폐암과 전립선암 검진

김 열
국립암센터 가정의학과

건강검진의 필요성

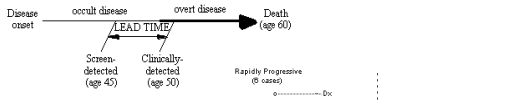
- **건강검진(Screening)**
  - 질병의 증상이 없는 사람들 중에서 질병을 지니고 있을 가능성이 높은 사람들을 빠르고 분명하게 가려내기 위해 적절한 검사를 시행하여 조기에 질병 유무를 밝혀내는 것
- **검진의 목적**
  - 질병의 조기발견 및 조기치료 – 2차예방
    (Cf, 1차예방 – 건강생활실천)
  - 국민의료비 절감 – 연구결과 : 비용효과(4.1-16.6배)
  - 질병의 사전예방으로 국민건강 수준의 향상

집단 검진의 조건

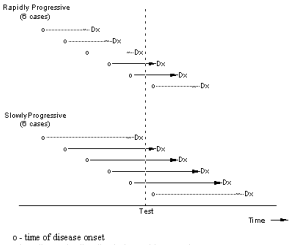
- 국내 역학상 사망률이나 치명률이 높은 질병
- 조기발견에 따른 효과적 치료방법 확립
- 치료가능한 조기에 발견할 수 있는 검사
- 검진방법의 민감도, 특이도, 예측도
- 비용이 싸고, 받아들일 수 있는 검사

Screening bias

- Lead time bias



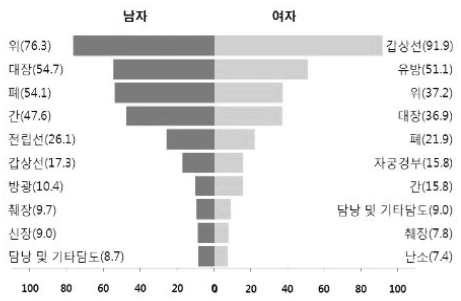
- Length time bias



암종별 발생 현황 (2008)

순위	암종	발생자수	분율(%)	조발생률	연령표준화 발생률*
	모든암	**178,816**	100.0	361.9	286.8
1	**위**	28,078	15.7	56.8	43.8
2	**갑상선**	26,923	15.1	54.5	47.6
3	**대장**	22,623	12.7	45.8	35.1
4	**폐**	18,774	10.5	38.0	28.1
5	**간**	15,663	8.8	31.7	24.5
6	**유방**	12,659	7.1	25.6	21.3
7	**전립선**	6,471	3.6	13.1	9.6
8	**담낭 및 기타담도**	4,378	2.4	8.9	6.5
9	**췌장**	4,320	2.4	8.7	6.5
10	**자궁경부**	3,888	2.2	7.9	6.6

성별 10대암 조발생률 (2008)



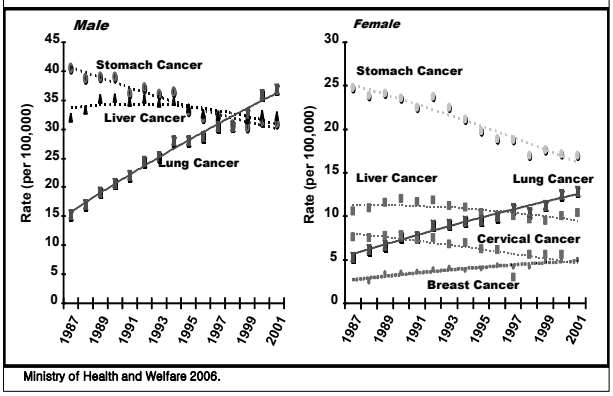
미국과 우리나라 암발생 순위 비교

순위	남자		여자	
	미국(2007)	한국 (2007)	미국 (2007)	한국 (2007)
1	**전립선(156.9)**	위(70.4)	유방(120.4)	갑상선(73.5)
2	**폐(80.5)**	**폐(52.1)**	**폐(54.5)**	유방(47.4)
3	대장(52.7)	대장(49.7)	대장(39.7)	위(35.0)
4	방광(36.0)	간(45.2)	자궁(24.1)	대장(33.9))
5	악성흑색종(23.5)	**전립선(21.5)**	갑상선(17.2)	**폐(20.4)**
6	비호즈킨림프종 (22.6)	갑상선(12.8)	비호지킨림프종 (15.7)	간(15.4)
7	신장(20.8)	방광(10.0)	악성흑색종(15.4)	자궁경부(14.8)
8	구강, 인두(16.1)	췌장(8.9)	난소(12.2)	담낭, 담도(8.5)
9	백혈병(15.0)	담낭, 담도(8.4)	신장(10.9)	난소(7.5)
10	췌장(13.2)	신장(8.0)	췌장(10.2)	췌장(7.1)

※( )안의 숫자는 인구 10만명당 해당 암의조발생률

폐암 검진

암사망율의 변화



Ministry of Health and Welfare 2006.

