ICSN2010(Oxford, July **2010)**

Estimation of overdiagnosis by new technologies for cancer screening

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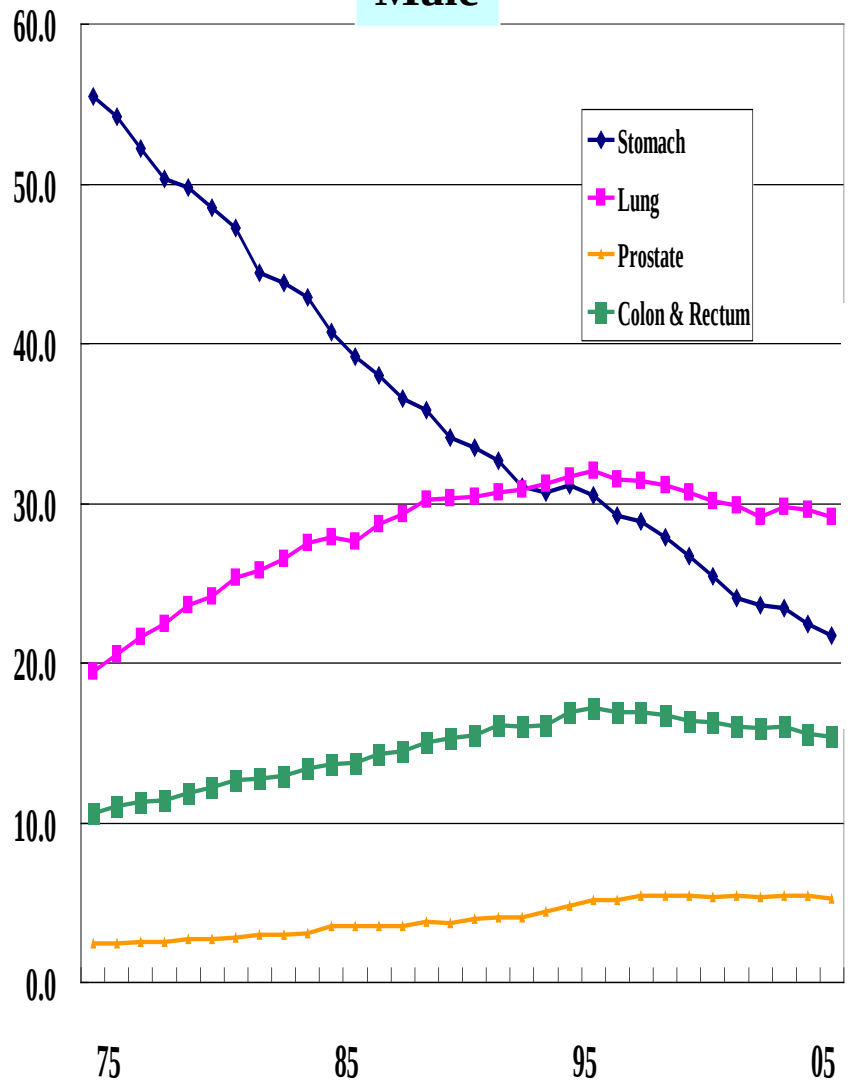
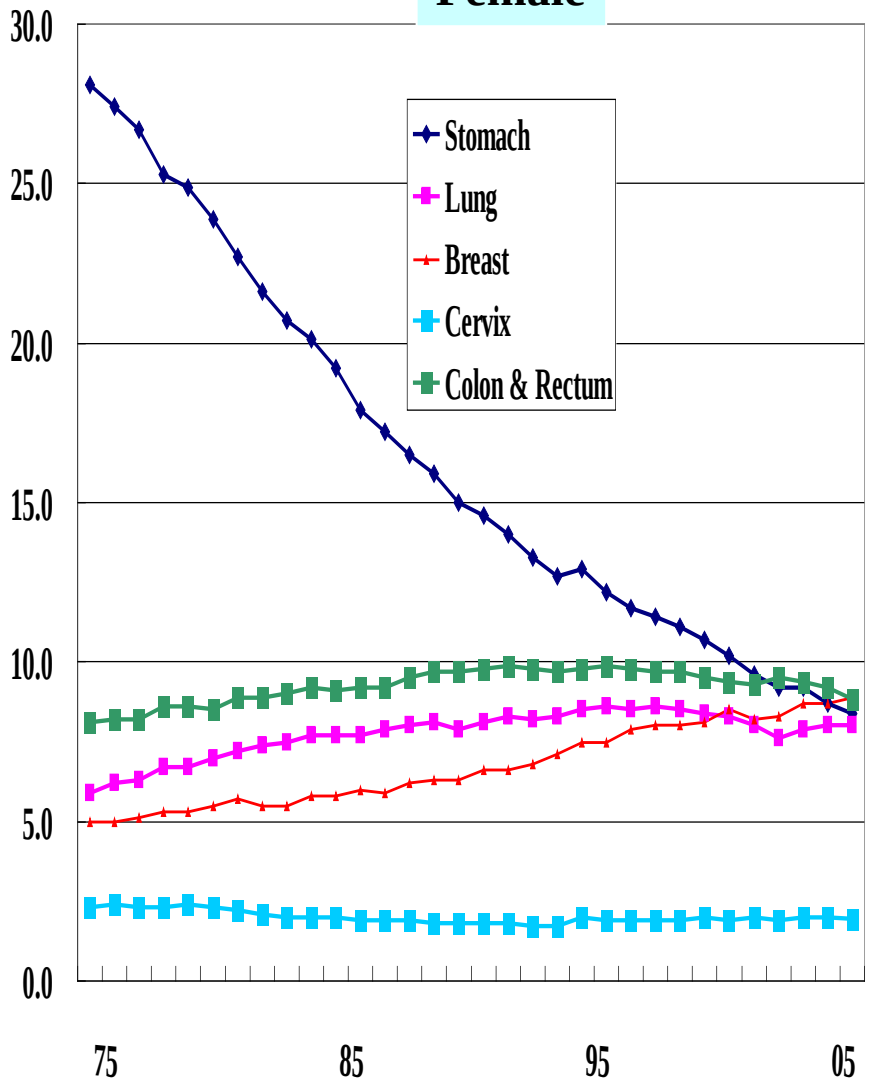
Trends in age-standardized cancer mortality rates





