Update on Screening

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Prostate Cancer Early Detection

NCCN Guidelines Index
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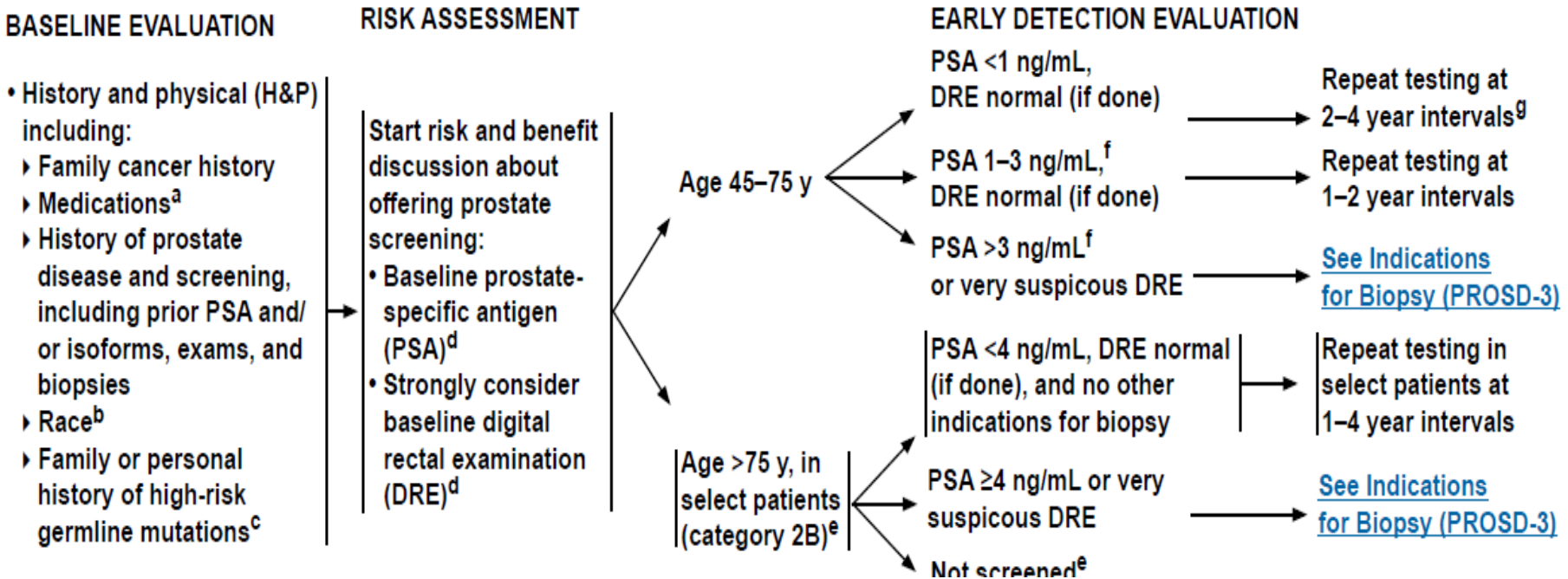
Discussion



JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Role of Genetic Testing for Inherited Prostate Cancer Risk: Philadelphia Prostate Cancer Consensus Conference 2017

Veda N. Giri, Karen E. Knudsen, William K. Kelly, Wassim Abida, Gerald L. Andriole, Chris H. Bangma, Justin E. Bekelman, Mitchell C. Benson, Amie Blanco, Arthur Burnett, William J. Catalona, Kathleen A. Cooney, Matthew Cooperberg, David E. Crawford, Robert B. Den, Adam P. Dicker, Scott Eggener, Neil Fleshner, Matthew L. Freedman, Freddie C. Hamdy, Jean Hoffman-Censits, Mark D. Hurwitz, Colette Hyatt, William B. Isaacs, Christopher J. Kane, Philip Kantoff, R. Jeffrey Karnes, Lawrence I. Karsh, Eric A. Klein, Daniel W. Lin, Kevin R. Loughlin, Grace Lu-Yao, S. Bruce Malkowicz, Mark J. Mann, James R. Mark, Peter A. McCue, Martin M. Miner, Todd Morgan, Judd W. Moul, Ronald E. Myers, Sarah M. Nielsen, Elias Obeid, Christian P. Pavlovich, Stephen C. Peiper, David F. Penson, Daniel Petrylak, Curtis A. Pettaway, Robert Pilarski, Peter A. Pinto, Wendy Poage, Ganesh V. Raj, Timothy R. Rebbeck, Mark E. Robson, Matt T. Rosenberg, Howard Sandler, Oliver Sartor, Edward Schaeffer, Gordon F. Schwartz, Mark S. Shahin, Neal D. Shore, Brian Shuch, Howard R. Soule, Scott A. Tomlins, Edouard J. Trabulsi, Robert Uzzo, Donald J. Vander Griend, Patrick C. Walsh, Carol J. Weil, Richard Wender, and Leonard G. Gomella