Chest X-ray + Sputum cytology

RCTs of Lung Cancer Screening with Chest Radiography with or without Sputum Cytology

Study	Intervention	No. of Participants	No. of Lung Cancers Detected at First Screening (Prevalence)	No. of Lung Cancers Detected After First Screening	No. of Stage III and IV Cancers*	Lung Cancer Mortality†‡	5-year Survival (%)†
Memorial Sloan-Kettering (11,12)					173	NA	35
Experimental arm	Annual chest radiography, sputum cytology every 4 mo	4968	30	146	…	…	…
Control arm	Annual chest radiography	5072	23	155	…	…	…
Johns Hopkins (13,14)					NA		NA
Experimental arm	Annual chest radiography, sputum cytology every 4 mo	5226	39	194	…	3.4/1000 PY	…
Control arm	Annual chest radiography	5161	40	202	…	3.8/1000 PY	…
Mayo Lung Project (15–17)			91 in all§				
Experimental arm	Chest radiography, sputum cytology every 4 mo	4618	…	206	123‖	4.4/1000 PY	35
Control arm	Recommended annual chest radiography, sputum cytology	4593	…	160	119‖	3.9/1000 PY	19
Czechoslovakian RCT (18,19)			19 in all§				NA
Experimental arm	Chest radiography and sputum cytology every 6 mo × 3 years, annually after year 3	3171	…	108	53	7.8%	…
Control arm	Chest radiography and sputum cytology annually after year 3	3174	…	82	46	6.8%	…

CT screening for lung cancer

- 85%(412명/484명)가 stage I
- 10년 생존율 88%
- underwent surgical resection(302명) – 10년 생존율 92%
- Stage I 에서 치료받지 않은 8명은 5년 내 사망

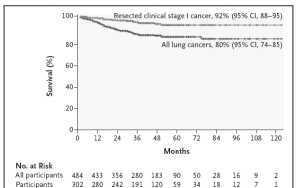
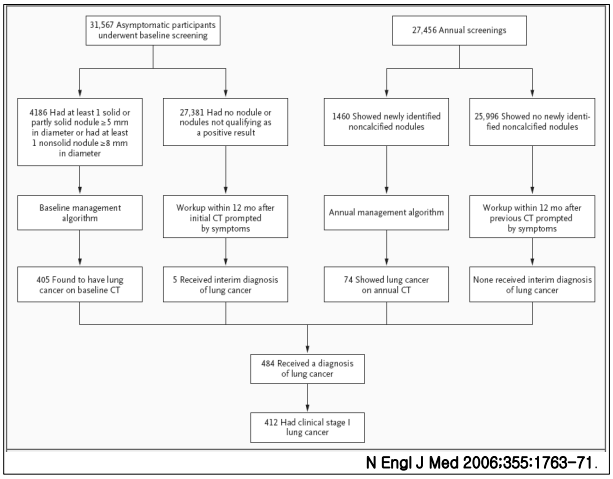
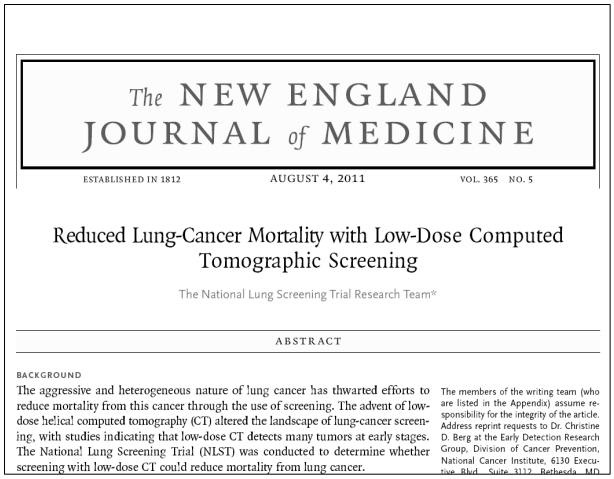


Figure 2. **Kaplan–Meier Survival Curves for 484 Participants with Lung Cancer and 302 Participants with Clinical Stage I Cancer Resected within 1 Month after Diagnosis.**
The diagnoses were made on the basis of CT screening at baseline combined with cycles of annual CT.