Recommendation of Japanese guideline for cancer screening

Screening	*Methods*	*Population-based screening*	*Opportunistic screening*
Gastric cancer	*Photofluorography*	*Recommended (Grade B)*	*Recommended (Grade B)*
	Endoscopy	*Not recommended*	**Decision making at individual level (Grade I)**
Colorectal cancer	*FOBT (immunological test)*	*Recommended (Grade A)*	*Recommended (Grade A)*
	Total colonoscopy	*Not recommended*	*Can be used (Grade C)*
Lung cancer	*Combination of chest radiography and sputum cytology (limited to current smokers)*	*Recommended (Grade A)*	*Recommended (Grade A)*
	Low-dose CT	*Not recommended*	**Decision making at individual level (Grade I)**
Cervical cancer	*Conventional cytology & Liquid-based cytology*	*Recommended (Grade A)*	*Recommended (Grade A)*
	1) HPV testing (alone) *2) Combination of HPV testing and cytology* *3) HPV testing with cytology triage*	*Not recommended*	**Decision making at individual level (Grade I)**
Prostate cancer	*Prostate specific antigen (PSA)*	*Not recommended*	**Decision making at individual level (Grade I)**

Background

- **New technologies have been expected to be used for cancer screening because of the high detection rate of cancer.**
- **In Japan, multiple health check-ups including cancer screening have been popular at clinical settings. New technologies are often included in such programs.**
- **Even in population based screening, new modalities for cancer screening have been introduced in several local municipalize without evaluation by reliable studies.**

Outlines of research based screening programs

- **One arm prospective study to evaluate the efficacy of cancer screening programs using new modalities**
- **Participants are enrolled on a volunteer basis**
- **Follow-up studies including hospital-based cancer registry, medical chart survey, and response to a questioner survey, are done at every year.**
- **At a minimum requirement, 5 years follow-up have been continued.**

