Kanserde Erken Teşhis Tarama Yöntemleri

Dr. Deniz Tural Tıbbi Onkoloji

Kaynaklar

Bu seminer için aşağıdaki kavuzlardan ve bu kılavuzların oluşmasında etkili makalelerden yararlanılmıştır

National Cancer Institute(NIH), National Comprehensive Cancer Network(NCCN)
European Society For Medical Oncology (ESMO)
United States Preventive Services Task Force (UPSTF)
American Cancer Society
American Society for Colposcopy and Cervical Pathology, American Society for Clinical Pathology
Uptodate

Ders Plani

- Kanserde tarama yöntemlerini neden kullanırız
- Tarama yöntemleri nelerdir
- Tarama yöntemlerin kazançları
- Tarama yöntemleri handikapları ve olası zararlı sonuçları
- Kolon kanseri, serviks, meme, akciğer, prostat ve diğer kanserlerde erken teşhis ve tarama yöntemleri

Kanserde Tarama Yöntemleri Amaç

- ☐ Tarama, semptom(bulgu) olmadan, kanser durumunun değerlendirilmesidir
- Temel amaç, erken tanı koymak
- ☐ Erken evrede yakalayarak kür elde edilebilirliği artırmak
- ☐ Tarama yöntemi ile erken teşhis konarak, kansere bağlı ölümleri azaltmak.

Kanserde Tarama Yöntemleri

- Anemnez, fizik muayene
- Laboratuar testleri, kan, idrar, doku örnekleri
- Görüntüleme yöntemleri
- ☐ Genetik testler

Tarama Yöntemlerinin Handikapları

Tarama testleri yapılırken gerçekleşen komplikasyonlar (örn: kolonoskopi kanama)
Yalancı pozitiflik, buna bağlı anksiyete, yapılan fazladan tetkikler, bunlarır komplikasyonları
Yalancı negatiflik, gecikmiş tanı
Overdiagnosis , yavaş seyir gösteren hastalığın erken tanısının konmasıyla gereksiz(fazladan)yapılan tedaviler(örn: erken evre prostat ca)
Bazı kanser türlerinde erken teşhisi yaşam kalitesini ve sağkalımı artırmaz

Erken Teşhis ile Sağkalımı Uzatan Tarama Yöntemleri

- ☐ Ba**ğırsak kanseri;** Kolonoskopi, sigmoidoskopi, gaita gizli kan testleri
- ☐ Akciğer kanseri; Düşük doz helikal bilgisayarlı tomografi
- ☐ Meme kanseri; Mamografi
- ☐ Rahim ağzı kanseri; Pap smear ve HPV testi

Kolonoskopi, sigmoidoskopi, Gaita gizli kan testleri

- ☐ Bu testler kolorektal kansere bağlı ölümleri azaltır
- Aynı zamanda kolonoskopi ve sigmoidoskopi anormal polipleri erken teşhis ederek kolorektal kanser oluşmasında engeller
- □ 50-75 Yaş gurubunda kolonoskopi ve sigmoidoskopi ve gaitada gizli kan testi tarama amaçlı önerilir.

Kolorektal Kanser Tarama

- ☐ U.S.Preventive Services Task Force(UPSTF) kolorektal kanser için tarama genel popülasyon için 50 yaşında önermektedir
- ☐ Fakat, ailesel kanser ve polip öyküsü olan, İnflamatuar bağırsak hastalığı olanlarda, 45 yaş ve sonrası için tarama önerir.
- ☐ Tarama intervali daha kısa ve tarama daha sık yapılabilir.

Kolorektal Kanserler Tarama Gaita gizli kan testleri

High-sensitivity fecal occult blood tests (FOBT): Polip ve kansere bağlı kanamayı tespit eder. Bening nedenlere bağlı sebeplere bağlı yalancı pozitiflik olabilir(Hemoroid vs.)
Guaiac FOBT kandaki Heme tespit eder.
Bu test öncesi yalancı pozitifliği engellemek için gıda kısıtlaması gerekmektedir(Et ve ürünleri) yalancı pozitifliğe sebep olabilir.
Fekal immünohistokimyasal yöntem, insan hemoglobinine karşı geliştirilmiş antikor kullanılarak yapılır, diyet kısıtlaması yoktur(İFOBT)
Gaitada yüksek sensitif gizli kan tarama testleri 1 ve 2 yılda bir 45-80 yaşları arasında önerilir.
Bu testlerle kolorektal kanserlere bağlı mortalite %15-33 oranında azaltılır.
UPSTF, Gaitada yüksek sensitif gizli kan arama testleri kolorektal kanser taramasında kullanılan tek test ise yılda bir tekrarlamasını önerir.

Kolorektal Kanserler Tarama Sigmoidoskopi

50 yaş sonrası sigmoidoskopi ile yapılan taramada kolorektal kanserlere bağlı mortalitede %60-70 oranında azalma saptanmış. Sigmoidoskopi ile rektum ve aşağı kolon görüntülenebilir UPSTF her beş yılda bir Sigmoidoskopi ile birlikte 3 yılda bir Gaitada yüksek sensitif gizli kan tarama testleri ile tarama testi önerir.

Kolorektal Kanserler Tarama Kolonoskopi

- Rektum ve tüm kolon bu yöntem ile incelenebilir.
- Kolonoskopi ile yapılan tarama ile Kolorektal kanserlere bağlı mortalite %60-70 oranında azaltılabilir.
- ☐ UPSTF, 45 yaş sonrası her 10 yılda bir Kolonoskopi ile tarama önerir.

Kolorektal Kanserler Tarama



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RISK ASSESSMENT FOR COLORECTAL CANCER

Average risk:

- Age ≥45 years^a
- · No personal history of adenoma or sessile serrated polyp/sessile serrated lesion (SSP/SSL)b or CRC
- · No personal history of inflammatory bowel disease (IBD)
- No personal history of high-risk CRC genetic syndromes
- · No personal history of cystic fibrosis
- · No personal history of childhood cancer
- Negative family history for confirmed advanced adenoma (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology) or an advanced SSP/SSL^{b,c} (≥1 cm, any dysplasia) in first-degree relatives.^d
- Negative family history for CRC in first-, second-, or third-degree relatives^é

Average-Risk Screening and Evaluation (CSCR-3)

Increased risk:

 Personal history Follow-up of Clinical Findings: Adenoma or SSP/SSLb Polyp Found at Colonoscopy (CSCR-4) ▶ CRC Diagnosis of Colorectal Cancer (CSCR-7) Increased Risk Screening Based on Personal History of ▶ IBD (ulcerative colitis, Crohn's colitis) Inflammatory Bowel Disease (CSCR-8) Increased Risk Based on Personal History of Cystic Fibrosis (CSCR-11) Cystic fibrosis ► Increased Risk Based on Positive Family History (CSCR-12) Positive family history Personal history of childhood, adolescent, and young adult cancer (including Increased Risk Based on Personal History of Childhood, individuals who meet criteria for therapy-Adolescent and Young Adult Cancer (CSCR-13) associated polyposis)

Kolorektal Kanserler Diğer Tarama Yöntemleri

Kolonoskopi, sigmoidoskopi, Gaita gizli kan Standard kabul edilen ve UPSTF önerdiği testlerdir.
Cologuard®: Fekal immünohistokimyasal yöntem ile gizli kan ile birlikte, 3 genin(APC, KRAS, p53) varlığını gösteren(PCR yöntemi ile 21 mutasyonu tarayarak yapılıyor)
kanser ve pre-kanser(polip) durumunu gösteren test.
Gaitada gizli kana göre sensitivitesi daha yüksek
Bu test pozitif geldiğinde Kolonoskopi öneriliyor.
FDA onayı var, fakat UPSTF tarama metodu olarak henüz kabul etmedi.