N Engl J Med 2006;355:1763-71.



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Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

ABSTRACT

BACKGROUND

The aggressive and heterogeneous nature of lung cancer has thwarted efforts to reduce mortality from this cancer through the use of screening. The advent of low-dose helical computed tomography (CT) altered the landscape of lung-cancer screening, with studies indicating that low-dose CT detects many tumors at early stages. The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer.

The members of the writing team (who are listed in the Appendix) assume responsibility for the integrity of the article. Address reprint requests to Dr. Christine D. Berg at the Early Detection Research Group, Division of Cancer Prevention, National Cancer Institute, 6130 Executive Blvd., Suite 3112, Bethesda, MD

Methods

- Trial Oversight
  - ✓ a randomized trial of screening
  - ✓ the control group: Chest radiography
  - ✓ 53,454 persons enroll
    - ❑ 26,722 (low-dose CT) vs 26,732 (chest radiography)

Participants

- Screening: August 2002 -September 2007
- Data collect: events that occurred through December 31, 2009
- **Participant**
  - ✓ **55-74 years**
  - ✓ **history of cigarette smoking of at least 30 packyears,**
  - ✓ **ex- smokers(quit within the previous 15 years.)**
- Excluded Participants
  - ✓ previously received a diagnosis of lung cancer
  - ✓ undergone chest CT within 18 months before enrollment
  - ✓ hemoptysis
  - ✓ unexplained weight loss of more than 6.8 kg in the preceding year

Screening

- three screenings (T0, T1, and T2) at 1-year intervals
- first screening (T0) performed soon after the time of randomization
- Positive ("suspicious for" lung cancer)
  - ✓ noncalcified nodule or mass (>4mm in CT, any size in CPA), adenopathy , effusion

Results

Table 1. **Selected Baseline Characteristics of the Study Participants.***

Characteristic	Low-Dose CT Group (N = 26,722)	Radiography Group (N = 26,732)
	number (percent)	
Age at randomization		
<55 yr†	2 (<0.1)	4 (<0.1)
55–59 yr	11,440 (42.8)	11,420 (42.7)
60–64 yr	8,170 (30.6)	8,198 (30.7)
65–69 yr	4,756 (17.8)	4,762 (17.8)
70–74 yr	2,353 (8.8)	2,345 (8.8)
≥75 yr†	1 (<0.1)	3 (<0.1)
Sex		
Male	15,770 (59.0)	15,762 (59.0)
Female	10,952 (41.0)	10,970 (41.0)
Race or ethnic group‡		
White	24,289 (90.9)	24,260 (90.8)
Black	1,195 (4.5)	1,181 (4.4)
Asian	559 (2.1)	536 (2.0)
American Indian or Alaska Native	92 (0.3)	98 (0.4)
Native Hawaiian or other Pacific Islander	91 (0.3)	102 (0.4)
More than one race or ethnic group	333 (1.2)	346 (1.3)
Data missing	163 (0.6)	209 (0.8)
Hispanic ethnic group‡		
Hispanic or Latino	479 (1.8)	456 (1.7)
Neither Hispanic nor Latino	26,079 (97.6)	26,039 (97.4)
Data missing	164 (0.6)	237 (0.9)
Smoking status		
Current	12,862 (48.1)	12,900 (48.3)
Former	13,860 (51.9)	13,832 (51.7)

* CT denotes computed tomography.
† Patients in this age range were ineligible for inclusion in the screening trial but were enrolled and were included in all analyses.
‡ Race or ethnic group was self-reported.