Research programs for screening

Target age

Male : 50 years and over
Female: 40 years and over

Exclusion criteria

Previous diagnosis of cancer
Follow-up for precancerous lesions

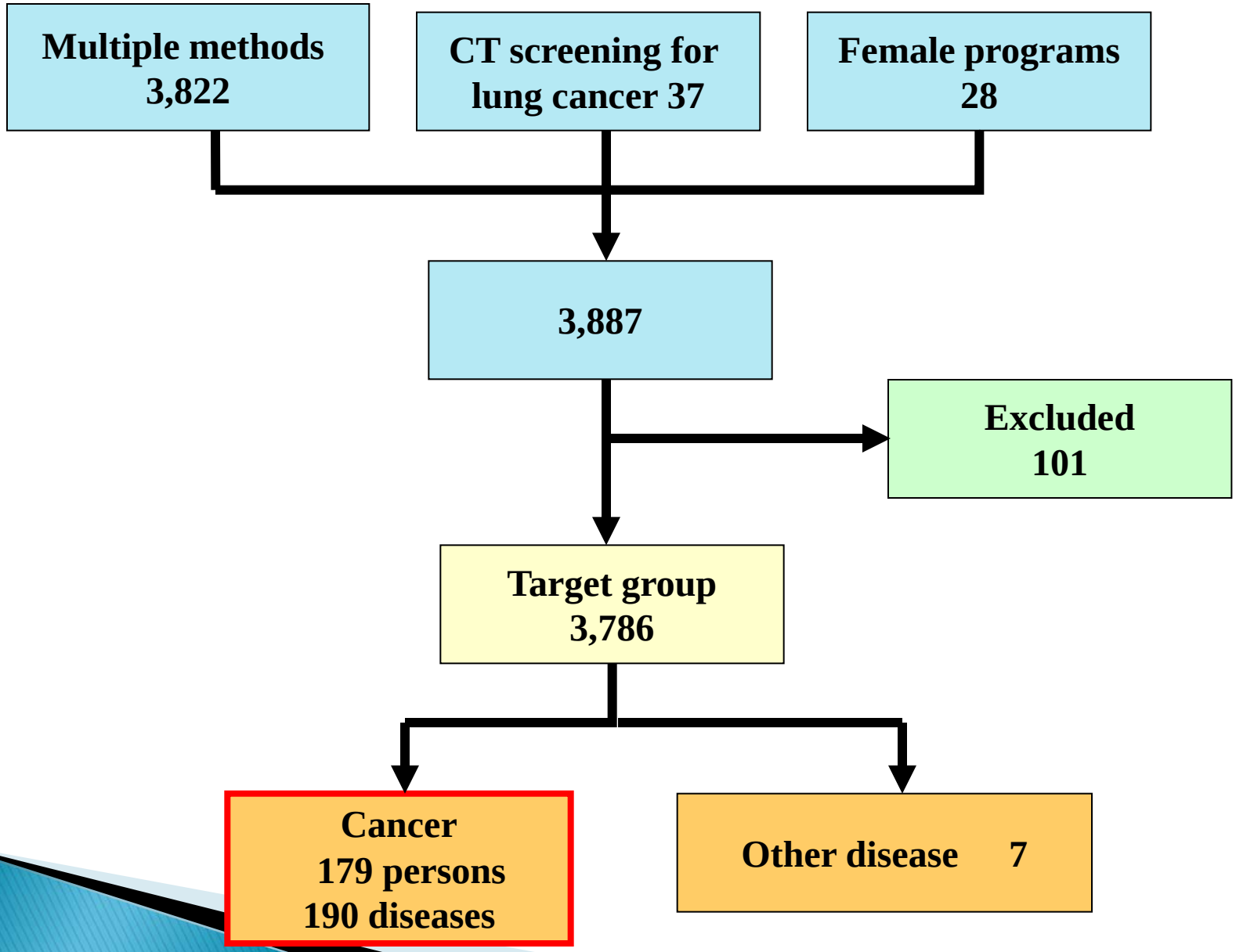
Three research programs

1) Multiple screening for whole body using new technologies including PET
2) Lung cancer screening using low-dose CT
3) Female screening programs for breast, uterus and ovarian cancer