Representation: Urology (National and International), Medical Oncology, Radiation Oncology, Clinical Cancer Genetics, Genetic Counseling, Health Policy, Bioethics, Population Science, Molecular Epidemiology, Pathology, Breast/GI/Gyn Oncology, Genetic Basic Science Research, Patient Advocates, Patient Stakeholders, NCCN, NCI, ACS

Giri, et al J Clin Oncol. 2017 Dec 13 [Epub ahead of print].

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INDICATIONS FOR BIOPSY[h]

- Repeat PSA
- DRE, if not performed during initial risk assessment
- Workup for benign disease

→ **MANAGEMENT**

- Consider biomarkers that improve the specificity of screening[i]
- Consider multiparametric MRI[j]

→ Transrectal ultrasound (TRUS)-guided biopsy[k] → See Management of Biopsy Results (PROSD-4)

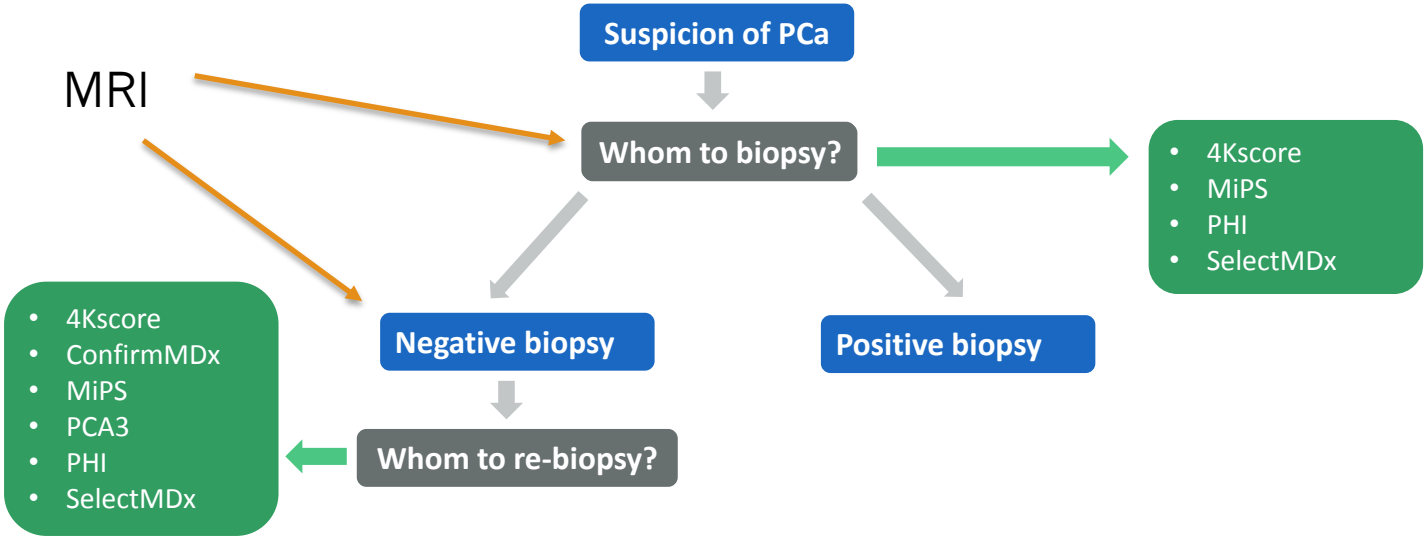
or

Follow-up in 6–12 mo with PSA/DRE[i,l]

TRUS-GUIDED BIOPSY
Initial and Repeat
Extended-pattern biopsy (12 cores)

- Number of cores:
  - Sextant (6),
  - Lateral peripheral zone (6), and
  - Lesion-directed at palpable nodule or suspicious image
- Anteriorly directed biopsy is not supported in routine biopsy. However, the addition of a transition zone biopsy to an extended biopsy protocol may be considered in a repeat biopsy if PSA is persistently elevated.
- Multiparametric MRI followed by lesion targeting may maximize the detection of higher-risk disease and limit the detection of lower-risk disease.[j]
- Local anesthesia can decrease pain/discomfort associated with prostate biopsy and should be offered to all patients.

