Korean gastric cancer screening program, algorithms and experience.

Jun Haeng Lee, MD.

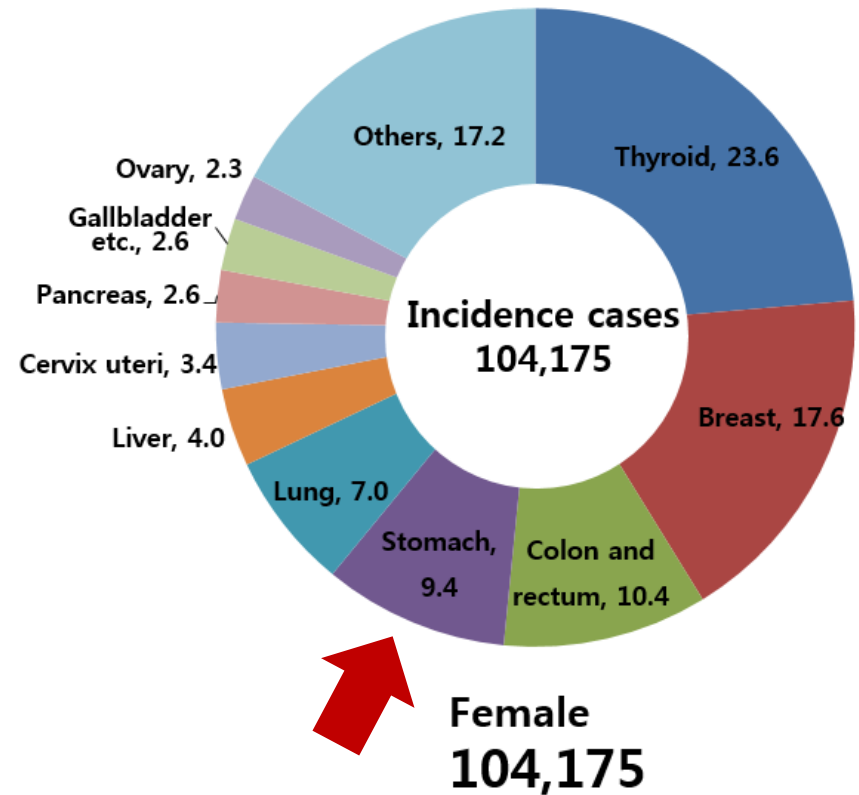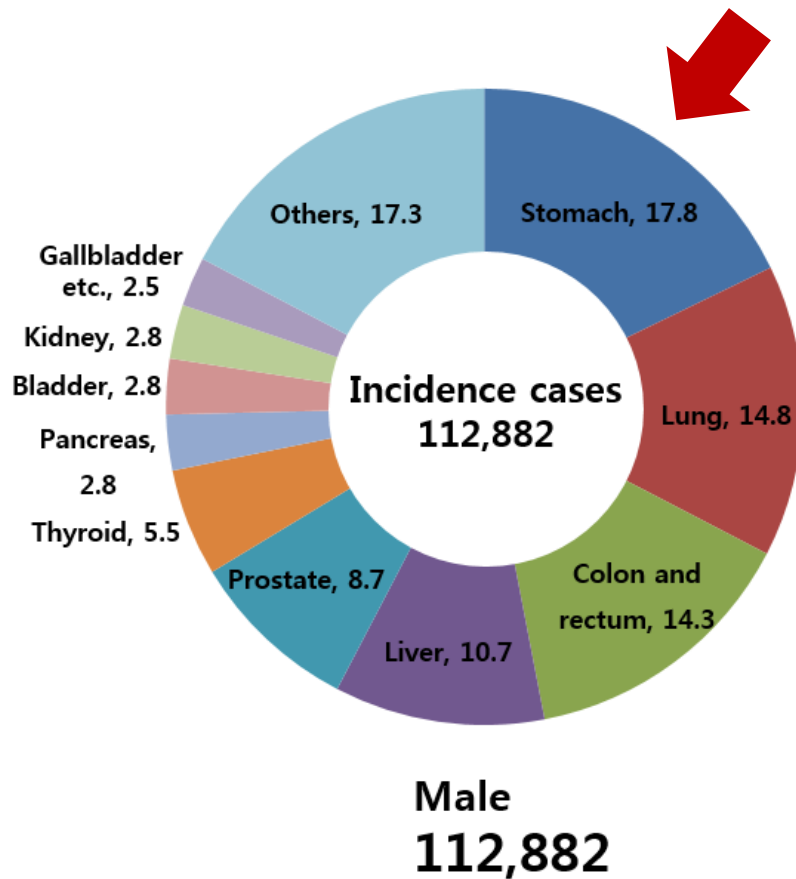Department of Medicine, Sungkyunkwan University School of Medicine, Seoul, Korea

