

Ideas for the Prostate Cancer Study Committee (PCSC)
Submitted by: Ron Gimbel, PhD – Professor & Director, Clemson Rural Health

Background: The SC Prostate Cancer Study Committee (PCSC) held its first meeting at the Gressette Building on November 29, 2023. During the meeting, the committee reviewed a written document submitted by the MUSC Hollings Cancer Center that addresses key points related to objectives of the first meeting. The document specifically related to a statistical “snapshot” of prostate cancer in SC, current awareness of men on the condition, and treatment options available. Legislators, clinicians, and other members contributed to discussion that followed. Department of Health and Environmental Control (DHEC) data, state summary and by county on incidence and mortality, were also presented and discussed. On November 30th, USC Professor James Hébert provided a detailed summary of his view of the problem facing the PCSC and recommended next steps toward targeting virulent prostate cancer.

What these comments add to the discussion: The text below contributes to the education and awareness of prostate cancer piece (focal point 3 in proviso), potential pilot project approaches for reducing PrCA mortality in counties with poor outcomes, a review of biomarkers and innovation, and a few comments on a necessary continuum of care for PrCA patients (focal point 2 in proviso).

Education and awareness about prostate cancer:

Increasing awareness of PrCA, the importance of screening in high-risk individuals, and related education requires targeted messaging and dissemination efforts that span from the individual to communities. The messaging should be tailored to the intended audiences and employ the best of what is known in dissemination science. For some audiences, educational materials and decision support tools will need to be developed or adapted (based on work of others). For health professionals the messaging and potential decision support may be extensive and will need to be grounded in evidence. For others, a general awareness and emotional appeal may be the optimal strategy.

Messaging and education of PrCA and importance of PrCA screening to high-risk men:

Professor Hébert has delivered compelling ideas on targeting screening of virulent prostate cancer in high-risk men. Should the PCSC and the legislature agree, a primary group for messaging and education about PrCA and screening would be the high-risk men. Hope at effectively communicating to this key stakeholder group would require very strategic and targeted messaging. A “general education” approach to messaging that would translate into action would take years, if not longer, to generate substantial interest. PrCA and PrCA screening is complicated and would require addressing the documented fears and uncertainty men have on PrCA and screening. In research on PrCA screening and surveillance, some identified themes that have surfaced include ***Social prompting*** (trusting professional opinion, motivation from family and friends, proximity and prominence of cancer); ***gaining decisional confidence*** (overcoming fears, survival imperative, peace of mind, mental preparation, prioritizing wellbeing); ***preserving masculinity*** (bodily invasion, losing sexuality, threatening manhood, medical avoidance); ***avoiding the unknown and uncertainties*** (taboo of cancer-related death, lacking tangible cause, physiological and costs.¹

Messaging and education of PrCA and importance of PrCA screening to women:

While perhaps not immediately intuitive, evidence suggests that women are information-seekers and can disseminate information to men and facilitate their efforts to make more informed decisions about prostate cancer screening. With respect to men, women have demonstrated their ability to recognize early cancer signs, and it is, therefore, relevant to include women in strategies to improve the early detection of PrCA.²⁻⁴ Furthermore, spouses and significant others in relationships have influenced men to pursue PrCA screening through encouragement and persistent “nagging”¹. With respect to early stage cancer diagnosis, a systematic review has uncovered a positive effect of being married to early stage cancer diagnosis as compared to unmarried men.⁵ For this stakeholder group, it is likely that messaging should be more strategically focused / targeted than general in nature.

Messaging and education of PrCA to health professionals:

Health professionals, including primary care providers operating in rural and underserved communities, have struggled with conversations about PrCA. These struggles have been fueled by the controversies surrounding the use of PSA tests⁶ and provider uncertainty about the true cost-benefit of PSA screening. Family practice physicians have reported patient interest in the discussion about screening often based on the patient’s exposure to advocacy messaging/news prompt or personal relationship with an individual diagnosed with PrCA.⁶ In some health professional setting, PSA conversations happen without the benefit of infographics or decision aids to support the conversation.⁶ There currently exists clinical guideline-driven decision aids and tools to help educate the health professionals on latest approaches to screening as well as specific practice points aimed at assisting the provider.⁷ Additionally, most health care organizations deploy a electronic health record (e.g., Epic, Cerner) that is used in clinical practice and can be designed to promote cancer screening recommendations based on specific criteria and best evidence. Messaging and the education of health professionals is often delivered via continuing medical education or continuing education seminars (in-person, virtual) and other platforms designed to help maintain and enhance clinical skill. Efforts to expand PrCA testing in primary care should optimally consider providing health provider education or training with useful decision tools to aid in discussions with patients.