Kolorektal Kanserler Diğer Tarama Yöntemleri

Sanal Kolonoskopi: Kolon temizliği ve BT öncesi karbondioksit pompalayarak bağırsaklarda ki görüntü kalitesi artırılır Sedasyon gerekmez, komplikasyon az ve tanı koyma kesinliği Standard Kolonoskopi ile benzer. Fakat polip ve anormal görüntü durumunda kolonoskopi ile biyopsi gerekir Sanal Kolonoskopi ile yapılan tarama ile sağkalımın artıp artmadığı bilinmemektedir UFST ve diğer bazı sağlık sigortaların ödeme kapsamına girmez

Kolorektal Kanserler Diğer Tarama Yöntemleri



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SCREENING MODALITY AND SCHEDULE

Screening Test*	Recommended Testing	Sen	Specificity	
	Interval**,1,2,3,4	Colorectal Cancer	Advanced Adenoma	
Colonoscopy	Every 10 years	95% ⁶	89%–98% (≥10 mm) ⁷ 75%–93% (≥6 mm) ⁷	90%8
Flexible sigmoidoscopy***	Every 5–10 years	58%-75% ⁹	72%–86% ⁹	92%8
CT colonography	Every 5 years	96% ⁶	67%–94% (≥10 mm) ⁷ 73%–98% (≥6 mm) ⁷	86%–98% (≥10 mm) ⁷ 80%–93% (≥6 mm) ⁷
High-sensitivity guaiac-based test	Annually	62%-79% ⁷	7%10	87%-96% ⁷
FIT	Annually	76%-95% ⁷	27%-47% ⁷	89%-96%7
Stool DNA test (includes high- sensitivity FIT)	Interval uncertain; however, every 3 years is suggested ⁵	92%5	42% ⁵	87% ⁵

^{*}A blood test that detects circulating methylated SEPT9 DNA has been FDA-approved for CRC screening for those who refuse other screening modalities. It is not recommended for routine screening. The interval for repeating testing is unknown.

^{**} Frequency based upon normal (negative) results.

^{***}Data for the sensitivity and specificity of flexible sigmoidoscopy are for the entire colon and are based on the completion of colonoscopy for those found to have a distal colon lesion on flexible sigmoidoscopy.

Kolorektal Kanserler Tarama Yöntemleri



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INCREASED RISK BASED ON POSITIVE FAMILY HISTORY

(Not meeting criteria for consideration of a hereditary cancer syndrome or appropriate testing for a hereditary cancer syndrome nondiagnostic or not done)bbb

SCREENINGeee **FAMILY HISTORY CRITERIA** Repeat every 5 vccc,eee,fff,ggg Colonoscopy beginning at age 40 y or ≥1 first-degree relative with CRC at any age or if positive, repeat per 10 y before earliest diagnosis of CRC colonoscopy findings Repeat every 10 y Second- and third-degree relatives with CRC ➤ Colonoscopy beginning at age 45 y^{ccc} or if positive, repeat per at any age colonoscopy findings First-degree relative with confirmed advanced Repeat every 5-10 yeee,fff adenoma(s) (ie, high-grade dysplasia, ≥1 cm, Colonoscopy beginning at age 40 y or villous or tubulovillous histology, TSA), or at age of onset of adenoma in relative, or if positive, repeat per advanced SSPs/SSLs (≥1 cm, any dysplasia) at any age^{ddd,hhh,iii} whichever is first colonoscopy findings

bbb If a patient meets the criteria for an inherited colorectal syndrome, see Assessment for Hereditary CRC Syndrome (HRS-1) in the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal.

ccc While current risk estimates for a family history of CRC in only second- and third-degree relatives may not be sufficiently elevated to recommend increased screening (Taylor DP, et al. Gastroenterology 2010;138:877-885; Taylor DP, et al. Genet Med 2011;13:385-391; Samadder NJ, et al. Gastroenterology 2014;147:814-821; Tian Y, et al. BMJ 2019;364:1803), there are some data showing that having a second- and, to a lesser degree, a third-degree relative with early-onset (<50 years old) CRC increases risk of both CRC and early-onset CRC (Ochs-Balcom HM. Cancer Epidemiol 2021;73:101973). Some combinations of affected first-, second-, and third-degree relatives may increase risk sufficiently to alter screening guidelines. If there are multiple distant relatives affected,

consider evaluation for an inherited colorectal syndrome in the family.

ddd It is important for endoscopists to add specific recommendations to endoscopy reports for first-degree relatives (ie, siblings, parents, children) or alternatively generate a letter meant to be shared with first-degree relatives to increase adherence when this applies. Examples of patient letters can be found at National Colorectal Cancer Roundtable. Cottet V, et al. Gastroenterology 2007:133:1086-1092; Ng S, et al. Gastroenterology 2016;150:608-616.

eee Colonoscopy intervals may be further modified based on personal and family history as well as on individual preferences. Factors that modify age to begin screening and colonoscopy intervals include: age of individual undergoing screening; specifics of the family history, including number and age of onset of all affected relatives, whether relatives had an inciting cause such as IBD; size of family; completeness of the family history; participation in screening; and colonoscopy findings in family members. See Discussion.

fff Multiple (2 or more) negative colonoscopies may support stepwise lengthening in the colonoscopy interval.

999 Samadder NJ, et al. Am J Gastroenterol 2017;112:1439-1447.

hhh Advanced SSPs/SSLs are generally considered to have a comparable cancer risk and are managed similarly to advanced adenomas. While there are limited data concerning the specific risk of CRC in first-degree relatives of individuals with advanced serrated polyps, it is reasonable to follow the same recommendations used for first-degree relatives of those with advanced adenomas. Cottet V, et al. Gastroenterology 2007;133:1086-1092; Ng S, et al.

Gastroenterology 2016;150:608-616.

Cottet V, et al. Gastroenterology 2007;133:1086-1092; Ng SC, et al. Gastroenterology 2016;150:608-616.