Clinical application of diagnostic biomarker tests



JAMA | Original Investigation

Effect of a Low-Intensity PSA-Based Screening Intervention on Prostate Cancer Mortality

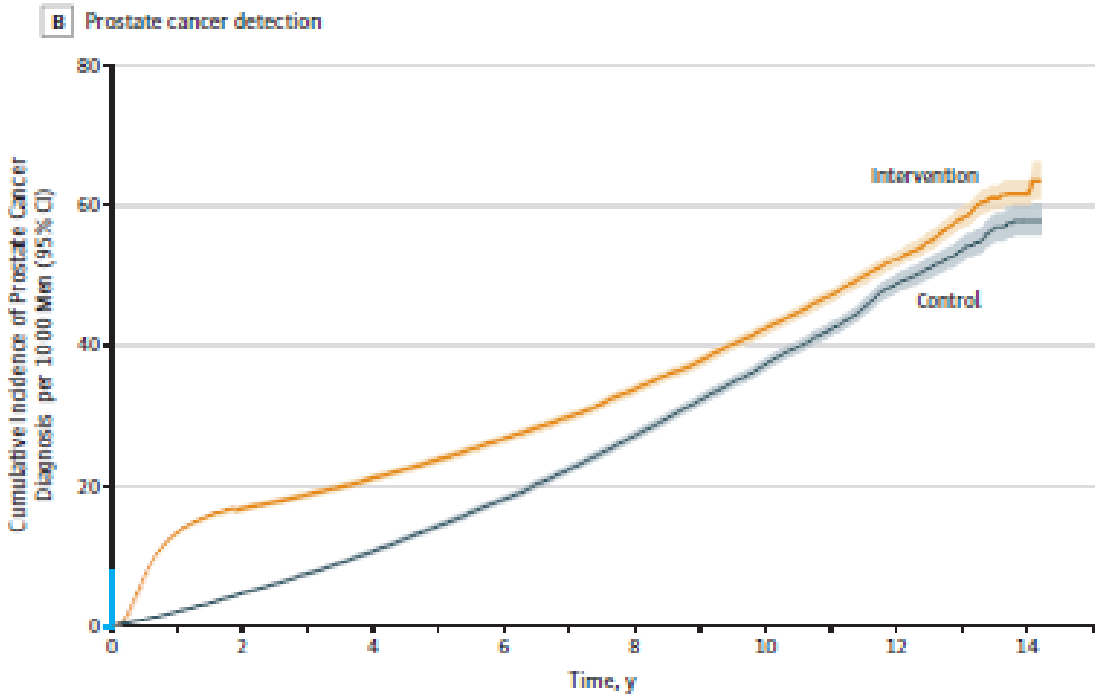
The CAP Randomized Clinical Trial

Richard M. Martin, PhD; Jenny L. Donovan, PhD; Emma L. Turner, PhD; Chris Metcalfe, PhD; Grace J. Young, MSc;

DESIGN, SETTING, AND PARTICIPANTS The Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP) included 419 582 men aged 50 to 69 years and was conducted at 573 primary care practices across the United Kingdom. Randomization and recruitment of the practices occurred between 2001 and 2009; patient follow-up ended on March 31, 2016.

INTERVENTION An invitation to attend a PSA testing clinic and receive a single PSA test vs standard (unscreened) practice.