Today's topics…

- Korean cancer screening program

- Biases of cancer screening

- Outcome of Korean National Gastric Cancer Screening

- Not only screening, but also prevention by *H. pylori* eradication

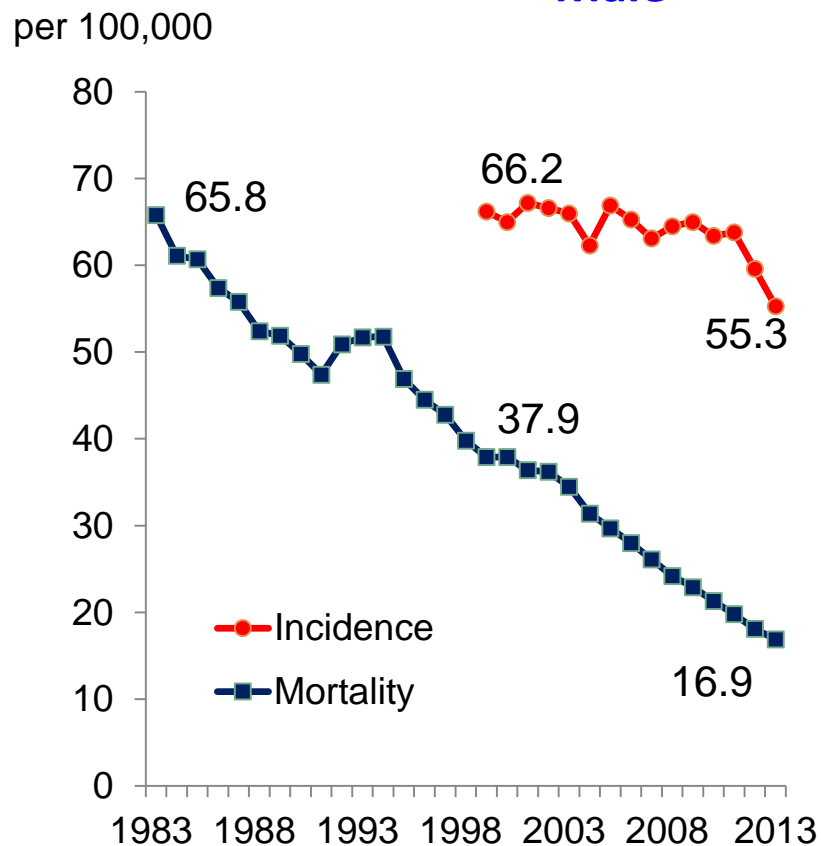# Korean cancer statistics (2014)

(Unit: %)

Male
112,882

Incidence cases 112,882
- Stomach, 17.8
- Lung, 14.8
- Colon and rectum, 14.3
- Liver, 10.7
- Prostate, 8.7
- Thyroid, 5.5
- Pancreas, 2.8
- Bladder, 2.8
- Kidney, 2.8
- Gallbladder etc., 2.5
- Others, 17.3

Female
104,175

Incidence cases 104,175
- Thyroid, 23.6
- Breast, 17.6
- Colon and rectum, 10.4
- Stomach, 9.4
- Lung, 7.0
- Liver, 4.0
- Cervix uteri, 3.4
- Pancreas, 2.6
- Gallbladder etc., 2.6
- Ovary, 2.3
- Others, 17.2

The incidence is still high, but two third of all gastric cancers are curatively treated.