- demographic characteristics and smoking history of the participants -identical in the two groups
- **Median duration of follow-up: 6.5 years**
- The rate of adherence to the screening protocol: 95% (low-dose CT) /93% (radiography group)

Results of Screening

Table 2. Results of Three Rounds of Screening.*

Screening Round	Low-Dose CT				Chest Radiography			
	Total No. Screened	Positive Result	Clinically Significant Abnormality No Suspicious for Lung Cancer	No or Minor Abnormality	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer	No or Minor Abnormality
		no. (% of screened)				no. (% of screened)		
T0	26,309	7191 (27.3)	2695 (10.2)	16,423 (62.4)	26,035	2387 (9.2)	785 (3.0)	22,863 (87.8)
T1	24,715	6901 (27.9)	1519 (6.1)	16,295 (65.9)	24,089	1482 (6.2)	429 (1.8)	22,178 (92.1)
T2	24,102	4054 (16.8)	1408 (5.8)	18,640 (77.3)	23,346	1174 (5.0)	361 (1.5)	21,811 (93.4)

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. Results of screening tests that were technically inadequate (7 in the low-dose CT group and 26 in the radiography group, across the three screening rounds) are not included in this table. A screening test with low-dose CT was considered to be positive if it revealed a nodule at least 4 mm in any diameter or other abnormalities that were suspicious for lung cancer. A screening test with chest radiography was considered to be positive if it revealed a nodule or mass of any size or other abnormalities suspicious for lung cancer.

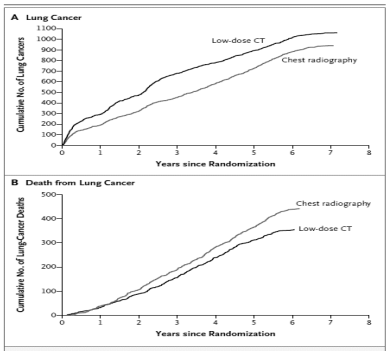
Mortality

	the low-dose CT group	the radiography group
The incidence of lung cancer	645 /100,000 person-years (1060 cancers)	572 /100,000 person-years (941 cancers)
deaths from lung cancer	247/ 100,000 person-years	309/100,000 person-years

relative reduction in the rate of death from lung cancer with low-dose CT screening of 20.0% (95% CI, 6.8 to 26.7; P=0.004).

The rate of death from any cause was reduced in the low-dose CT group, as compared with the radiography group, by 6.7% (95% CI, 1.2 to 13.6; P=0.02).
-> 1877 deaths in low-dose CT group: 2000 deaths in radiography group.

Cumulative Numbers of Lung Cancers and of Deaths from Lung cancer.



전립선암 검진

전립선암 선별검사로 시행되는 있는 검사

- Digital rectal exam
- PSA blood test(Prostate Specific Antigen)
  - Measures protein made by prostate cells
  - Increased PSA levels in blood are usually not due to cancer. common causes include :
    - Benign Prostatic Hypertrophy(BPH)
    - Prostatitis
    - Post-biopsy/surgery

서로 상반되는 3가지 대규모 RCT

찬성
- European Randomized Study of Prostate Cancer(ERSPC)
- Göteborg(Swedish) Trial

→ 유럽

반대
- Prostate, Lung, Colon and Ovarian Trial(PLCO)

→ 미국

European Randomized Study of Prostate Cancer (ERSPC)

- 1991년, 유럽 7개국에서 시작
- 162,000명, 55-69세
- randomized to screening vs. usual care
- Median follow-up : 약 9년
- More cancers detected with screening
  - 5990 vs. 4307
- Fewer prostate cancer deaths in screening group
  - 261 vs. 363
- Conclusion : **20% lower risk** of prostate cancer death in the group invited to screening

Göteborg(Swedish) Trial

- 1995년, 스웨덴의 Goteborg시에서 시작
- 20,000명, 50-64세
- randomized to screening(PSA per 2 years) vs. usual care
  - ERSPC data에 포함시킴.
- Median follow-up 14years
- More cancers detected with screening
  - 1138 cancers vs. 718 cancers
- Fewer prostate cancer deaths in screening group
  - 44 deaths vs. 78 deaths
- Conclusion : **40% lower risk** of prostate cancer death in the group invited to screening

Prostate, Lung, Colon and Ovarian Trial(PLCO)

- 1993년, 미국의 10개 center에서 시작
- 73000명, 55-74세
- Randomized to screening annually vs. routine follow-up
- Median follow-up about 10years
- At 7years, screening found more cases of cancer
  - 2820 cancers vs2332 cancers
- More prostate cancer deaths in screening arm
  - 7 years : 50 deaths vs. 44 deaths
  - 10years : 92 deaths vs. 82 deaths
- Conclusion : **no mortality benefit** among those invited to screening