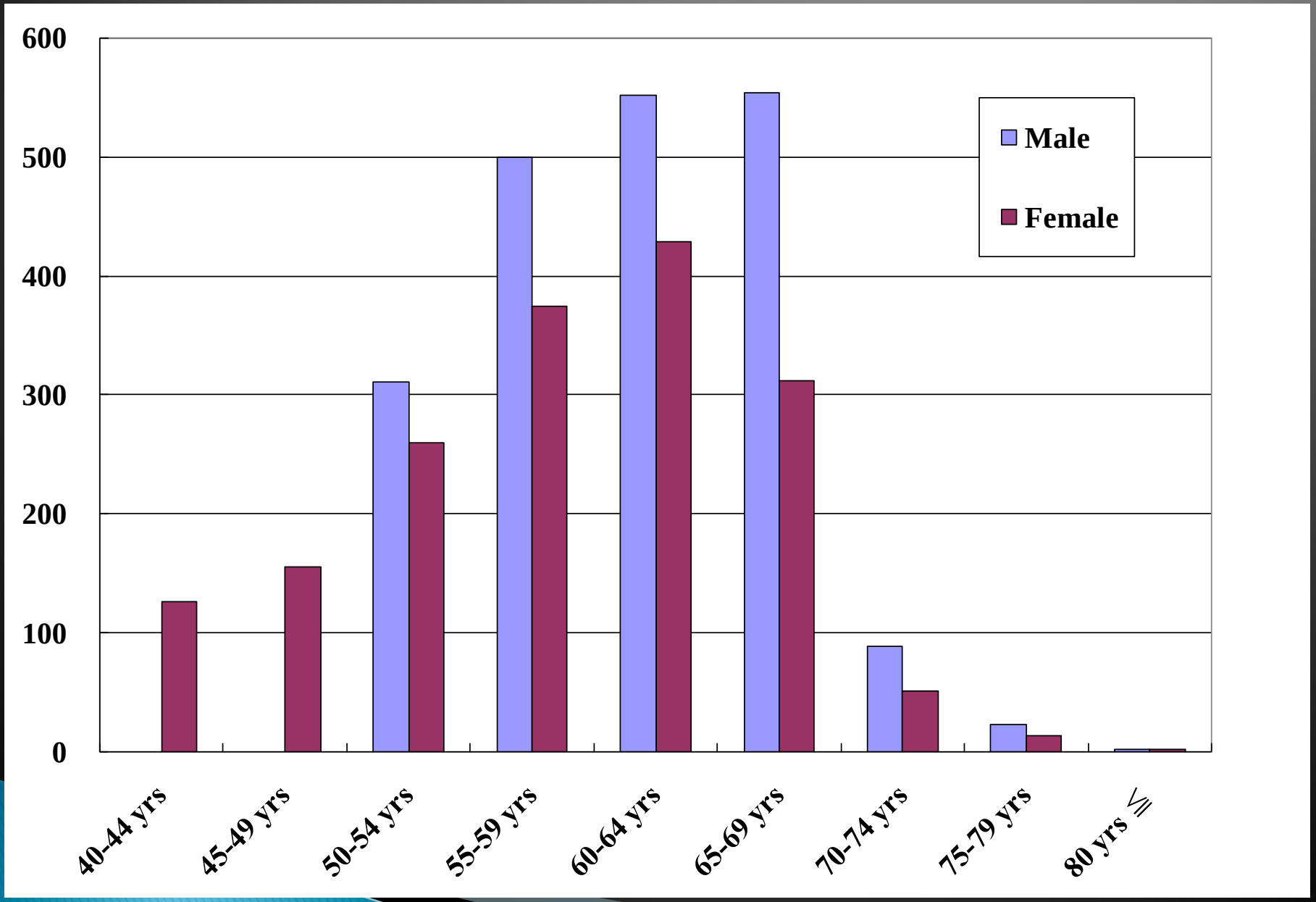
Screening methods of research programs

Target	Recommended screening by the Japanese Cancer Screening Guidelines	Research programs
Esophagus	Not recommended	Endoscopy
Stomach	Radiography	Endoscopy
Cervix	Pap smear	Pap smear
Breast	Combination of mammography and physical examination	Combination of mammography , ultrasonography and physical examination
Lung	Chest X-ray and sputum cytology (limited to current smoker)	Low-dose CT and sputum cytology
Colon & rectum	Fecal occult blood test	Total colonoscopy or barium enema
Liver	Not recommended	Abdominal ultrasonography
Gall bladder Pancreas Kidney	Not recommended	Combination of CA19-9 and ultrasonography
Prostate	Not recommended	PSA
Corpus uteri	Not recommended	Magnetic resonance imaging
Ovary	Not recommended	Magnetic resonance imaging and CA125