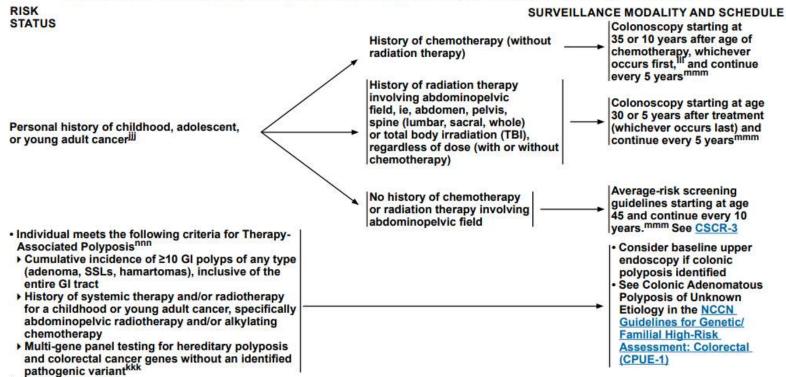
Kolorektal Kanserler Tarama Yöntemleri Lynch Sendromu



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INCREASED RISK BASED ON PERSONAL HISTORY OF CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCER



The adolescent and young adult (AYA) oncology patient is defined as an individual aged 15–39 years of age at the time of initial cancer diagnosis. This definition is based on the National Cancer Institute (NCI) Progress Review Group recommendations for a national agenda to advance AYA oncology. See NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology.

kkk Multi-gene testing should include all polyposis and colorectal cancer genes (Stanich P, et al. Clin Gastroenterol Hepatol 2019;17:2008-2015). Pathogenic variants associated with adenomatous polyposis include, but are not limited to monoallelic pathogenic variants in APC, GREM1, POLE, POLD1, and AXIN2, and biallelic pathogenic variants in MUTYH, NTHL1, and MSH3.

III Biller L, et al. Cancer Prev Res 2020;13:291-298

mmm Children's Oncology Group Long-Term Follow-up Guidelines for survivors of childhood, adolescent, and young adult cancers - Version 5.0-October 2018.

nnn Therapy-associated polyposis is an acquired phenotype that presents years after exposure to chemotherapy and/or radiotherapy.

Low-dose helical computed tomography (CT)
55-74 Yaşları arasında, 30 yıl/paket sigara içen bireylere önerilir
Yılda bir yapılması önerilir
The National Lung Screening Trial (NLST) çalışması NEJM 2011 tarihinde yayınlaması ile kavuzlara girmiştir.
Bu çalışmaya göre düşük doz helikal tomografi ile semptom , bulgu ve akciğer kanseri tanısı olmayan bireylerde tarama ile akciğer kanserine bağlı ölüm %15-20 oranında daha az görülmektedir.
Düşük doz helikal tomografi ile 1000 taramada %24.2 , PA akciğer ile taramada %6.9 oranında akciğer kanseri erken tanısı konmuş.
Akciğer adeno ve skuamöz kanser erken evrede saptanmış, fakat küçük hücreli akciğer kanseri erken evre tespit edilme oranı çok düşük oranda saptanmış.
Düşük doz helikal tomografi ile 1000 kişiye uygulanan tarama ile 3 kansere bağlı ölüm engellenmiştir.

Akciğer Kanserine Yönelik Tarama Testi Handikapları

- ☐ Yıllık akciğer kanseri taraması yapılan bireylerde
- Düşük doz helical BT %39.1
- ☐ PA akciğer kolunda %16 şüpheli bulgu saptanmış
- ☐ Bu bireylerde ileri tetkik yapılma zorunluluğunda kalınmış

Patient and Physician Guide: National Lung Screening Trial (NLST)

What is the purpose of this guide?

To explain the benefits and harms of low-dose computed tomography (CT) screening for lung cancer in people at high risk for the disease. The NLST showed a reduction in deaths from CT screening compared to chest X-ray screening. The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial recently showed that chest X-ray screening (compared to no screening) did NOT reduce the chance of dying from lung cancer.

Who participated in the NLST?

Current or former cigarette smokers within the past 15 years, 55 to 74 years of age, with at least 30 pack-years of smoking [Pack-years = packs per day x number of years smoking]. Participants must have had no symptoms or signs of lung cancer or other serious medical conditions, and be medically fit for surgery.

Study Findings: Low-dose CT versus Chest X-ray screening

53,454 current and former smokers were randomly assigned to be screened once a year for 3 years with low-dose CT or chest X-ray. Here's what happened after an average of 6.5 years:

	Low-dose CT 26,722 people		Chest X-ray 26,732 people
Benefit: How did CT scans help compared to chest X-ray, an ineffective screening test?			
3 in 1,000 fewer died from lung cancer	18 in 1,000	versus	21 in 1,000
5 in 1,000 fewer died from all causes	70 in 1,000	versus	75 in 1,000
Harm: What problems did CT scans cause compared to chest X-ray?			
223 in 1,000 more had at least one false alarm	365 in 1,000	versus	142 in 1,000
18 in 1,000 more had a false alarm leading to an invasive procedure, such as bronchoscopy, biopsy, or surgery	25 in 1,000	versus	7 in 1,000
2 in 1,000 more had a major complication from Invasive procedures	3 in 1,000	versus	1 in 1,000

USPSTF yıllık düşük doz helikal thoraks BT aşağıdaki bireylere önerir 55–80 yaşları arasında, 30 yıl/paket sigara içen ve içmekte olan Yada 30 yıl sigara içen ve 15 yıl içinde bırakan Yaşam beklentisi uzun, ciddi sağlık problemi olmayan, Küratif akciğer kanseri cerrahisine uygun ve istekli bireylere önerir Oneri derecesi: Grade B, orta düzeyde yarar.



NCCN Guidelines Version 1.2024 Lung Cancer Screening

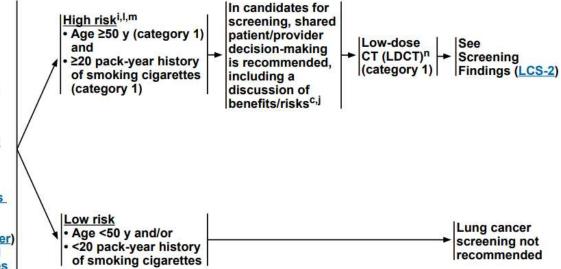
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RISK ASSESSMENT^{a,b,c} RISK STATUS SCREENING

- Cigarette smoking history^d
- Radon exposure^e
- · Occupational exposuref
- Cancer history^g
- Family history of lung cancer in first-degree relatives
- Disease history (chronic obstructive pulmonary disease [COPD] or pulmonary fibrosis)
- Cigarette smoking exposure^{ff} (second-hand smoke)
- Risk calculator to enhance determination of risk status^{i,j}

Patients not eligible for lung cancer screening:

- Symptoms of lung cancer (see <u>NCCN Guidelines</u> for Non-Small Cell Lung Cancer)
- Previous lung cancer (see <u>Surveillance in the NCCN Guidelines for Non-Small Cell Lung Cancer)</u>
- Functional status and/or comorbidity that would prohibit curative intent treatment^k (see <u>Principles</u> of <u>Surgery in the NCCN Guidelines for Non-Small</u> <u>Cell Lung Cancer</u>)



Meme Kanseri Tarama Yöntemleri

Mamografi

- ☐ Çok sayıda çalışma yıllık mamografi ile 40–74 yaşları arasında tarama ile meme kanserine bağlı mortalitenin %15–20 oranında azaldığı gösterilmiştir
- ☐ Özelikle 50 yaş sonrası bu yarar daha belirgin
- 40 yaş öncesi mamografi ile yapılan taramada sağkalım yararı gösterilmemiş.