JAMA. 2018;319(9):883-895. doi:10.1001/jama.2018.0154



No. at risk								
Intervention	189386	181301	175057	168234	159939	91419	36222	1589
Control	219439	212739	205021	196022	185601	103578	22905	1747
No. of events								
Intervention	3133	792	976	1203	1106	644	197	3
Control	1010	1260	1507	1787	1550	612	127	0

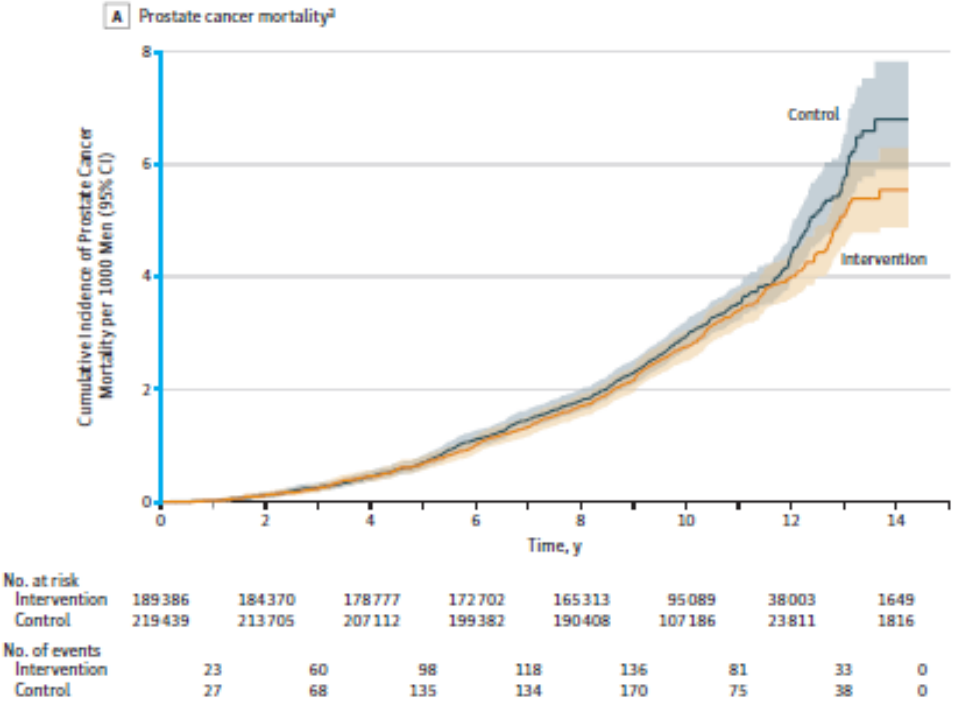

A Prostate cancer mortality[a]
Cumulative Incidence of Prostate Cancer Mortality per 1000 Men (95% CI)
Control
Intervention
Time, y
0
2
4
6
8
10
12
14
No. at risk
Intervention 189386 184370 178777 172702 165313 95089 38003 1649
Control 219439 213705 207112 199382 190408 107186 23811 1816
No. of events
Intervention 23 60 98 118 136 81 33 0
Control 27 68 135 134 170 75 38 0

Table 2. Prostate Cancer-Specific and All-Cause Mortality in the Single Prostate-Specific Antigen (PSA) Testing Intervention Group vs Standard Practice (Control)

	Intervention Group (n = 189 386)[a]		Control Group (n = 219 439)[b]						
	No. of Deaths	Rate/1000 Person-Years (95% CI)	No. of Deaths	Rate/1000 Person-Years (95% CI)	Rate Difference/1000 Person-Years (95% CI)	Rate Ratio (95% CI)[c]	*P* Value	Rate Ratio (95% CI)[d]	*P* Value
Primary Outcome: Prostate Cancer Mortality[e]									
Intention-to-screen cohort	549	0.30 (0.27 to 0.32)	647	0.31 (0.29 to 0.33)	−0.013 (−0.047 to 0.022)	0.96 (0.85 to 1.08)	.50	0.93 (0.67 to 1.29)	.66
Secondary Outcome: All-Cause Mortality									
Intention-to-screen cohort	25 459	13.74 (13.57 to 13.91)	28 306	13.51 (13.35 to 13.67)	0.229 (−0.001 to 0.460)	0.99 (0.94 to 1.03)	.49	1.07 (0.93 to 1.23)	.35

Trial Limitations

- One-time screen
  - Cancers discovered in initial screening worse than in subsequent rounds in PLCO and ERSPC
- Poor adherence
  - Only 40% in intervention arm had PSA and subsequent evaluation
  - But that is the “real world” and one way in which PLCO and ERSPC differed
- Rel. Short follow-up
  - Few CaP deaths