Whole body	Not recommended	Positron emission tomography and CEA

Target number of the present study



Distribution of participant in research programs



Detection numbers of research programs

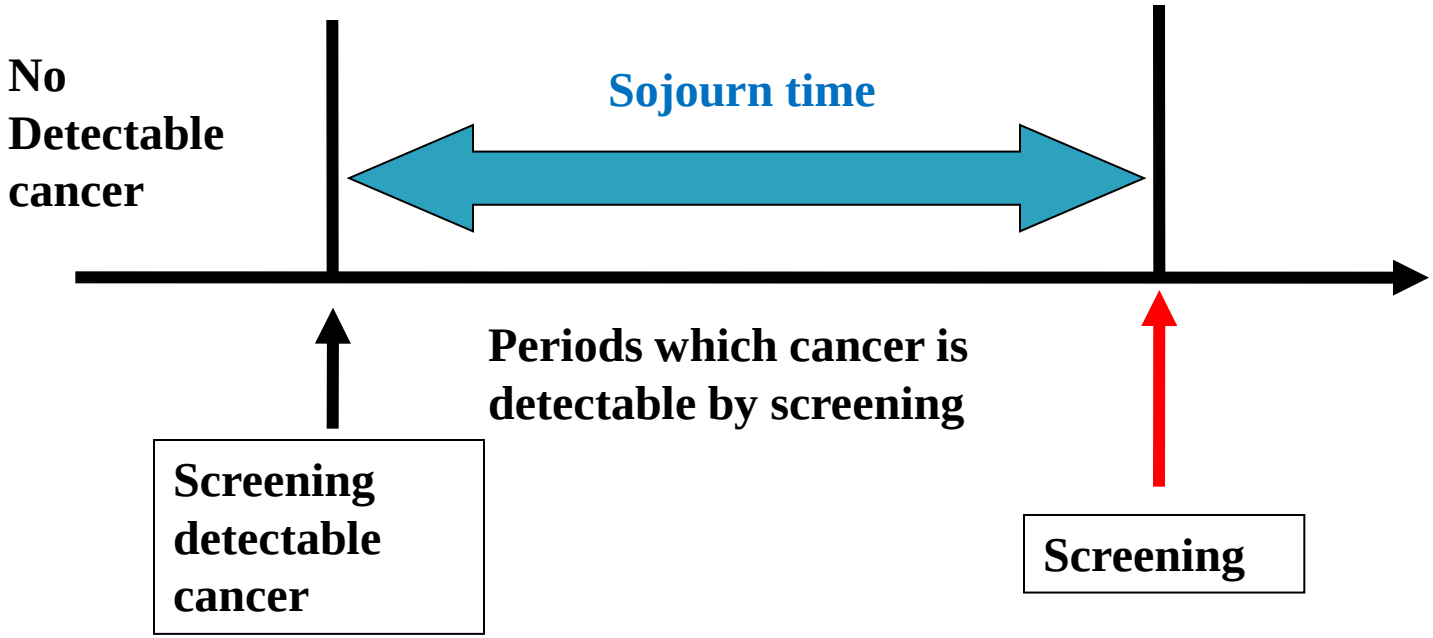
Target for Cancer screening	Method	Sex	Numbers of examinees	Detection numbers	Detection rate (%)
Esophagus	Endoscopy	Male	2,040	8	0.39
		Female	1,684	0	0.00
Stomach	Endoscopy	Male	2,042	28	1.37
		Female	1,684	7	0.42
Colon and rectum	Barium enema	Male	317	4	1.26
		Female	342	4	1.17
Colon and rectum	Total colonoscopy	Male	1,723	26	1.51
		Female	1,342	15	1.12
Lung	CT	Male	2,061	14	0.68
		Female	1,697	18	1.06
Prostate	PSA	Male	2,042	24	1.18
Breast	Combination of mammography , ultrasonography and physical examination	Female	1,712	15	0.88
Others		Male	2,061	15	0.73
		Female	1,725	12	0.70
All		Male	2,061	119	5.77
		Female	1,725	71	4.12