Messaging and education of PrCA to communities:

Evidence suggests that community education can improve the PrCA knowledge of African American men.⁴ Successful models of community education in PrCA have addressed barriers specific communities face in accessibility of screening, the screening and diagnostic process, and treatment.⁴ Research has demonstrated that the methods by which patients prefer to receive education varies, and by using preferred methods and format improves participant knowledge.⁴ Effectiveness of PrCA education programming has been dependent on the presenter. Community leaders / stakeholders are key to helping identify individuals credible to engage high-risk men in such sessions. Prostate cancer survivors have been deemed credible presenters and preferable to health care providers.⁴

Another strategy to promote PrCA awareness and education has been the engagement of barbershops in rural African American communities. Rural barbers have been receptive to the addressing PrCA with their customers. The barbershops represent feasible venues for delivering

PrCA education to high-risk men.⁸ As with other cancer, diabetes, and chronic diseases and conditions, churches and pastors in rural African American communities are yet another key stakeholder in delivering messaging and education on PrCA.

Use of virtual PrCA decision tools to convey education:

While some African American men have voiced preference in interpersonal engagement in lieu of watching prepared educational videos related to PrCA screening and PrCA more generally⁸, several systematic reviews have documented the utility of leveraging mobile health (mHealth), web-based, social media, and other virtual modalities to deliver PrCA messaging and education.^{9,10} A key principle of success in deploying PrCA (and other cancer) education via virtual modalities has been a multimodal publicity effort prior to the introduction of the material.¹¹ There are commercially available mobile phone applications for PrCA education. One study comparatively reviewed 14 of these applications and found serious deficits. For example, none of the apps fully embraced the American Cancer Society’s Prostate Cancer Prevention and Early Detection Guideline, only half had content consistent with topics inclusive with the guideline, and only 4 (about 29%) were culturally sensitive to African Americans.¹¹ Despite mixed results, mHealth and social medical approaches for promotion of PrCA screening and education of PrCA appear to be growing in number and typically do increase testing.^{9,10,12}

Dissemination science frameworks to guide and evaluate education and awareness of PrCA:

Dissemination and implementation science intends to bridge the gap between research, practice, and policy by building a knowledge base about how health information, effective interventions, and new clinical practices, guidelines, and policies are communicated and integrated for public health and health care service use in specific settings. *Dissemination* is the targeted distribution of information and intervention materials to a specific public health or clinical practice audience. The intent is to spread knowledge and the associated evidence-based interventions.¹³ Wide adoption of evidence-based, health promotion practices depend on developing and testing effective dissemination approaches.¹⁴ There are numerous published dissemination science frameworks to shape both messaging and evaluation of that messaging. There are classic approaches, outlined in *Health Behavior and Health Education: Theory, Research, and Practice*, 4th 15th edition as well as contemporary approaches often with delivery facilitated in digital/electronic spaces.¹⁶

Pilot project ideas:

Beyond promoting messaging and education about PrCA in high-risk men, the PCSC may want to consider the idea of developing, implementing, and evaluating pilot studies aimed at enhancing PrCA annual screening/surveillance to identify early-stage diagnosis and treatment that will ultimately lead to reduced PrCA mortality. Two options in how to do this are offered below. One option is to focus pilot projects on increasing screening and coordination of treatment in PrCA, with the focus exclusively on PrCA. An alternative option would be to not focus pilot projects on PrCA, but rather in a cluster of screenings related to “men’s health”. The potential “pros” and “cons” of each are offered.

Pilot project options:

I. Regional pilot projects aimed at increasing testing and reducing prostate cancer (PrCA) mortality among high-risk men:

An approach to reducing PrCA mortality in high-risk individuals would be to conduct pilot projects delivered in counties for which high-risk men reside. The pilot projects would generate substantial evidence on what works, optimal strategies for dissemination and implementation of annual screening and follow-up and expand understanding of cost for a continuum of care from prevention, screening, treatment, survivorship, and annual screening/surveillance. Strategies to determine location and pilot project leadership are identified below.

As with option II below, a thoughtful approach to annual PrCA screening in pilot project counties is critically important. In addition to understanding the messaging (above) and how to roll-out annual screening processes, follow-up for positive findings must be mapped and support harnessed. This includes, but is not limited to, access to urology clinics for follow-up screening, diagnosis, and treatment. For men with health insurance, the majority of costs should be covered by the health insurance plan. This is not the case for men living without health insurance. A comprehensive process that incorporates men with and without health insurance will need to be created, implemented, and retained.