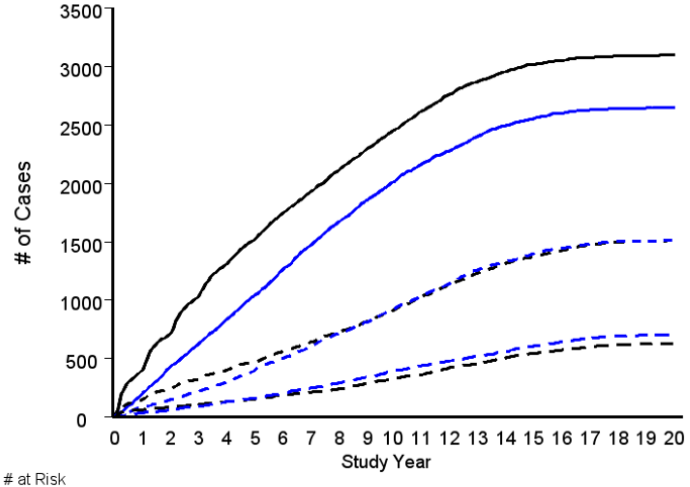
Secondary prostate cancer screening outcomes by race in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Screening Trial

Results: Black men were slightly more likely (14.5%) to have a false-positive PSA test compared to white men (12.4%; $P = 0.02$) but less likely to have a false-positive digital rectal exam (DRE) (10.9% vs 14.2%, respectively; $P < 0.001$). Among all men who were screened, black men were significantly more likely to undergo a biopsy than white men (16.5% vs 13.8%, respectively [$P = 0.003$]) but there was no difference when limited to those with a positive PSA test. Prostate cancer tumors were more likely to be aggressive and to have metastasized in black men compared to white men. Disparities in incidence, mortality, and survival rates were comparable to those seen in population-based data.

The Prostate. 2018;**78**:830–838.

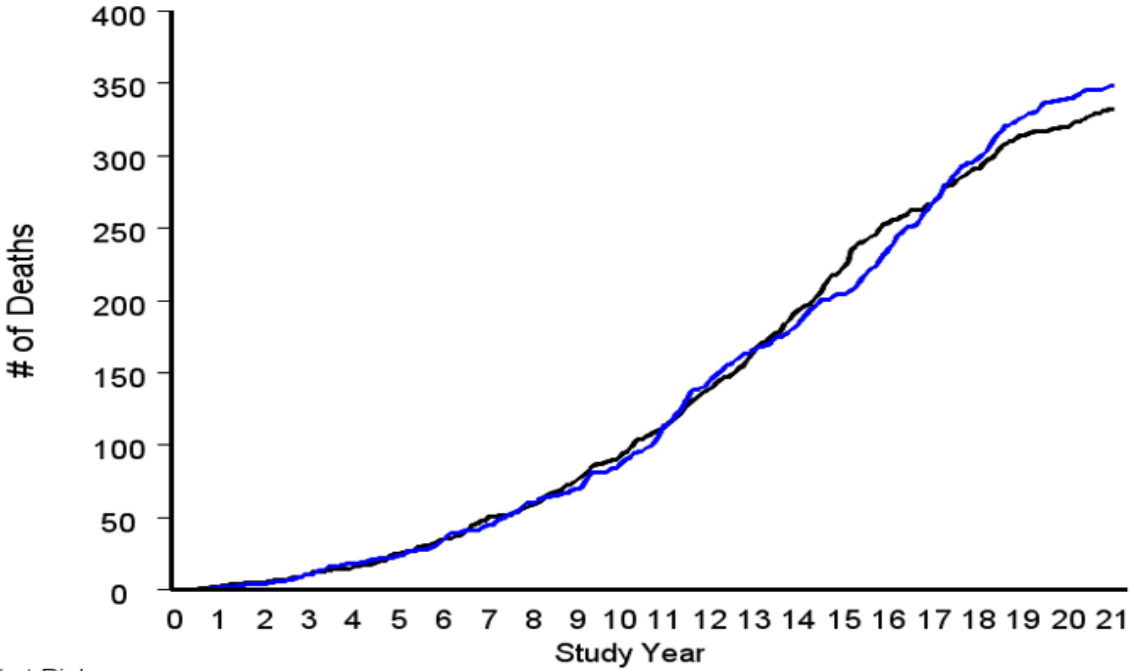
Extended PLCO Follow-up at 16.7 yrs

Figure 2B. Cumulative PCa cases by arm by Gleason category. Black lines are intervention arm, blue lines are usual care arm. Solid, dotted and dashed lines are (biopsy) Gleason 2-6, Gleason 7 and Gleason 8-10 cases, respectively.