Screening history within a year

Examination	Modality	Previous examination within a year			
		Male (%)		Female (%)	
Stomach	XP	43.5	（887/2040）	30.0	（505/1684）
	GFS	28.7	（586/2040）	23.3	（393/1684）
Colon and rectum	FOBT	52.7	（1074/2040）	40.7	（685/1684）
	BE	4.9	（99/2040）	3.0	（50/1684）
	TCF	15.4	（315/2040）	8.3	（139/1684）
Lung	Chest X-ray	73.9	（1524/2061）	62.0	（1052/1697）
Breast	MMG	-		18.5	（317/1712）

Estimation based on simple model

Expected numbers
＝（Incidence rate/100,000)
×(Numbers of participants)×(Sojourn time)×(Sensitivity)



Three patterns based on screening history

- **Prevalence Screening**

Expected numbers
＝（Incidence rate/100,000)
×(Numbers of participants)×(Sojourn time)×(Sensitivity)

- **Incidence screening for participants tested by same method for screening within 1 year**

Expected numbers
＝（Incidence rate/100,000)
×(Numbers of participants)×(1 year)×(Sensitivity)
+（False negative cases）×(Sensitivity)

- **Incidence screening for participants tested by different method for screening within 1 year**

Assumption of sojourn time and sensitivity

- **Estimation for sojourn time:**
  sojourn time was constant in all age groups

- **Estimation for sensitivity:**
  sensitivity was constant in all age groups
  sensitivity was constant throughout sojourn time