2010 ACS guideline

- 기대 여명이 10년 이상 남은 사람에게만 권유
- Informed decision (uncertainties, riks, and potential benefits)
  - Average risk : 50세 부터
  - High risk : 45세 부터
    - African American men
    - 65세 이전에 전립선 암을 진단 받은 first-degree relative 가 있는 경우
  - 75세 이상은 권고하지 않음

2010 ACS guideline

- Informed decision 후 선별검사를 하겠다고 한 경우 선별검사는 PSA로!
- DRE는 optional. (The digital rectal exam may also be done as a part of screening)
- 검사 간격은 PSA 결과에 따라
  - <2.5ng/mL : 2년 마다
  - 2.5-3.9ng/mL : 1년 마다
  - >4.0ng/mL : further evaluation and/or biopsy

2010 ACS guideline

- Factors that influence the risk of prostate cancer
  - African American race
  - Family history of prostate cancer
  - Incresing age
  - Abnormal digital rectal exam
  - Prior negative prostate biopsy lowers risk
- Web based risk assessment tool

http://deb.uthscsa.edu/URORiskCalc/Pages/calcs.jsp

HEALTH TiPS
WHAT YOU CAN DO

http://www.acpfoundation.org

Screening for Prostate Cancer

Medical groups do not agree on screening men for prostate cancer, this is why...

The screening test for prostate cancer is a blood test. The test can be abnormal for several reasons not just prostate cancer.

The screening test for prostate cancer is a blood test.

Talk to your doctor about screening if you are:

- A man age 50 to 75.
- An African American man.
- A man who has a father or brother with prostate cancer.

Men over age 75 should not be screened.

Most prostate cancers found by screening:

- Are small and slow growing.
- May not be fatal.

Some men may have a faster growing prostate cancer and will benefit from early treatment.
The only way to know if an abnormal test is due to cancer is to do a biopsy.
A biopsy is a minor surgery to get small pieces of the prostate to look at under a microscope.
If the biopsy shows that there are cancer cells then your doctor will recommend treatment.

전립선 선별 검사는 유용할까?

- Overtreatment(발견되지 않았으면 아무런 해를 끼치지 않았을 암을 찾아서 치료하는 것) : 전립선암 치료가 삶을 바꿔놓을 심각한 합병증과 부작용을 일으킬 수 있다.

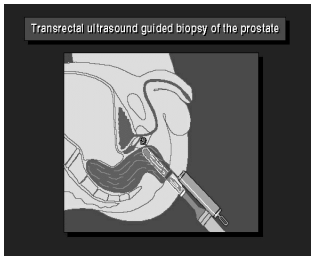
Treatment	Side Effect	Frequency
Radical prostatectomy	Erectile dysfunction	20-70%
	Urinary incontinence	15-50%
External beam radiation therapy	Erectile dysfunction	20-45%
	Urinary incontinence	2-16%
Androgen deprivation therapy	Sexual dysfunction	20-70%
	Hot flashes	50-60%
	Cardiovascular Dz	?
	Diabetes	?

USPSTF

- The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer. **This is a grade D recommendation.**
- US Preventive Services Task Force recommendations, **the PSA screening would be downgraded from an 'I' as in inconclusive to a 'D – no benefit' as in don't. (2011)**
- **기존 recommendation**
  - The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of prostate cancer screening in men younger than age 75 years. Grade: I statement.
  - The USPSTF recommends against screening for prostate cancer in men age 75 years or older. Grade: D recommendation.

전립선암 조기검진-전립선 초음파

- 1° screening에는 이용되지 않음.
  (low sensitivity, specificity)
- DRE와 PSA로 screening 후
  → prostate biopsy에 이용.



요약

- 현재 다수의 건강인을 대상으로 하는 폐암, 전립선암 검진은 그 유용성에 대한 근거가 제한적이거나, 논란이 있음.
- 폐암의 경우 최근 미국의 대규모 비교연구에서 30PY이상 흡연한 그룹에서 매년 저선량흉부CT검사를 받는 경우 폐암 발견율이 높고, 사망률을 감소시켰다고 보고됨.
- 전립선암의 경우 지금까지 시행된 대규모 비교연구의 결과가 상의하여 논란이 있음.
- 개별 진료실 세팅에서는 폐암, 전립선암 검진의 과학적 근거와 한계에 대한 정보를 나눈 후 수검자와 함께 결정하는 것이 바람직할 것임.