SF CAN San Francisco Cancer Initiative

UCSF

Smarter Screening and Smarter Treatment (S3T) for Prostate Cancer

Research Summary

Developed in a multidisciplinary collaboration of UCSF
Internal Medicine, Primary Care, and Urology - Launched by SF-CAN

It is now possible to greatly reduce the harms of PSA testing (over-diagnosis and over-treatment) by:

Smarter Screening = ***early baseline, targeted,*** *and* ***less frequent*** PSA testing; use of secondary markers and imaging prior to diagnosis

Smarter Treatment = ***risk-stratified, guideline-concordant treatment*** that aims to minimize both over- and under-treatment

TARGETED BASELINE (SMARTER) PSA TESTING

- Prostate cancer (PCa) is not one disease. Most PCa is indolent and does not threaten length or quality life. PCa that is aggressive/high-grade causes substantial morbidity and kills more men in the US annually than any cancer save lung cancer- but can be detected early enough to extend life and often to cure.
  - The goal of screening is to *find aggressive prostate cancer e*arly and cure it before it spreads beyond the prostate
- *African American* men have more aggressive PCa starting at younger ages. The greatest of all cancer disparities is African Americans' 40-60% excess incidence and >2.5-fold higher mortality rate compared to other groups.[1,2]
  - Recent research that includes rigorous statistical modeling[3] and a large retrospective cohort of US veterans[4] shows a *greater mortality benefit for more intensive PSA-based screening for African Americans*
- Men should get a baseline PSA test at an early age (~45-50) before benign prostatic hyperplasia and other conditions associated with aging cloud the interpretation of PSA. Those at high risk for lethal prostate cancer (those with blood relatives who have died from PCa; African American men; men exposed to Agent Orange) should have a baseline PSA at an *earlier age*.[5]
  - Recent research shows that a baseline PSA starting at age 45 can reliably predict *the occurrence of aggressive prostate cancer* up to 25 years later across multiple racial and national sub-groups.[6,7]
- Of note, a 2018 meta-analysis found a "considerable lack of evidence" of the efficacy of the digital rectal exam for detecting prostate cancer in primary care.[8] DRE has little value particularly when PSA is tested early using a low threshold to drive further workup.
- Offer PSA **baseline** testing in mid-life (45 to 55). A large majority of the population will test <1 ng/ml.[6]
- At any age, men with a PSA <1 ng/ml ("normal") need not test again for 5 or more years. [9,10,11]

RISK-STRATIFIED (SMARTER) DIAGNOSIS & TREATMENT

- In our S3T protocol at UCSF, we define a "marginal" PSA for men ≤60 years old is 1-2 ng/ml; over age 60 the marginal PSA is 1-3 ng/ml
  - ✓ For men with marginal PSA, consider early repeat testing to assess trends, vs. early work-up (see below) based on risk factors and patient preferences.
  - ✓ A PSA >2 (45-60 yrs old) or >3 (61-75 yrs old) indicates a workup/referral to urology
    - **Workup** means secondary testing with blood or urine tests, and/or MRI – *not* automatic biopsy
    - **Secondary testing (e.g., 4K, phi, SelectMDx , MRI**) is explicitly intended to reduce the number of biopsies performed, and to avoid detection of low-grade, indolent prostate cancer.

Age	PSA	Protocol
45-60	<1	Recheck in 5+ years
	1-2	Recheck in 6-12 mos vs. early referral based on family history, anxiety, etc + SDM
	>2	Referral
61-75	<1	Recheck in 5+ years
	1-3	Recheck in 6-12 months vs. early referral based on family history, anxiety, etc + SDM
	>3	Referral

- ✓ **Biopsies** should be reserved for men considered at risk for high-grade PCa

- Active Surveillance (AS) is known to *greatly reduce over-treatment* for men with low-risk PCa[12]
  - ✓ Nearly all low-risk disease should be managed by AS.[13,14]
  - ✓ African Americans with aggressive PCa are often under-treated; their higher-grade disease often requires surgery, radiation, and/or hormone therapy, or a combination.
- The literature is mixed on whether African American men have an increased risk of progression during AS; in most studies race is not an independent predictor of progression. However, more consistent use of confirmatory testing and closer follow is advisable; the same is true for those with strong family history and/or germline genetic mutations in BRCA 1/2, ATM, or related genes.[15]

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[1] National Cancer Institute Surveillance, Epidemiology, and End Results Program. NCI, DCCPS, Surveillance Research Program Surveillance Systems Branch. https://seer.cancer.gov/statfacts/html/disparities.html Accessed 8/17/22.