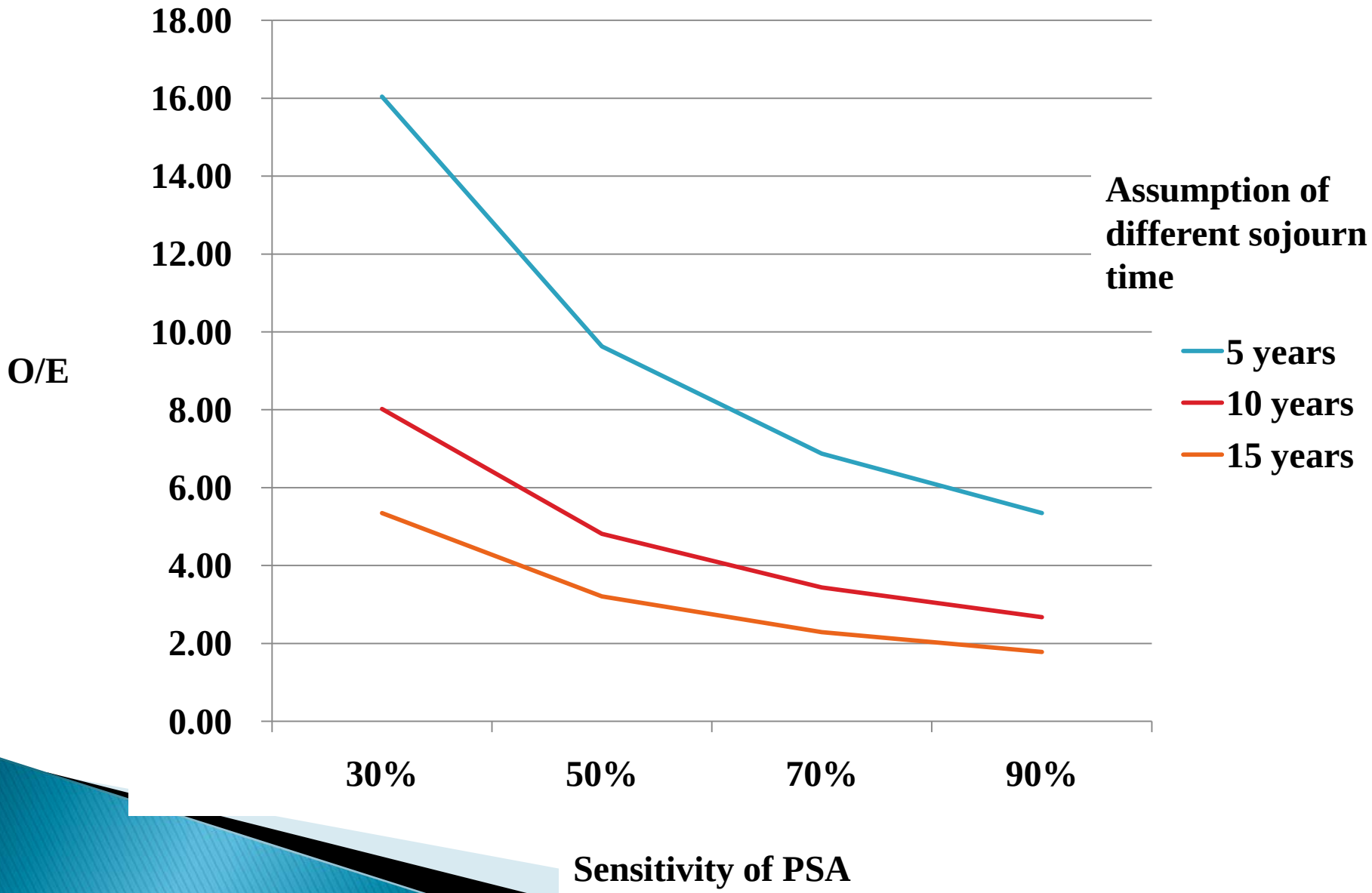
Target for Cancer screening	Method	Baseline assumption Sensitivity（%）	Sojourn time（year）
Stomach	Endoscopy	70	5
Colon &rectum	Barium enema	70	5
	Total colonoscopy	70	10
Lung	CT	80	5
Prostate	PSA	70	10
Breast	Combination of mammography , ultrasonography and physical examination	80	5

Comparison of the observed and expected numbers

Target for cancer screening	Method	Male			Female		
		Observed number	Expected number	O/E	Observed number	Expected number	O/E
Stomach	Endoscopy	28	15.31	1.83	7	3.69	1.9
Colon and rectum	Barium enema	4	2.25	1.78	4	1.08	3.7
	Total colonoscopy	26	21.9	1.19	15	7.64	1.96
Lung	CT	14	10.86	1.29	18	2.38	7.56
Prostate	PSA	24	7	3.43	-	-	-
Breast	Combination of mammography , ultrasonography and physical examination	-	-	-	15	6.22	2.41

$P<0.05$

Sensitivity analysis of prostate cancer screening



Limitations

- **Simple model**

  Estimation of exspected numers of cancers was calucultaed by simple model ignored different sojourn times and senstivity in target age group.

- **Selection bias**

  Participants were volunteers who had health conscious

- **Limited information of screening history**

  Screening history was obtained from a questioner survey but its limited to the previous 1year

- **Short follow-up**

  Observed numbers were limited to the results of first year of screening program. Since cancer detection rate is decreased in subsequent screening, the O/E might be changed.

How should we inform overdiagnosis?

- Screening using new technologies has been supported by briefs of early detection and enthusiasm.
- Overdiagnosis is serious harm for cancer screening. It is common in current screening programs, as well as new technologies.
- Appropriate information related to overdiagnosis is needed to help decision whether or not participate in cancer screening.
- We have developed leaflets for cancer screening guidelines with public involvement, but methods of informing subjects about 'overdiagnosis' are immature.

Conclusions

- **Although cancer screening programs in the present study increased the detection of potentially curable cancers, these modalities, particularly lung, breast and prostate screening, might detect cancers that would not necessarily be clinically significant.**

- **We should weigh the benefits and harms of new technologies and develop methods to inform subjects about overdiagnosis.**