Meme Kanseri Tarama Yöntemleri Mamografi

Handikap-Yalancı Pozitiflik		
	Genç yaş	
	Daha önce meme biyopsisi	
	Aile öyküsü	
	Östrojen bazlı tedavi görenlerde	
	Yalancı pozitifliğe bağlı ek test	
	Hasta üzerinde oluşturduğu stres	
	Armış maliyet	

Meme Kanseri Tarama Yöntemleri Mamografi

Overdiagnosis – Overtreatment

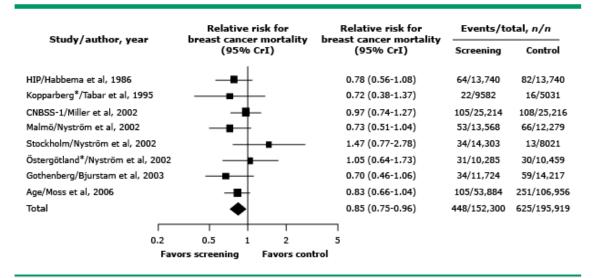
- □ Ductal carcinoma in situ gibi invazif olmayan kanserlerin mamografide saptanması
- Bu hastaların bir kısmında, hastanın hayat boyu sorun yaratacak invazif kanser gelişmeyeceğine rağmen tedavi edime zorunluluğu

Meme Kanseri Tarama Yöntemleri Mamografi –Handikaplar

- ☐ Yaklaşık olarak %20 yalancı negatiflik mevcut
 - Genç yaş
 - Meme yapısı yoğun olanlarda daha yüksek
- ☐ Meme kanserine bağlı ölüme neden olmayacak indolent erken kanserlerin saptanması buna bağlı ek tanı ve tedaviler
- Rutin taramalara bağlı X ışınlarına maruziyet ve bunun olası zararları

Meme Kanseri Tarama Yöntemleri Mamografi

Pooled relative risk for breast cancer mortality from mammography screening trials compared with control for women aged 39 to 49 years



CNBSS-1: Canadian National Breast Screening Study-1; CrI: credible interval; HIP: Health Insurance Plan of Greater New York; %: percent.

39–49 YAŞLARI ARASINDA MEME KANSERİNE BAĞLI ÖLÜMLER %15 AZALTIR

^{*} Swedish Two-County trial.

Meme Kanseri Tarama Yöntemleri Mamografi

Table 1. Pooled RRs for Breast Cancer Mortality From Mammography Screening Trials for All Ages

Age	Trials Included, <i>n</i>	RR for Breast Cancer Mortality (95% Crl)	NNI to Prevent 1 Breast Cancer Death (95% Crl)
39–49 y	8*	0.85 (0.75-0.96)	1904 (929-6378)
50-59 y	6 †	0.86 (0.75-0.99)	1339 (322–7455)
60-69 y	2‡	0.68 (0.54-0.87)	377 (230-1050)
70–74 y	1§	1.12 (0.73–1.72)	Not available

CrI = credible interval; NNI = number needed to invite to screening; RR = relative risk.

† Canadian National Breast Screening Study-1 (28), Stockholm (26), Malmö (26), Swedish Two-County trial (2 trials) (26, 31), and Gothenburg trial (30).

‡ Malmö (26) and Swedish Two-County trial (Östergötland) (26).

395 49 YAŞLARLARASINDA MEMEKANSERİNE BAĞLI 1 ÖLÜMÜ AZALTMAK İÇİN 1904 TARAMA YAPMAK LAZIM org

^{*} Health Insurance Plan of Greater New York (27), Canadian National Breast Screening Study-1 (28), Stockholm (26), Malmö (26), Swedish Two-County trial (2 trials) (26, 31), Gothenburg trial (30), and Age trial (29).

Meme Kanseri Tarama Yöntemleri Mamografi –Yıllık? İki Yılda bir?

Chances of breast cancer-related outcomes among 1000 women screened annually or biennially, starting at age 40 or 50 and continuing through age 69 or 74

Screening program			Cumulative consequences of screening program			
Mammogram frequency Starting age Ending age			Lives saved, number	Life-yrs gained, number	False-positive mammograms, number	Unnecessary biopsies, number
Annual			`			
	40	69	8.3	164	2250	158
	50	69	7.3	132	1350	95
	40	74	10.5	188	2470	173
	50	74	9.5	156	1570	110
Biennial						
	40	69	6.1	120	1250	88
	50	69	5.4	99	780	55
	40	74	8.2	142	1410	99
	50	74	7.5	121	940	66

Adapted and calculated from: Mandelblatt JS, Cronin KA, Bailey S, et al. Effects of Mammography Screening Under Different Screening Schedules: Model Estimates of Potential Benefits and Harms. Ann Intern Med 2009; 151:738.

Yıllık Mamografi, iki Yıllık Mamografiye göre Meme kanserine bağlı ölümü bir miktar azaltıyor. Fakat bunu artmış yanlış pozitif ve artmış gereksiz girişim ile sağlıyor

Meme Kanseri Tarama Yöntemleri Mamografi –Yıllık? İki Yılda bir?

Medline ® Abstract for Reference 55

of 'Screening for breast cancer: Strategies and recommendations'

PubMed

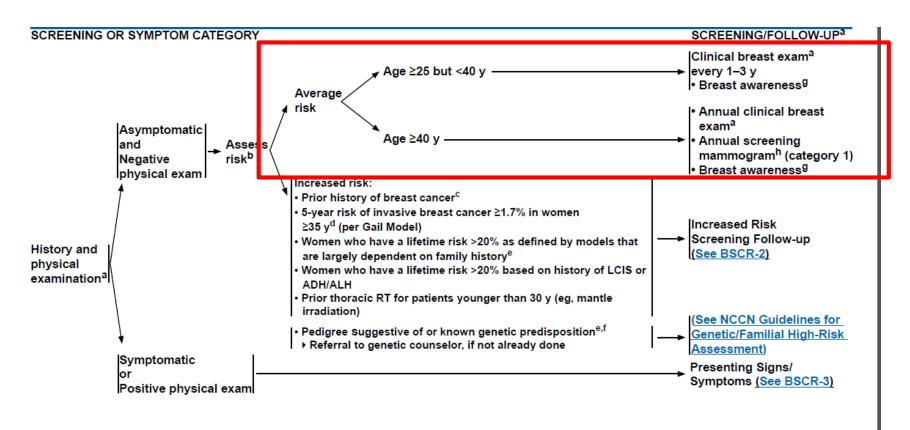
Outcomes of screening mammography by frequency, breast density, and postmenopausal hormone therapy.

Kerlikowske K, Zhu W, Hubbard RA, Geller B, Dittus K, Braithwaite D, Wernli KJ, Miglioretti DL, O'Meara ES, Breast Cancer Surveillance Consortium JAMA Intern Med. 2013:173(9):807.