[2] DeSantis CE, Siegel RL, Sauer AG, et al. Cancer statistics for African Americans, 2016: progress and opportunities in reducing racial disparities. *CA Cancer J Clin*. 2016;66(4):290-308. doi:10.3322/caac.21340

[3] Tsodikov A, Roman G, Tiago de Carvalho, Eveline AM Heijnsdijk, Rachel A. Hunter-Merrill, Angela B. Mariotto, Harry J. de Koning, and Ruth Etzioni. "Is prostate cancer different in black men?" Cancer 123, no. 12 (2017): 2312-2319.

[4] Sherer MV, Qiao EM, Kotha NV, Qian AS, Rose BS. Association Between Prostate-Specific Antigen Screening and Prostate Cancer Mortality Among Non-Hispanic Black and Non-Hispanic White US Veterans. *JAMA Oncol*. Published online August 04, 2022. doi:10.1001/jamaoncol.2022.2970

[5] Cooperberg MR. "The New US Preventive Services Task Force" C" Draft Recommendation for Prostate Cancer Screening." *European Urology* 72, no. 3 (2017): 326-328.

[6] Preston MA, Batista JL, Wilson KM, et al. Baseline Prostate-Specific Antigen Levels in Midlife Predict Lethal Prostate Cancer. *J Clin Oncol*. 2016;34(23):2755–2711. doi:10.1200/JCO.2016.66.7527.

[7] Nyame YA, Gulati R, Heijnsdijk EAM, Tsodikov A, Mariotto AB, Gore JL, Etzioni R. "The impact of intensifying prostate cancer screening in black men: a model-based analysis." JNCI: 113, no. 10 (2021): 1336-1342.

[8] Naji L, Randhawa H, Sohani Z, Dennis B, Lautenbach D, Kavanagh O, Bawor M, Banfield L, and Profetto J. 2018. Digital rectal examination for prostate cancer screening in primary care: a systematic review and meta-analysis. *The Annals of Family Medicine*, *16*(2), pp.149-154.

[9] Mottet N, Vanden Bergh RCN, Briers E., et al., AU-ESTRO-ESUR-SIOG Guidelines on Prostate cancer. https://uroweb.org/guidelines/prostate-cancer. Accessed August 18, 2022.

[10] Vickers AJ, Ulmert D, Sjoberg DD, Bennette CJ, Björk T, Gerdtsson A, Manjer J, Nilsson PM, Dahlin A, Bjartell A, Scardino PT. "Strategy for detection of prostate cancer based on relation between prostate specific antigen at age 40-55 and long-term risk of metastasis: case-control study." *BMJ* 346 (2013).

[11]Ferraro S, Bussetti M, Panteghini M. "Serum prostate-specific antigen testing for early detection of prostate cancer: Managing the gap between clinical and laboratory practice." *Clinl Chemistry* 67, no. 4 (2021): 602-609.

[12] Chen RC, Rumble RB, Loblaw DA, Finelli A, Ehdaie B, Cooperberg MR, Morgan SC, Tyldesley S, Haluschak JJ, Tan W, Justman S. "Active surveillance for the management of localized prostate cancer (Cancer Care Ontario Guideline): American Society of Clinical Oncology clinical practice guideline endorsement." *J Clin Onc*: Official Journal of the American Society of Clinical Oncology 34, no. 18 (2016): 2182-2190.

[13] Carlsson S, Benfante N, Alvim R, Sjoberg DD, Vickers A, Reuter VE, Fine SW, Vargas HA, Wiseman M, Mamoor M, Ehdaie B. "Long-term outcomes of active surveillance for prostate cancer: the Memorial Sloan Kettering Cancer Center experience." *The Journal of Urology* 203, no. 6 (2020): 1122-1127.

[14] Sanda MG, Cadeddu JA, Kirkby E, Chen RC, Crispino T, Fontanarosa J, Freedland SJ, Greene K, Klotz LH, Makarov DV, Nelson JB. "Clinically localized prostate cancer: AUA/ASTRO/SUO guideline. Part I: risk stratification, shared decision making, and care options." *The Journal of Urology* 199, no. 3 (2018): 683-690.

[15] Vigneswaran HT, Mittelstaedt L, Crippa A, Eklund M, Vidal A, Freedland SJ, Abern MR. "Progression on active surveillance for prostate cancer in Black men: a systematic review and meta-analysis." *Prostate Cancer and Prostatic Diseases* 25, no. 2 (2022): 165-173.