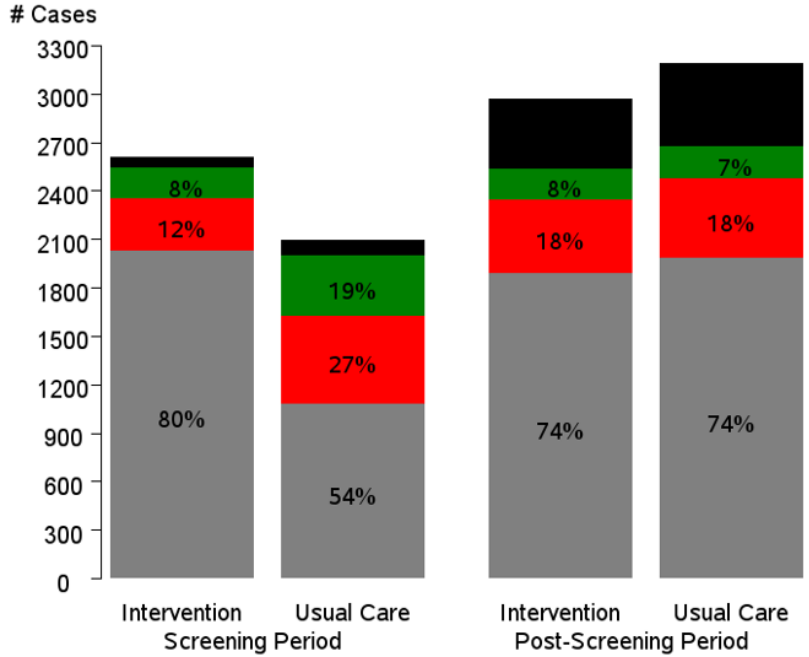
# at Risk							
Intervention	38340	35841	33417	30736	26715	20202	8893
Usual Care	38343	36309	33770	30882	26370	19364	8470

Figure 1. Prostate cancer deaths by trial arm. Black is intervention arm, blue is usual care arm.



# at Risk								
Intervention	38340	36873	35863	33941	31206	26572	14643	5268
Usual Care	38343	37276	35760	33825	30891	25798	13878	4934

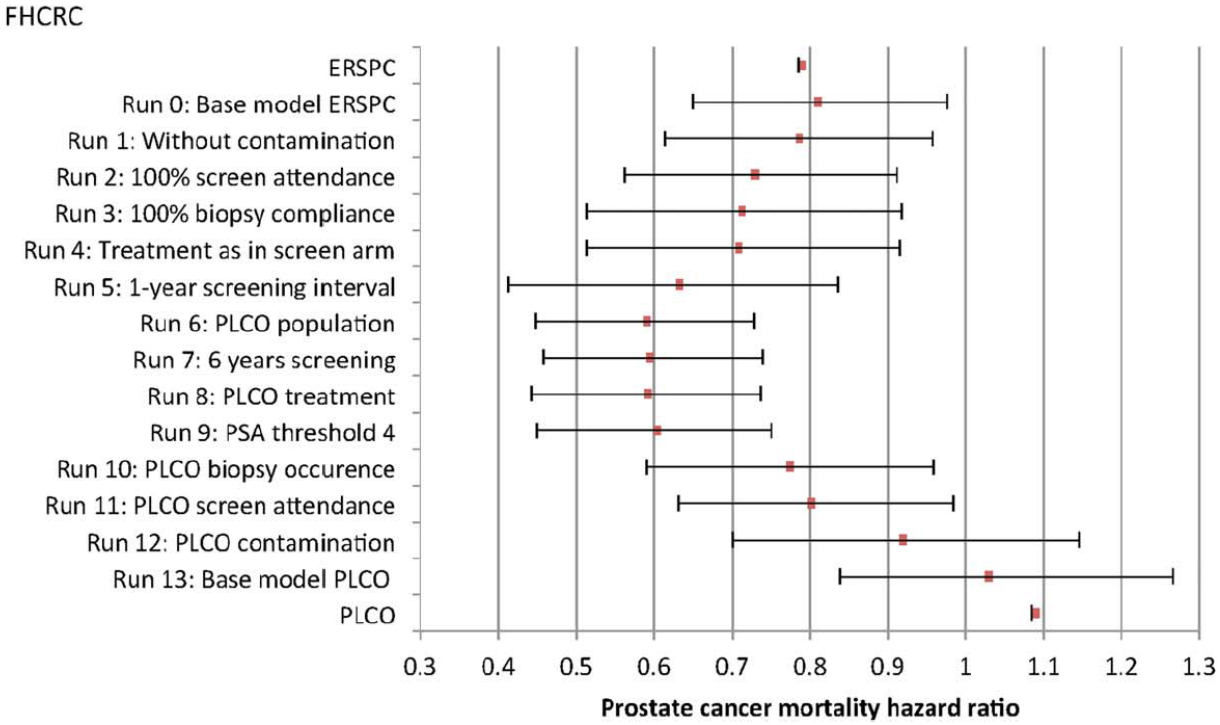
Figure 3. Number and percent of cases by trial arm, trial period and mode of detection. Grey is screen-detected cases, red is symptomatically detected, green is other-detected and black is unknown. Percentages exclude unknown.