IMPORTANCE Controversy exists about the frequency women should undergo screening mammography and whether screening interval should vary according to risk factors beyond age. OBJECTIVE To compare the benefits and harms of screening mammography frequencies according to age, breast density, and postmenopausal hormone therapy (HT) use. DESIGN Prospective cohort. SETTING Data collected January 1994 to December 2008 from mammography facilities in community practice that participate in the Breast Cancer Surveillance Consortium (BCSC) mammography registries. PARTICIPANTS Data were collected prospectively on 11 474 women with breast cancer and 922 624 without breast cancer who underwent mammography at facilities that participate in the BCSC. MAIN OUTCOMES AND MEASURES We used logistic regression to calculate the odds of advanced stage (IIb, III, or V) and large tumors (>20 mm in diameter) and 10-year cumulative probability of a false-positive mammography result by screening frequency, age, breast density, and HT use. The main predictor was screening mammography interval. RESULTS Mammography biennially for women aged 50 to 74 years does not increase risk of tumors with advanced stage or large size regardless of women's breast density or HT use. Among women aged 40 to 49 years with extremely dense breasts, biennial mammography versult was high among women undergoing annual mammography with extremely dense breasts who were either aged 40 to 49 years (65.5%) or used estrogen plus progestogen (65.8%) and was lower among women aged 50 to 74 years who underwent blennial or triennial mammography with scattered fibroglandular densities (30.7% and 21.9%, respectively) or fatty breasts (17.4% and 12.1%, respectively). CONCLUSIONS AND RELEVANCE Women aged 50 to 74 years, even those with high breast density or HT use, who undergo biennial screening mammography have similar risk of advanced-stage disease and lower cumulative risk of false-positive results than those who undergo annual mammography. When deciding whether to undergo

Meme yoğunluğunun fazla oldu 40–49 yaşları arasında, yanlış pozitifliğe rağmen yıllık, 50–74 yaşları arasında iki yılda bir mamografi önerilebilinir.

Meme Kanseri Tarama Yöntemleri Mamografi



Meme Kanseri Tarama Yöntemleri Dijital—Mamografi

- ☐ Dijital mamografi; bilgilerin saklanması, eski ile karşılaştırma olanağının olması ve konsültasyon amaçlı elektronik posta ile yollanması gibi avantajları var
- ☐ Fakat normal mamografiye göre meme kanserine bağlı kanser mortalitesini azatlığına dair bulgu yok
- ☐ Yoğun(dens) Meme yapısı, BRCA mutasyonu olanlarda daha avantajlı olduğuna dair veriler mevcut.

Meme Kanseri Tarama Yöntemleri 3D—Mamografi

Three -dimensional(3D) mamografi

- ☐ Üç boyutlu mamografi X ışınlarına maruziyet daha fazladır
- ☐ Üç boyutlu mamografinin standart(iki boyutlu) mamografiden üstün olduğunu gösteren karşılaştırmalı çalışma yoktur
- Standart mamografiye göre artı ve eksileri bilinmemektedir.

Meme Kanseri Tarama Yöntemleri Yüksek Risk Gruplarında

BREAST SCREENING CONSIDERATIONS

RECOMMENDATIONS FOR BREAST MRI SCREENING AS AN ADJUNCT TO MAMMOGRAPHY^{3,4}
(FOR AGE TO BEGIN SCREENING EXCEPT WHERE NOTED BELOW: SEE BSCR-2)

Recommend Annual MRI Screening (Based on Evidence):5

BRCA mutation, commence at age 25 y

- First-degree relative of BRCA carrier, but untested: commence at age 25 y
- Lifetime risk 20% or greater, as defined by models that are largely dependent on family history⁶

Recommend Annual MRI Screening (Based on Expert Consensus Opinion):⁷

- Radiation to chest between age 10 and 30 years
- Li-Fraumeni syndrome⁷ and first-degree relatives
- Cowden and Bannayan-Riley-Ruvalcaba syndromes⁸ and first-degree relatives
- · Consider MRI screening for LCIS and ALH/ADH based on emerging evidence

Insufficient Evidence to Recommend for or Against MRI Screening:9

- Lifetime risk 15%-20%, as defined by models that are largely dependent on family history⁶
- Heterogeneously or extremely dense breast on mammography
- Women with a personal history of breast cancer, 10 including ductal carcinoma in situ (DCIS)

Recommend Against MRI Screening (Based on Expert Consensus Opinion):

Women at <15% lifetime risk

Serviks Kanserine Yönelik Tarama Testi

United States Preventive Services Task Force (UPSTF9), American Cancer Society, American Society for Colposcopy and Cervical Pathology, American Society for Clinical Pathology
Mart 2012 tarihinde konsesus olarak serviks kanserine yönelik tarama testini belirlediler
Kadınlarda Pap smear testinin 21–29 yaşında 3 yılda bir yapılmasını,
30–65 yaşları arasında Pap smear ve HPV DNA 5 yılda bir bakılması ya da 3 yılda bir Pap smear bakılması önerilir.
Fakat HIV, immün supresyon olan, dietilsitilbestrol maruziyeti, serviks pre-kanser ya da kanser öyküsü olanlarda 65 yaş sonrası taramaya devam edilmesi önerilir.
Histerektomi(Uterus ve serviks operasyon ile alınmışsa) yapılan kadılarda tarama gerekmez
HPV aşısı yapılanlar tarama programına dahil edilmelidir.

Serviks Kanserine Yönelik Tarama Testi

- ☐ Pap smear testinin yanında neden HPV-DNA önerilir
- ☐ Pap- Smear serviks skuamöz karsinomunda ki anormaliteyi gösterirken, adeno ca değişimlerini göstermede daha az hasas
- ☐ HPV-DNA ile birlikte kullanıldığında adeno ca erken evre yakalama oranı artıyor.

Serviks Kanserine Yönelik Tarama Testi

■Table 1■ Summary of Recommendations

Population	Page Numbers	Recommended Screening Method [*]	Management of Screen Results	Comments
Aged <21 y	521-522	No screening		HPV testing should not be used for screening or management of ASC-US in this age group
Aged 21-29 y	522-523	Cytology alone every 3 y	HPV-positive ASC-US [†] or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US [†] : Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group
Aged 30-65 y	523-529	HPV and cytology "cotesting" every 5 y (preferred)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines ² HPV positive, cytology negative: Option 1: 12-mo follow-up with cotesting Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive: refer to colpos: • If HPV16 or HPV16/18 negative: 12-mo follow-with cotesting Cotest negative or HPV-negative ASC-US: Rescreen with cotesting in 5 v	000 0 M (0 M)
		Cytology alone every 3 y (acceptable)	HPV-positive ASC-US [†] or cytology of LSIL or more severe: Refer to ASCCP guidelines ² Cytology negative or HPV-negative ASC-US [†] : Rescreen with cytology in 3 y	
Aged >65 y	529-531	No screening following adequate negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y
After hysterectomy	531	No screening		Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer ever
HPV vaccinated	531-533	Follow age-specific recommendations (san as unvaccinated wome		de reducer esperante de 15 de em regission entre de production de 15 de 15 de 15 de 15 de 15 de 15 de 15 de 15

ASCCP, American Society for Colposcopy and Cervical Pathology; ASC-US, atypical squamous cells of undetermined significance; CIN2, cervical intraepithelial neoplasia grade 2; HPV, human papillomavirus; LSIL, low-grade squamous intraepithelial lesion.

^{*} Women should not be screened annually at any age by any method.

