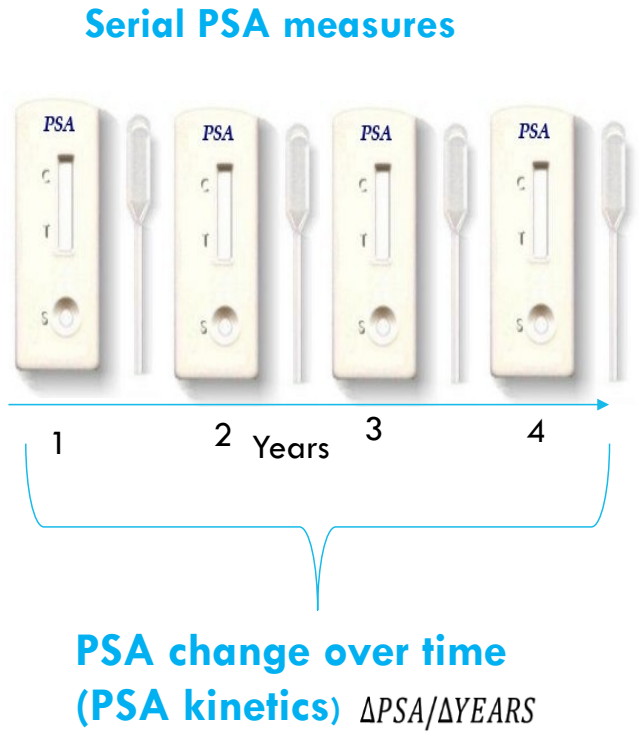
Population	Recommendation	Grade (What's This?)
Men: Screening with PSA	The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer.	D

Table 1. Distribution of baseline demographic and urologic history variables among men in the intervention arm of the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial

Baseline variable	% of category ($N = 38\,350$)*
Race/ethnicity	
White, Non-Hispanic	86.2
Black, Non-Hispanic	4.5
Hispanic	2.1
Asian	4.0
Pacific Islander or American Indian	0.8
Missing	2.4

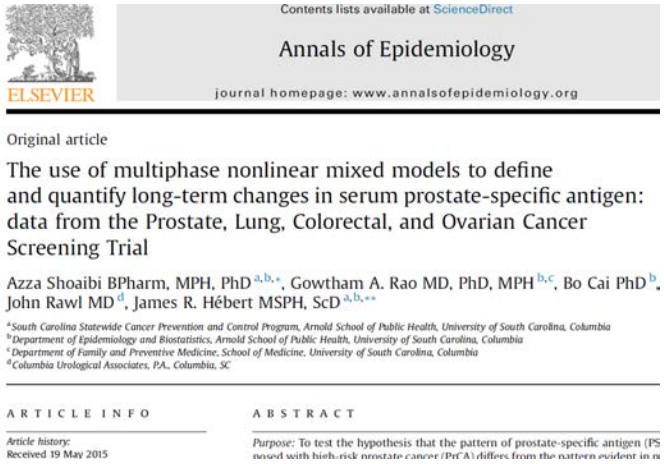
THE USE OF SERIAL PSA MEASUREMENT

- A controversy that refuses to die
- Statistical and computational advances allowed for accurate, comprehensive and flexible method to detect and quantify PSA change over time in magnitude and direction



Investigated Retrospectively in the PLCO Data to answer:

Can PSA change over time (in magnitude and direction) be used to differentiate "high-risk prostate cancer (PrCA)" from any other prostate condition?



Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

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Original article

The use of multiphase nonlinear mixed models to define and quantify long-term changes in serum prostate-specific antigen: data from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial

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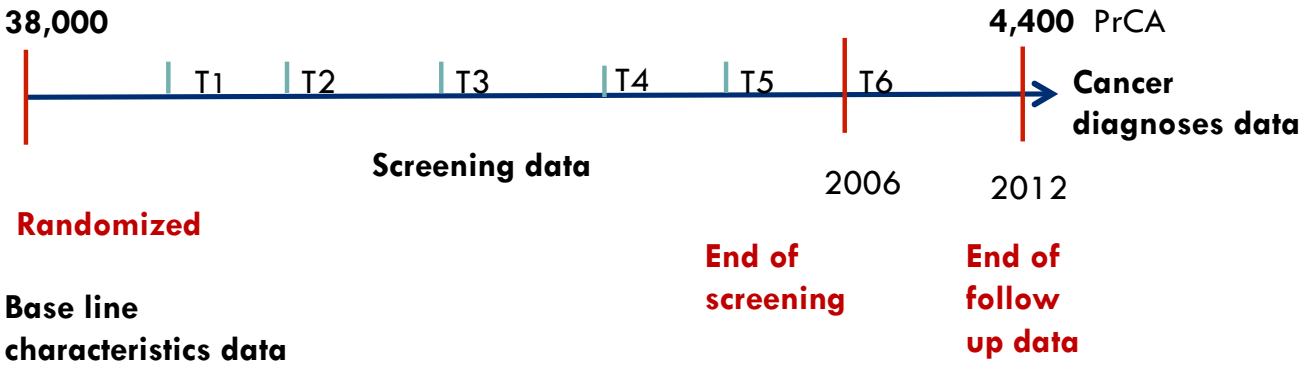
ARTICLE INFO