Any pilot project that targets high-risk men, especially from any given race/ethnicity, should not be exclusive (omitting other men who could be living with PrCA) but inclusive of all men in a geographic region who meet screening criteria. This being said, one way to ensure representation of younger African American men might be to consider the proportion of these men residing within a given county when determining where to start. Stated differently, a commitment to conduct pilot projects where the total percentage of African American residents is higher.

Potential pro's of PrCA pilot projects:

- Will attract high-risk men into annual PrCA screening which would heighten the number of earlier stage PrCA diagnoses and reduce the number/percentage of late stage diagnoses;
- An exclusive focus on PrCA mortality reduction and active annual PrCA screening program is consistent with the PCSC mission as identified in the initial legislative proviso;
- Implementation of PrCA screening could be delivered at multiple settings (fixed clinics, mobile health units, churches, workplace settings) targeting rural and underserved communities with poor health outcomes.

Potential con's of PrCA pilot projects:

- High-risk men for PrCA annual screening would be the focus, but as men are traditionally reluctant to seek primary health care, out pilot projects may miss the mark on early detection of other diseases/conditions that could have been identified with a more comprehensive men's health approach (described below); and
- While the cost of the proposed PrCA annual screening would be covered for the majority of men with health insurance, the cost for uninsured and underinsured men would need to be considered through some other mechanism to ensure their participation.

II. *Alternative approach – regional pilot projects aimed at reducing premature mortality from PrCA and other diseases and conditions within a new framework of men’s health:*

An alternative approach to reducing PrCA mortality in high-risk individuals, reducing racial and ethnic mortality rate disparities for cancers, chronic disease, other conditions, and improving the overall health of men in SC might be to bundle PrCA screening under a larger targeted program on “Men’s Health”. This in lieu of targeted regional pilot projects aimed exclusively at PrCA.

Primary care clinicians and outreach teams often observe a larger proportion of women seeking health care services than men. While many women pursue annual women’s health screenings, perhaps influenced by federal funding for cancer and cardiovascular screening of low-income women, men are less likely to seek preventive care (to include cancer screening).

An alternative approach is to design a robust annual screening program on men’s health that can address not only PrCA but also other conditions and diseases most likely to result in the premature death of men. A bundled men’s health screening could include:

- cancer screening (prostate, colon, lung*) per protocol,
- blood pressure measurement,
- weight/height/BMI measurement,
- lipid panel,
- depression screening, and
- assessment of high-risk behaviors (e.g., alcohol use, smoking status, poor eating behaviors).

While in high-risk individuals some cancer screening may require annual laboratory testing (e.g., PrCA), in others like lung cancer screening, via low dose CT scan, eligibility is determined by pre-defined smoking history and other factors, not applicable to all men. The evidence to support active colon cancer screening for early detection is strong and several options exist for testing (e.g., Cologuard, colonoscopy) that are typically covered by insurance.

Measuring blood pressure is a fundamental process in clinical workflow as is weight/height. The lipid panel is a relatively inexpensive blood test and depression screening, and assessment of high-risk behaviors is completed via surveys. The screening process can be streamlined, with effective and efficient clinical workflow, into a single 30–45-minute visit annually. This sort of men’s health screening could be delivered via current primary health care settings (e.g., rural health clinics, FQHCs, other) and alternative settings (e.g., mobile health units, workplace).

Potential pro’s of a men’s health bundle:

- Will attract men into annual health screening;
- No need to create extensive cancer specific PrCA messaging as this would be a component of annual men’s health package;
- In addition to PrCA, health professionals would identify high-risk men for heart disease, diabetes, hypertension, depression, and other major “killers” of men; and
- Implementation of men’s health screening could be delivered at multiple settings (fixed clinics, mobile health units, churches, workplace settings) targeting rural and underserved communities with poor health outcomes.

Potential con's of a men's health bundle:

- High-risk men for PrCA annual screening would be a focus, but not the exclusive focus of the annual men's health screening process. It is possible that the attention on PrCA could be minimized as hypertension and hyperlipidemia (high cholesterol) testing results may yield need for immediate action; and
- While the cost of the proposed men's health screening bundle would be covered for the majority of men with health insurance, the cost for uninsured and underinsured would need to be covered through some other mechanism to ensure their participation.