[†] ASC-US cytology with secondary HPV testing for management decisions.

Prostat Kanseri

- Otopsi serileri başka nedenlerle ölen erkeklerde %60–70 oranında prostat kanseri saptanmış.
- ☐ Yaşam boyunca erkeklerin %15-20 oranında prostat kanseri tanısı konuyor ve yalnızca %3 prostat kanserine bağlı ölüyor
- ☐ Düşük riskli prostat kanserli hastalarda cerrahi ya da hiçbir şey yapmadan gözlem arasında 20 yıllık takiplerde bir fark yok

Prostat Kanseri

Tarama amaçlı PSA

- ☐ 1986 yılında prostat kanserinin seyrini takip etmek için PSA kullanımı FDA onayı aldı.
- 1994 yılında rektal tuşe ile birlikte PSA kullanımı semptomu olmayan erkeklerde tarama testi olarak kullanımına onay verildi.
- ☐ PSA semptomu olan hastalarda problemin kaynağını anlamada yardımcı olabilir
- Bening prostat hipertrofisi, prostatit durumunda artabilir.

Prostat Kanseri Tarama amaçlı PSA

Yakın zamana kadar 50 yaş sonrası yılık PSA düzeyi ile tarama öneriliyordu.
Bazı riskli gruplarda, kardeş ve baba prostat kanseri, tarama yaşı 40-45 olarak öneriliyordu.
Ama son yapılan çalışmalar PSA taraması ile artmış aşırı tetkik ve girişim buna bağlı artan komplikasyonlar, PSA rutin kullanımını tartışmalı yapmış
PSA istenecek ise oluşabilecek zarar ve yarar konusunda hasta mutlaka bilgilendirilmelidir.
PSA 4 ng/ml üstünde olanlarda tekrarlanan test pozitif ise prostat biyopsisi önerilir

Prostat Kanseri PSA–Handikapları

Overdiagnosis ve Overtreatment

PSA ile tarama küçük semptomatik olmayan ve indolent gidecek tümörleri saptayabilir
Buna bağlı gereksiz girişim ve tedavilere neden olabilir
Yanlış pozitif buna bağlı gereksiz tetkik ve psikolojik stres
PSA yüksek olanların %25 prostat ca tanısı alıyor
Yanlış negatif PSA normal aralıkta olmasına rağmen prostat ca olabilir
İki büyük çalışma %17–50 oranında Overdiagnosis saptanmış

Prostat Kanseri PSA Tarama ERSPC Çalışması

N Engl J Med. 2012 Mar 15;366(11):981-90. doi: 10.1056/NEJMoa1113135.

Prostate-cancer mortality at 11 years of follow-up.

Schröder FH, Hugosson J, Roobol MJ, Tammela TL, Ciatto S, Nelen V, Kwiatkowski M, Lujan M, Lilja H, Zappa M, Denis LJ, Recker F, Páez A, Määttänen L, Bangma CH, Aus G, Carlsson S, Villers A, Rebillard X, van der Kwast T, Kujala PM, Blijenberg BG, Stenman UH, Huber A, Taari K, Hakama M, Moss SM, de Koning HJ, Auvinen A; ERSPC Investigators.

⊕ Collaborators (165)

Erratum in

N Engl J Med. 2012 May 31;366(22):2137.

Abstract

BACKGROUND: Several trials evaluating the effect of prostate-specific antigen (PSA) testing on prostate-cancer mortality have shown conflicting results. We updated prostate-cancer mortality in the European Randomized Study of Screening for Prostate Cancer with 2 additional years of follow-up.

METHODS: The study involved 182,160 men between the ages of 50 and 74 years at entry, with a predefined core age group of 162,388 men 55 to 69 years of age. The trial was conducted in eight European countries. Men who were randomly assigned to the screening group were offered PSA-based screening, whereas those in the control group were not offered such screening. The primary outcome was mortality from prostate cancer.

RESULTS: After a median follow-up of 11 years in the core age group, the relative reduction in the risk of death from prostate cancer in the screening group was 21% (rate ratio, 0.79; 95% confidence interval [CI], 0.68 to 0.91; P=0.001), and 29% after adjustment for noncompliance. The absolute reduction in mortality in the screening group was 0.10 deaths per 1000 person-years or 1.07 deaths per 1000 men who underwent randomization. The rate ratio for death from prostate cancer during follow-up years 10 and 11 was 0.62 (95% CI, 0.45 to 0.85; P=0.003). To prevent one death from prostate cancer at 11 years of follow-up, 1055 men would need to be invited for screening and 37 cancers would need to be detected. There was no significant between-group difference in all-cause mortality.

CONCLUSIONS: Analyses after 2 additional years of follow-up consolidated our previous finding that PSA-based screening significantly reduced mortality from prostate cancer but did not affect all-cause mortality. (Current Controlled Trials number, ISRCTN49127736.).

Prostat Kanseri PSA Tarama: ERSPC Çalışması

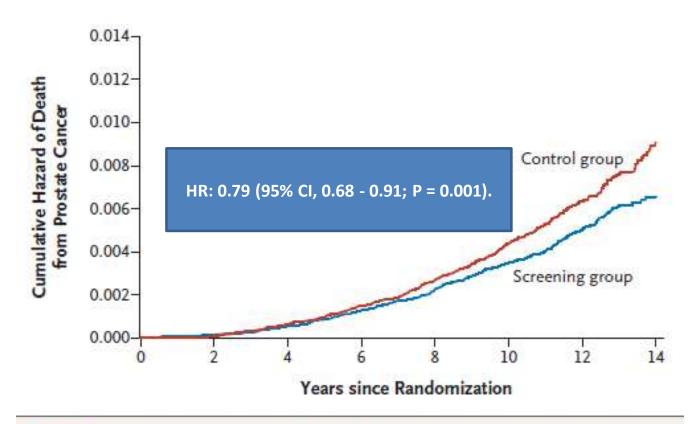


Figure 2. Cumulative Hazard of Death from Prostate Cancer among Men 55 to 69 Years of Age.

Values are not included for centers in France because of the short follow-up period (median, 4.6 years). The Nelson-Aalen method was used to calculate the cumulative hazard of death from prostate cancer.

Prostat Kanseri PSA Tarama–Handikapları





Bir Kırlangıç ile bahar gelmez

Bir tesadüf, iki bahar geliyor

Prostat Kanseri PLCO Çalışması

Abstract

Send to:

Send to:

J Natl Cancer Inst. 2012 Jan 18;104(2):125-32. doi: 10.1093/jnci/djr500. Epub 2012 Jan 6.

Prostate cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial: mortality results after 13 years of follow-up.

Andriole GL¹, Crawford ED, Grubb RL 3rd, Buys SS, Chia D, Church TR, Fouad MN, Isaacs C, Kvale PA, Reding DJ, Weissfeld JL, Yokochi LA, O'Brien B, Ragard LR, Clapp JD, Rathmell JM, Riley TL, Hsing AW, Izmirlian G, Pinsky PF, Kramer BS, Miller AB, Gohagan JK, Prorok PC; PLCO Project Team.