Article history:
Received 19 May 2015

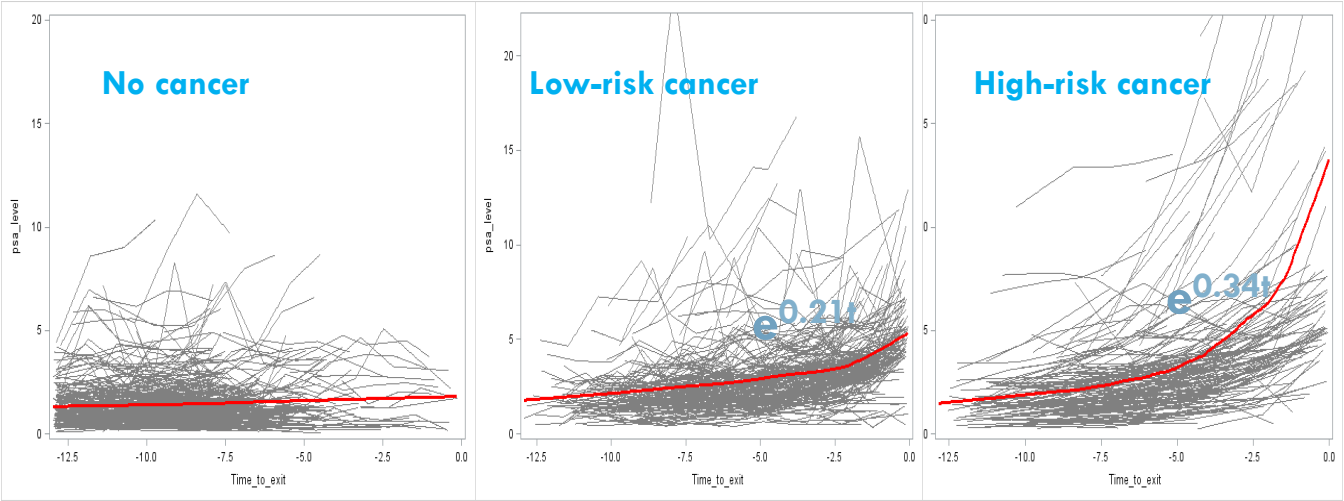
ABSTRACT

Purpose: To test the hypothesis that the pattern of prostate-specific antigen (PS



Median follow-up time: 12.4 years

We Developed a New PSA Growth Curve Algorithm

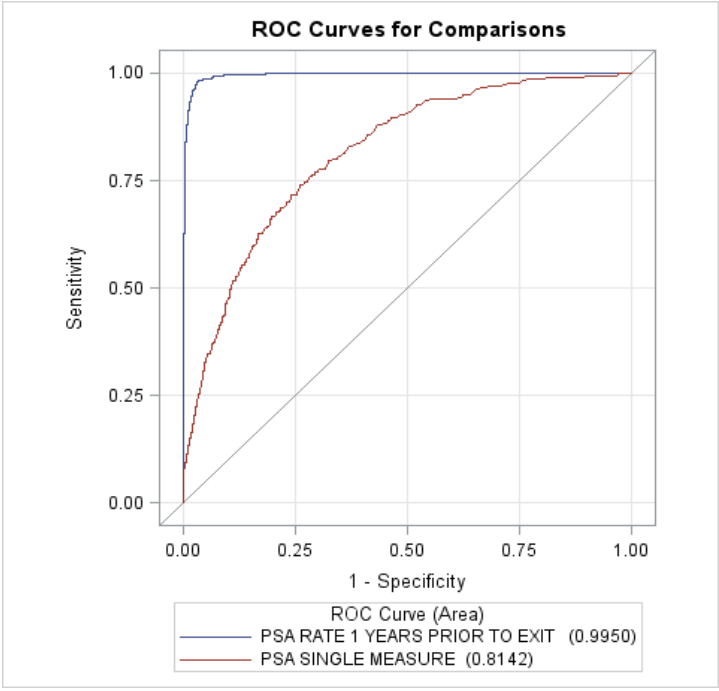


Longitudinal trajectories of PSA for all PLCO participants: PSA Growth Curve

RETROSPECTIVE “PREDICTABILITY”