The Efficacy of Prostate-Specific Antigen Screening: Impact of Key Components in the ERSPC and PLCO Trials

Harry J. de Koning, MD[1]; Roman Gulati, MS [2]; Sue M. Moss, PhD[3]; Jonas Hugosson, MD[4]; Paul F. Pinsky, PhD[5]; Christine D. Berg, MD[6]; Anssi Auvinen, MD[7]; Gerald L. Andriole, MD[8]; Monique J. Roobol, PhD[9]; E. David Crawford, MD[10]; Vera Nelen, MD[11]; Maciej Kwiatkowski, MD[12]; Marco Zappa, MD[13]; Marcos Luján, MD[14]; Arnauld Villers, MD[15]; Tiago M. de Carvalho, PhD [1]; Eric J. Feuer, PhD[16]; Alex Tsodikov, PhD[17]; Angela B. Mariotto, PhD[16]; Eveline A. M. Heijnsdijk, PhD [1]; and Ruth Etzioni, PhD[2]

CONCLUSIONS: The observed cancer mortality reduction in screening trials appears to be highly sensitive to trial protocol and practice settings. Accounting for these differences, the efficacy of PSA screening in the PLCO setting is not necessarily inconsistent with ERSPC results. ***Cancer*** **2018;124:1197-206.** *© 2017 American Cancer Society.*


FHCRC
ERSPC
Run 0: Base model ERSPC
Run 1: Without contamination
Run 2: 100% screen attendance
Run 3: 100% biopsy compliance
Run 4: Treatment as in screen arm
Run 5: 1-year screening interval
Run 6: PLCO population
Run 7: 6 years screening
Run 8: PLCO treatment
Run 9: PSA threshold 4
Run 10: PLCO biopsy occurence
Run 11: PLCO screen attendance
Run 12: PLCO contamination
Run 13: Base model PLCO
PLCO
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3
Prostate cancer mortality hazard ratio

ERSPC: Netherlands subset @ 19 yrs

	Screening arm		Control arm		Total Cohort	
	Number	%	Number	%	Number	%
T-stage						
T1	30	5.4	20	3	50	4
T2	27	5	24	4	51	5
T3	14	3	7	1.2	21	2
T4	1	0.2	6	1	7	1
N-stage						
NX	38	7	34	6	72	6
N0	34	6	19	3.3	53	4.7
N1	0	0	4	0.7	4	0.4
M-stage						
MX	25	5	25	4	50	4
M0	44	8	25	4	69	6
M1	3	1	7	1	10	1
Gleason score						
No PCa	482	87	524	90	1006	89
GS unknown	9	2	3	1	12	1
GS 3+3	40	7	26	4	66	6
GS ≥3+4	23	4	28	5	51	4
Survival status						
Alive	190	34	227	39	417	37
Death	364	66	354	61	718	63
Cause of death						
PCa	5	1	11	2	16	1
Other cause	359	65	343	59	702	62
Total	554	100	581	100	1135	100