M/I ratio was 0.31 in Korea
- Mortality/incidence ratio

Male

per 100,000

66.2
65.8
55.3
37.9
16.9

- Incidence
- Mortality

1983 1988 1993 1998 2003 2008 2013

Female

per 100,000

30.8
26.7
22.4
15.5
6.8
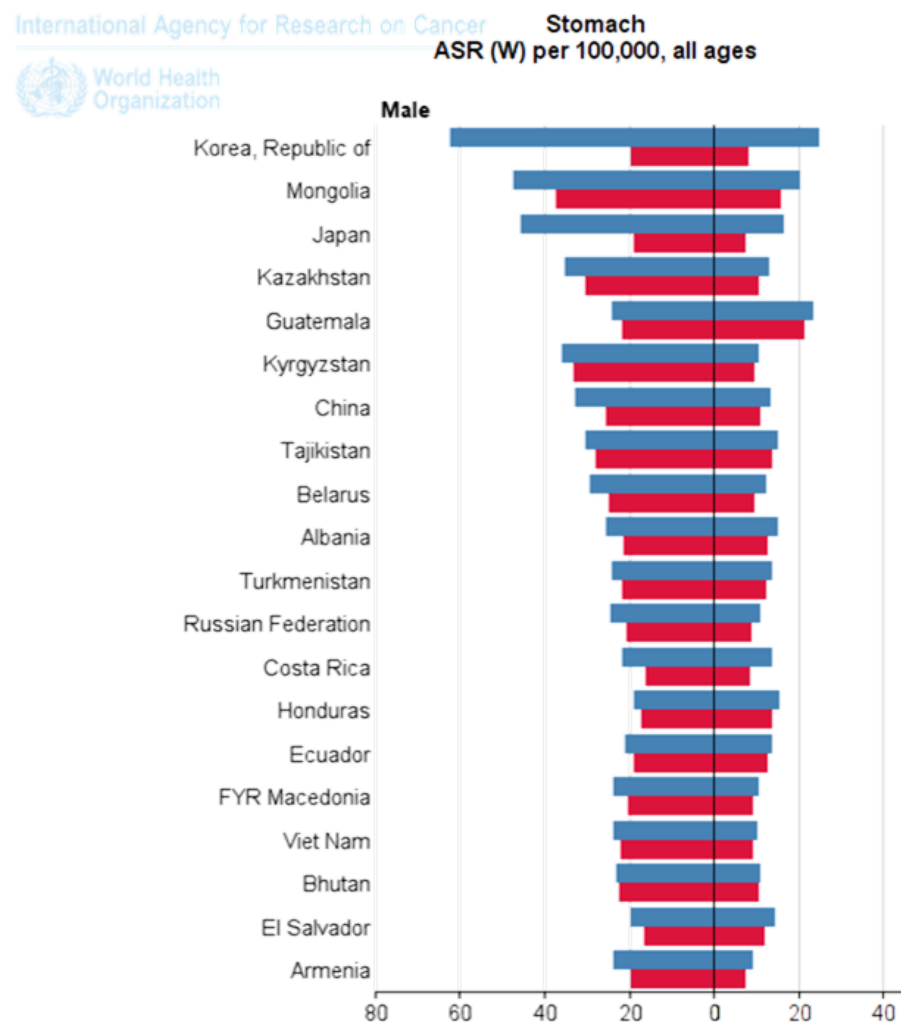
- Incidence
- Mortality

1983 1988 1993 1998 2003 2008 2013
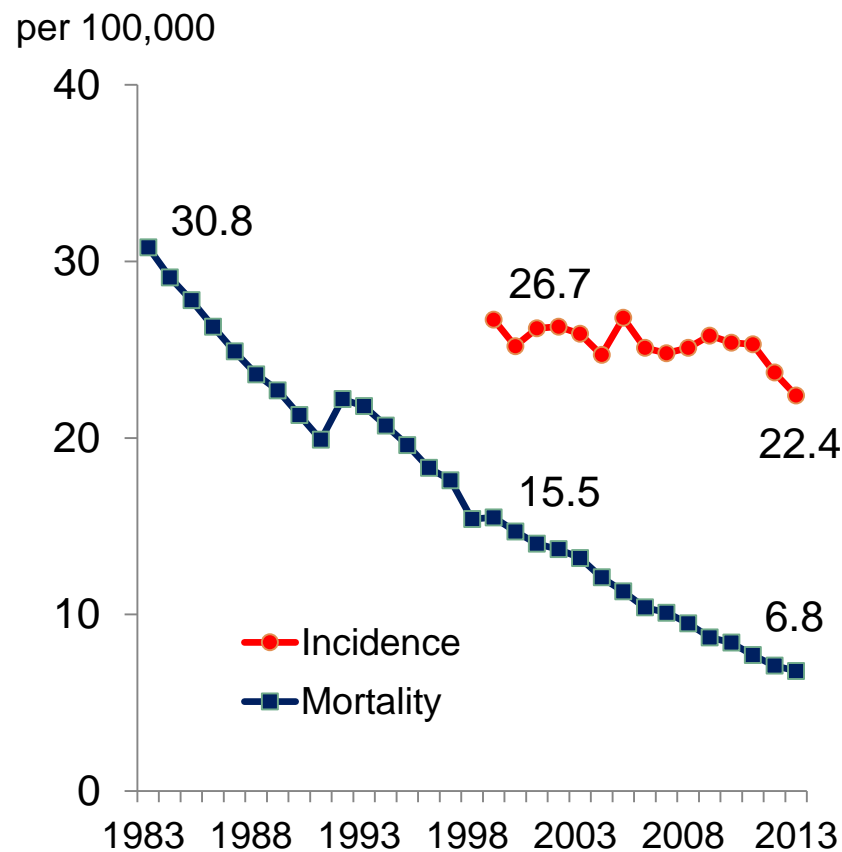
Age standardization was based on the Segi's world standard population