Measurements of test performance for the prediction of high-risk prostate cancer by selected annual PSA rate thresholds

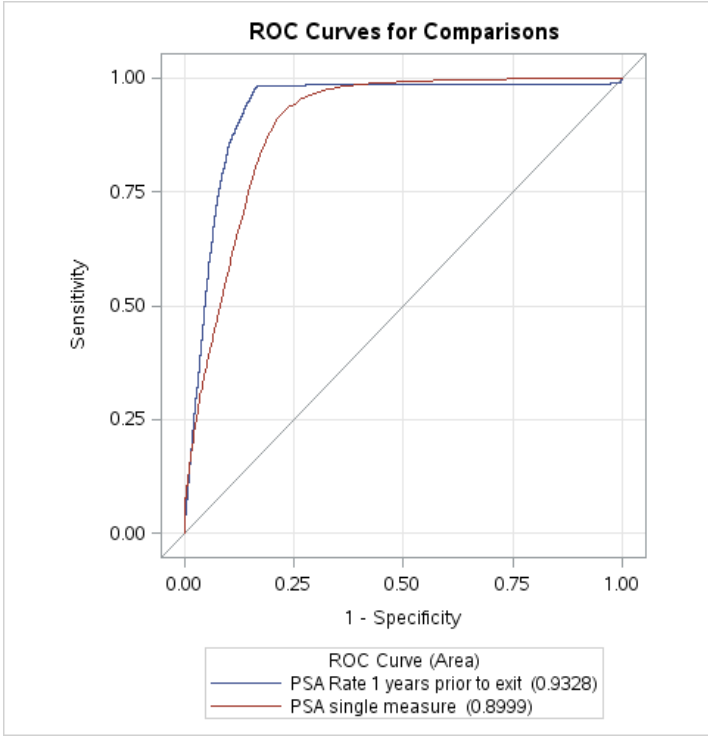
PSA rate cut off point (ng/ml/year)	Sensitivity	Specificity
All participants		
0.10	99.7%	90.9%
0.29	98.1%	96.7%
0.37	**97.2%**	**97.3%**
African Americans		
0.22	100.0%	97.8%
1.20	95.0%	99.8%



Retrospective “Predictability” in the VA (Validation Set)

- **Using the <u>VA Electronic Medical Data</u>**

	PSA rate cut off point (ng/ml/ year)	Sensitivity	Specificity
African American	1.20	89.0%	80%
	0.99	89.1%	80.0%
Non-African Americans	0.37	95.5%	86.7%
	0.80	90%	89.3%



Prospective Cohort is Needed to Confirm/ Refine Results from the PLCO, which had Very Limited (<4%) AA participation, and to overcome Deficiencies of the VA.

The goal would be to create a cohort of 48,000 African-American Men who would be willing to submit to annual PSA testing: 6 measurements.

The Primary Aim would be to test and validate PSA growth curve for screening purposes but can (and probably should) include other important secondary aims.

DESIGN CONSIDERATIONS

- Simple multicenter follow-up study design with extensive baseline data collection and follow-up data collected at regular (i.e., annual) intervals.
- Geographical consideration: African-American communities around the country
- Community based approach: Require strong community buy-in, commitment to providing information needed for informed decision-making, formulating rules for referring men out for diagnostic workup, and putting procedures in place for data linkage (e.g., to the cancer registries).

ONE PROPOSED SETTING

The VA system might be an ideal setting:

1. They already have the screening infrastructure in place
2. There isn't the financial incentive to over-diagnose and over-treat (though that may be less of a problem with healthcare reform under the ACA)
3. There is an excellent system of electronic medical records
4. There are many African-American veterans in the VA system (i.e., 40% of the total)
5. The medical home (for subsequent care) already is in place.

ANOTHER PROPOSED SETTING;

1. NCORP appears to understand the CBPR imperative
2. As such, they have good access to local, interested communities and in some regions of the country this includes large AA populations
3. Local “connectivity” could ensure a competent, caring ‘medical home
4. There could be good overlap with the VA
5. Could add an important element of academic medicine/ NCI imprimatur to the mix

IMPACT

- The Despite the general indolence of PrCA, AA are at relatively high risk of being diagnosed with a deadly, aggressive PrCA.
- Detecting aggressive disease represents a significant public health issue and unmet clinical need.
- This would be the first AA [male] national cohort that is specific for Prostate cancer and urology outcomes (but it also could be used for many other purposes
- An excellent way to engage African-American men who would otherwise not participate in research that could be of direct benefit to the wider community.

FURTHER DISCUSSION

- Definition of high-risk Prostate Cancer
- Enrolment (e.g., waves) strategy
- Eligibility criteria
- Family history matching
- Biopsy referral rules
- Follow-up time
- Follow-up mechanisms
- Cost estimations $$$