- Collaborators (18)
- Author information

Abstract

BACKGROUND: The prostate component of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial was undertaken to determine whether there is a reduction in prostate cancer mortality from screening using serum prostate-specific antigen (PSA) testing and digital rectal examination (DRE). Mortality after 7-10 years of follow-up has been reported previously. We report extended follow-up to 13 years after the trial.

METHODS: A total of 76 685 men, aged 55-74 years, were enrolled at 10 screening centers between November 1993 and July 2001 and randomly assigned to the intervention (organized screening of annual PSA testing for 6 years and annual DRE for 4 years; 38 340 men) and control (usual care, which sometimes included opportunistic screening; 38 345 men) arms. Screening was completed in October 2006. All incident prostate cancers and deaths from prostate cancer through 13 years of follow-up or through December 31, 2009, were ascertained. Relative risks (RRs) were estimated as the ratio of observed rates in the intervention and control arms, and 95% confidence intervals (CIs) were calculated assuming a Poisson distribution for the number of events. Poisson regression modeling was used to examine the interactions with respect to prostate cancer mortality between trial arm and age, comorbidity status, and pretrial PSA testing. All statistical tests were two-sided.

RESULTS: Approximately 92% of the study participants were followed to 10 years and 57% to 13 years. At 13 years, 4250 participants had been diagnosed with prostate cancer in the intervention arm compared with 3815 in the control arm. Cumulative incidence rates for prostate cancer in the intervention and control arms were 108.4 and 97.1 per 10 000 person-years, respectively, resulting in a relative increase of 12% in the intervention arm (RR = 1.12, 95% CI = 1.07 to 1.17). After 13 years of follow-up, the cumulative mortality rates from prostate cancer in the intervention and control arms were 3.7 and 3.4 deaths per 10 000 person-years, respectively, resulting in a non-statistically significant difference between the two arms (RR = 1.09, 95% CI = 0.87 to 1.36). No statistically significant interactions with respect to prostate cancer mortality were observed between trial arm and age (P (interaction) = .81), pretrial PSA testing (P(interaction) = .52), and comorbidity (P(interaction) = .68).

CONCLUSIONS: After 13 years of follow-up, there was no evidence of a mortality benefit for organized annual screening in the PLCO trial compared with opportunistic screening, which forms part of usual care, and there was no apparent interaction with age, baseline comorbidity, or pretrial PSA testing.

Prostat Kanseri PSA Tarama-PLCO Çalışması

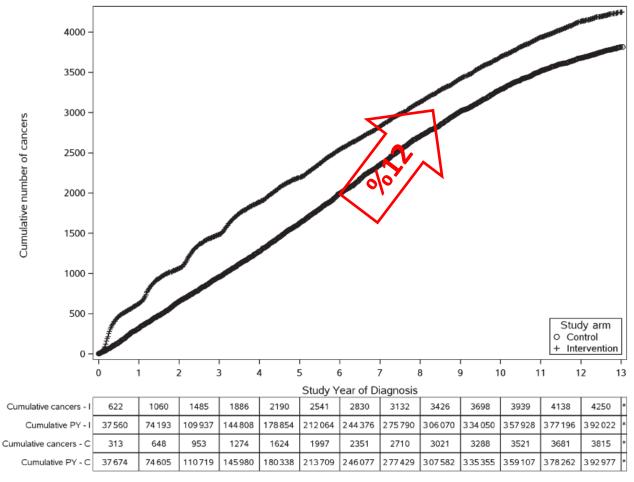


Figure 2. Cumulative number of prostate cancers in the intervention and control arms from year 1 to year 13. C = control arm; I = intervention arm; PY = person-years.

Prostat Kanseri PSA Tarama-PLCO Çalışması

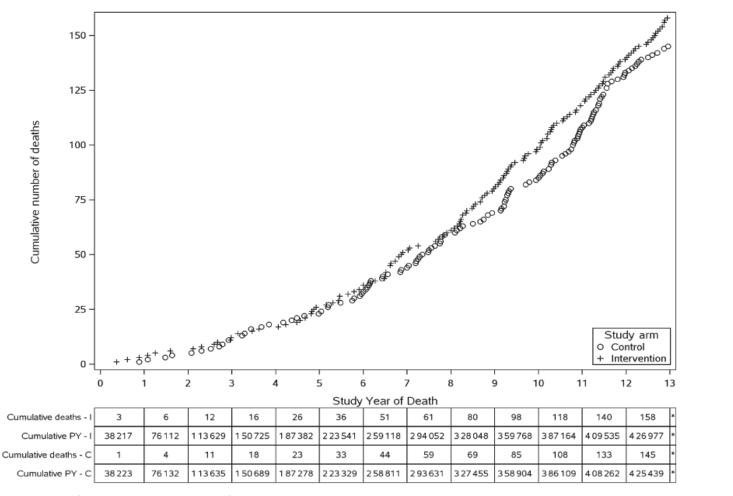


Figure 3. Cumulative deaths from prostate cancer in the intervention and control arms from year 1 to year 13. C = control arm; I = intervention arm; PY = person-years.

Prostat Kanseri PSA–Handikapları

Annals of Internal Medicine



SCREENING FOR PROSTATE CANCER

CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population		Adult Males				
Recommendation		Do not use prostate-specific antigen (PSA)-based screening for prostate cancer.				
		Grade: D				
Screening Tests	Contemporary recommendations for prostate cancer screening all incorporate the measurement of serum PSA levels; other methods of detection, such as digital rectal examination or ultrasonography, may be included.					
	prostate cano	nvincing evidence that PSA-based screening programs result in the detection of many cases of asymptomati- er, and that a substantial percentage of men who have asymptomatic cancer detected by PSA screening hav It either will not progress or will progress so slowly that it would have remained asymptomatic for the man's lifetime (i.e., PSA-based screening results in considerable overdiagnosis).				
Interventions	Management strategies for localized prostate cancer include watchful waiting, active surveillance, surgery, and radiation therapy. There is no consensus regarding optimal treatment.					
Balance of Harms and Benefits	The reduction in prostate cancer mortality 10 to 14 years after PSA-based screening is, at most, very small, even for men in the optimal age range of 55 to 69 years.					
	The harms	of screening include pain, fever, bleeding, infection, and transient urinary difficulties associated with prostate biopsy, psychological harm of false-positive test results, and overdiagnosis.				
	death. Bec	reatment include erectile dysfunction, urinary incontinence, bowel dysfunction, and a small risk for prematur ause of the current inability to reliably distinguish tumors that will remain indolent from those destined to be I men are being subjected to the harms of treatment for prostate cancer that will never become symptomati				
	The benefits of PSA-based screening for prostate cancer do not outweigh the harms.					
Other Relevant USPSTF Recommendations	Recomm	Recommendations on screening for other types of cancer can be found at www.uspreventiveservicestaskforce.org.				

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

Prostat Kanseri PSA Tarama–Handikapları

Figure 2. Relative risk of prostate cancer death for men screened with PSA versus control participants, by country.