Identifying counties for pilot projects (Option I or II):

Should the PCSC and the legislature support the concept of conducting pilot projects on option I or II above, or some other variant, a strategy to measure the impact on both rural and underserved populations would be to carefully select sites that would represent target high-risk men. Several variables should be considered in the selection. Such variables might include:

- **Region** – perhaps selecting one county for each of the four regions of the state;
- **Rural/Urban** – while the majority of pilot project locations should reflect the rural nature of the state, at least one project should be anchored in an urban county with underserved residents;
- **PrCA mortality rate** – the mortality rate should be a consideration with the selected project locations being allocated in at least the worst half of the SC counties;
- **PrCA mortality count** – the projects should be located within counties with a prostate cancer mortality count each year that might help the PCSC identify improvement; perhaps a minimum of 40. This is important to be able to reflect an observed change in mortality over time and acquire realistic expectation of project impact; and
- **% of men who are African American** – being an African American male is a variable that contributes to likelihood of contracting virulent prostate cancer.
- **Other** - TBD

Considering the above criteria, the following pilot project locations may be appropriate.

<i>Low Country Region:</i>	Orangeburg, Berkeley, or Colleton County
<i>Pee Dee Region:</i>	Williamsburg, Sumter, or Florence County
<i>Midlands Region:</i>	Aiken, Kershaw, or Richland County
<i>Upstate Region:</i>	Greenwood, Spartanburg, or Laurens County

Regional pilot project leadership and expectations:

Should the regional pilot project concept be adopted and funded, implementation will require a state-wide leader/oversight group and a coordinating team at the region/county level. The coordinating teams should have a designated leader and be populated by health professionals and other key stakeholders. As the regional pilot projects take hold, a likely outcome will be an increasing number of PrCA annual screenings delivered (and other screening if option II is selected). With a substantial increase in PrCA testing, the incidence of PrCA will likely increase and over time represent earlier-stage diagnosis of the cancer. Within several years, as early-stage cancer is detected and treated, the PrCA mortality rate and count should decrease in pilot counties and lessons learned.

Precision medicine and the introduction of various biomarkers and other innovation that will guide future PrCA screening, diagnosis and treatment.

The PSA test lacks specificity and results in inconclusive findings which leads to over treatment of biopsies and/or digital rectum exams (DREs). These next lines of screening can be invasive and expensive.¹⁷ Current research is focused on how to better detect PrCA in individuals using additional biomarkers and technology either with the PSA test or replace it all together.

The ExoDx Prostate(IntelliScore) (EPI) test is an example of a screening tool used with an inconclusive PSA test. EPI test is a urine exosome gene expression assay. EPI is a less invasive and more affordable secondary PrCA screening that can prevent unwarranted biopsies and DREs.¹⁸

The 4KScore test was approved by the FDA in December 2021. This test is another innovative assay that screens four biomarkers in the blood following an inconclusive PSA test. Results from the assay are calculated and are intended to be read with the patient's medical history/risk, clinical examinations and/or other findings.¹⁹ This unique approach makes the results more individualized and can better guide health care providers' and patients' decision-making for treatment options.

Recent research has found numerous PrCA biomarkers that can be detected via liquid (i.e. plasma, urine, serum, etc.) biopsies. The number and complexity of these biomarkers make it difficult to detect and treat PrCA accurately and consistently. Further research to understand these biomarkers will provide insight into how individuals may be diagnosed and treated with PrCA.²⁰

Continuum of care in prostate cancer (prevention, screening & diagnosis, treatment, survivorship, monitoring)

Messaging and education campaigns, pilot projects, and other initiatives to improve PrCA testing and early detection of PrCA will ultimately improve access to care, improve health outcomes, and reduce inequities. However, to sustain any gains over time and dramatically improve outcomes will require a continuum of care. This is especially challenging to do in rural and underserved communities where health professionals are not represented, counties lack essential health infrastructure (including hospitals), social determinant barriers are real, and mistrust is somewhat a norm. Thoughtful consideration and collaboration of key county-level and regional stakeholders is a must. While PrCA screening can happen in a variety of settings, there must be primary care and specialty care (urology) to follow-up with patients who present elevated PSA levels and/or abnormal DREs. When warranted, patients need access to biopsy for conclusive determination, and for some follow-on treatment. Following PrCA treatment, patients should be offered survivorship program and annual monitoring/testing to ensure the cancer has not returned. While some of the continuum support needs to be “brick and mortar” within the county, much the continuum can be delivered by telehealth or mobile health units to ensure access and reduce cost. With the good will of health professional organizations and community leaders, continuum of care support can be a reality and will optimize health outcomes for the individual, the community, and the state.

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Works Cited:

1. James LJ, Wong G, Craig JC, et al. Men's perspectives of prostate cancer screening: A systematic review of qualitative studies. *PLoS One*. 2017;12(11):e0188258.
2. Allen JD, Akinyemi, I.C., Reich, A., Fleary, S., Tendulkar, S., Lamour, N. African American women's involvement in promoting informed decision-making for prostate cancer screening among their partners/spouses. *Amer J Men's Health*. 2018;12(4):884-893.
3. Wiafe E, Mensah KB, Mensah ABB, Bangalee V, Oosthuizen F. Knowledge of prostate cancer presentation, etiology, and screening practices among women: a mixed-methods systematic review. *Sys Rev*. 2021(10):138.
4. Carthon B, Sibold HC, Blee S, D. Pentz R. Prostate cancer: Community education and disparities in diagnostics and treatment. *The Oncologist*. 2021;26(7):537-548.
5. Buja A, Lago L, Lago S, Vinelli A, Zanardo C, V. B. Marital status and stage of cancer at diagnosis: A systematic review. *Eur J Cancer Care (Engl)*. 2018;27(1):2755.
6. Driedger SM, Kirby S, Maier R, et al. Strategies used in managing conversations about prostate-specific antigen (PSA) testing among family physicians (FPs): a qualitative study. *BMJ Open*. 2023;13(4):e073415.
7. Carlsson SV, Vickers AJ. Screening for Prostate Cancer. *Medical Clinics of North America*. 2020;104(6):1051-1062.
8. Luque JS, Roy S, Tarasenko YN, Ross L, Johnson J, Gwede CK. Feasibility study of engaging barbershops for prostate cancer education in rural African American communities. *J Cancer Educ*. 2015;30(4).
9. Schliemann D, Tan M, Hoe W, et al. mHealth Interventions to Improve Cancer Screening and Early Detection: Scoping Review of Reviews. *J Med Internet Res* 2022;24(8):e36316.
10. Ruco A, Dossa F, Tinmouth J, et al. Social Media and mHealth Technology for Cancer Screening: Systematic Review and Meta-analysis. *J Med Internet Res* 2021;23(7):e26759.
11. Moghul M, Cazzaniga W, Croft F, Kinsella N, Cahill D, James ND. Mobile Health Solutions for Prostate Cancer Diagnostics—A Systematic Review. *Clin Pract*. 2023;13:863-872.
12. Loeb S, Katz MS, Langford A, Byrne N, Ciprut S. Prostate cancer and social media. *Nature Reviews Urology*. 2018;15(7):422-429.
13. Glasgow RE, Vinson C, Chambers D, Khoury MJ, Kaplan RM, C. H. National Institutes of Health approaches to dissemination and implementation science: current and future directions. *Am J Public Health*. 2012;102(7):1274-1281.
14. Harris JR, Cheadle A, Hannon PA, et al. A framework for disseminating evidence-based health promotion practices. *Prev Chronic Dis*. 2012;9:e22.
15. Glanz KE, Rimer BKE, Viswanath KE. *Health Behavior and Health Education: Theory, Research, and Practice*. San Francisco: Jossey-Bass; 2008.
16. Brownson RC, Eyster AA, Harris JK, Moore JB, RG. T. Getting the Word Out: New Approaches for Disseminating Public Health Science. *J Public Health Manag Pract*. 2018;24(2):102-111.

17. Teng Y, Li W, Gunasekaran S. Biosensors based on single or multiple biomarkers for diagnosis of prostate cancer. *Biosensors and Bioelectronics: X*. 2023;15:100418.
18. Tutrone R, Donovan MJ, Torkler P, et al. Clinical utility of the exosome based ExoDx Prostate(IntelliScore) EPI test in men presenting for initial Biopsy with a PSA 2-10 ng/mL. *Prostate Cancer Prostatic Dis*. 2020;23:607–614.
19. Vickers AJ, Cronin AM, Aus G, et al. A panel of kallikrein markers can reduce unnecessary biopsy for prostate cancer: data from the European Randomized Study of Prostate Cancer Screening in Göteborg, Sweden. *BMC Medicine*. 2008;6(1):19.
20. Alqualo NO, Campos-Fernandez E, Picolo BU, et al. Molecular biomarkers in prostate cancer tumorigenesis and clinical relevance. . *Critical Reviews in Oncology/Hematology*. 2023;104232.