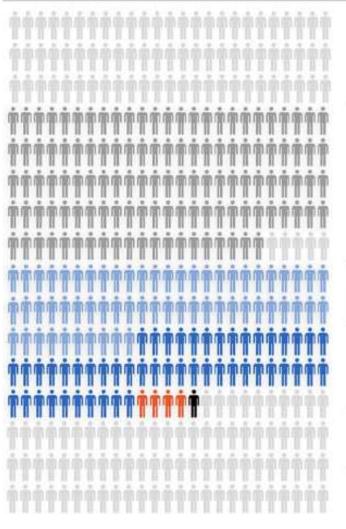
Country	Scree	ACTOR DE LOS	Con	The state of the s	Risk Ratio			Risk Ratio		
	Deaths	Total	Deaths	Total	(95% CI)			(95% CI)		
PLCO trial								8		
United States	158	38 340	145	38 345	1.09 (0.87–1.36)				3	
ERSPC trial										
Sweden	39	5901	70	5951	0.56 (0.38-0.83)		10	43		
Belgium	22	4307	25	4255	0.86 (0.48-1.52)		8		- 11	
Netherlands	69	17 443	97	17 390	0.71 (0.52-0.96)		9 7 - A			
Italy	19	7266	22	7251	0.86 (0.46-1.58)		19	100		
Finland	139	31 970	237	48 409	0.89 (0.72-1.09)			-		
Spain	2	1056	1	1141	2.15 (0.20-23.77)	<			-	->
Switzerland	9	4948	10	4955	0.89 (0.36-2.20)				<u></u>	
						0.2	0.5	1.0	2.0	5.
							Favors Scr		Favors Control	

ERSPC = European Randomized Study of Screening for Prostate Cancer; PLCO = Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; PSA = prostate-specific antigen.

Prostat Kanseri PSA–Handikapları

BENEFITS AND HARMS OF PSA SCREENING FOR PROSTATE ENLARGE C

1,000 men ages 55-69 screened every 1-4 years for 10 years with a PSA test



1,000 men screened.

Of these:

100-120

get false-positive results that may cause anxiety and lead to biopsy

(Possible side effects of biopsies include serious infections, pain, and bleeding)

110

get a prostate cancer diagnosis, and of these men:

· at least 50

will have treatment complications, such as infections, sexual dysfunction,or bladder or bowel control problems

. 4-5

die from prostate cancer (5 die among men who do not get screened)

. 0-1

death from prostate cancer is avoided

Prostat Kanseri PSA-Handikapları

CLINICAL GUIDELINE | Screening for Prostate Cancer: USPSTF Recommendation Statement

Table 1. What the USPSTF Grades Mean and Suggestion	ons for Practice
---	------------------

Grade	Definition	Suggestions for Practice		
4	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.		
3	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.		
c	Note: The following statement is undergoing revision. Clinicians may provide this service to selected patients depending on individual circumstances. However, for most persons without signs or symptoms there is likely to be only a	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.		
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.		
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.		

Prostat Kanseri PSA Tarama

- ☐ American Urological Association (AUA)
- ☐ American Cancer Society (ACS)
 - 45-75 Yaşları arasında bireylerin fayda ve zararları konusunda bilgilendirilmesi ve hasta onay verirse yapılması
- ☐ ESMO, rutinde önermez, yüksek riskli bireylerde önerilebilir
- ☐ American College of Physicians (ACP)
- ☐ Canadian Task Force on Preventive Health Care
 PSA rutin taramada kullanımı önermez

Prostat Kanseri Yüksek Risk Grubu

- ☐ Aile birinci derece akrabalarda 60 yaş öncesi prostat ca öyküsü, 2-2.5 x
- ☐ BRCA1, BRCA2 mutasyou 2-6x
- ☐ Lynch sendromu 2-5x
- ☐ BRCA mutasyonu olanlarda tarama yaşı 40

Prostat Kanseri PSA Tarama



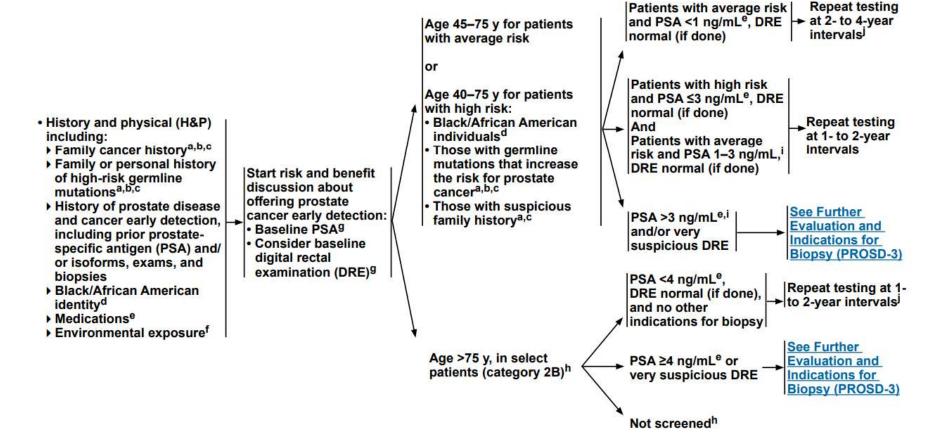
NCCN Guidelines Version 2.2023 Prostate Cancer Early Detection

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EARLY DETECTION EVALUATION



Diğer Tarama Testler

AFP/ Karaciğer USG

- ☐ Yüksek riskli hastalarda Hepatoselüler kanser erken teşhisinde katkıda bulunabilir
- ☐ Yanlış pozitiflik ve buna bağlı komplikasyonlar

Yanlış negatiflik ve buna bağlı geç tanı handikaplarıdır

Over, Fallop tüpleri, Primer periton kanserlerinde Erken Tanı- Tarama

☐ Pelvik Muayane

☐ Transvaginal USG

☐ Ca 125

National Cancer Institute çalışması, bu testlerin semptomsuz kadınlarda kombine olarak kullanılmasının sağkalım üzerinde olumlu bir etkisi saptamamış.

☐ Rutin tarama amaçlı önerilmez

SONUÇ

Kadınlar için önerilen ve yaşamı uzattığı gösterilmiş tarama testleri Kolonoskopi, sigmoidoskopi, Gaita gizli kan testleri, 45–70 yaşları arasında Pap smear testinin 21–29 yaşında 3 yılda bir yapılması. 30–65 yaşları arasında Pap smear ve HPV DNA 5 yılda bir bakılması ya da 3 yılda bir Pap smear bakılması önerilir. 25-40 yaşları arasında 1-3 yılda meme muayenesi, 40 yaş ve sonrası yıllık mamografi ya da 2 yılda bir mamografi 55-74 Yaşları arasında, 30 yıl/paket sigara içen bireylere düşük doz helikal tomografi

SONUÇ

Erkekle için önerilen ve yaşamı uzattığı gösterilmiş tarama testleri

- Kolonoskopi, sigmoidoskopi, Gaita gizli kan testleri, 45–70 yaşları arasında
- ☐ 55-74 Yaşları arasında, 30 yıl/paket sigara içen bireylere taramaya yönelik tomografi
- PSA istenmesi konusunda fikir birliği yoktur. Yüksek riskli olmayan bireylere yaygın görüş PSA ile taramama yönündedir. PSA istenecekse mutlaka fayda ve zararları konusunda bilgilendirme yapılmalıdır.