Estimated gastric cancer incidence and mortality in 2012 (Top 20 countries)

- Korea and Mongolia is number one and two in the incidence of gastric cancer.
- The survival rate is highest in Korea followed by Japan.
- It is probably due to early detection by screening program and high surgical and endoscopic techniques.
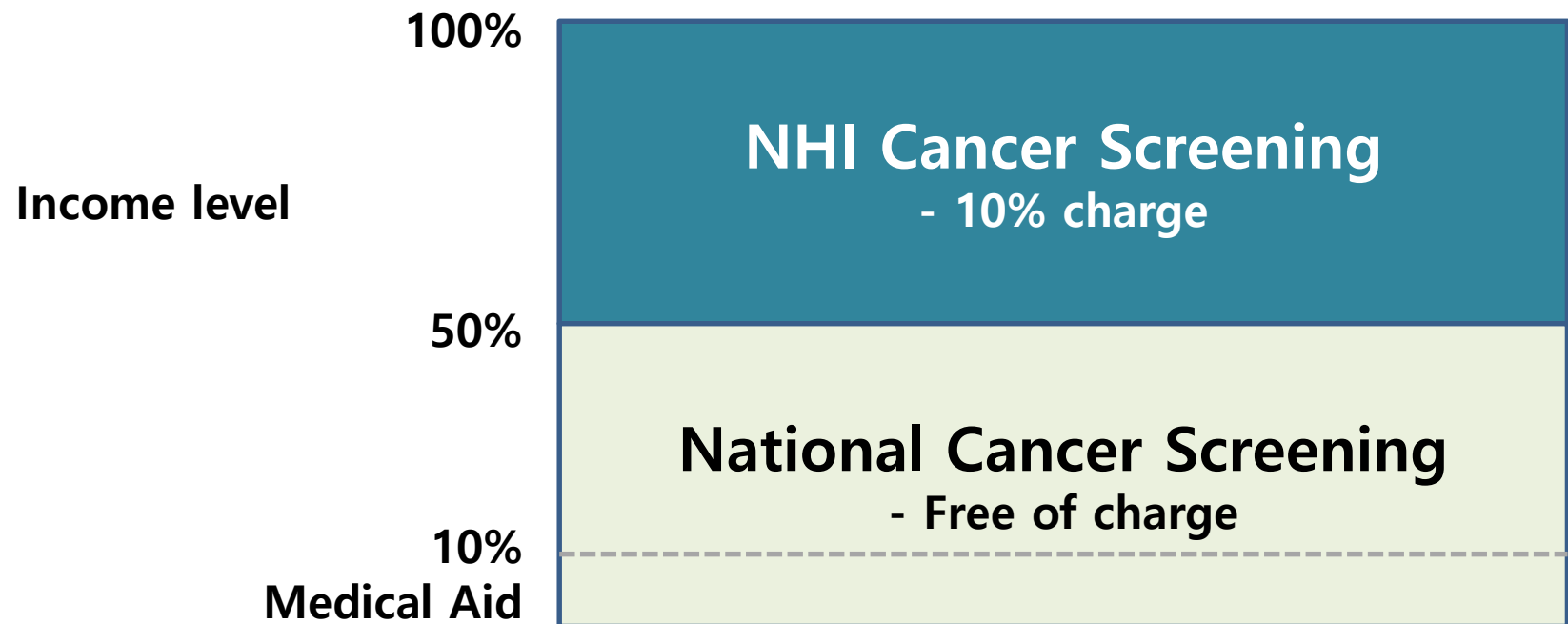
Korean Cancer Screening Program

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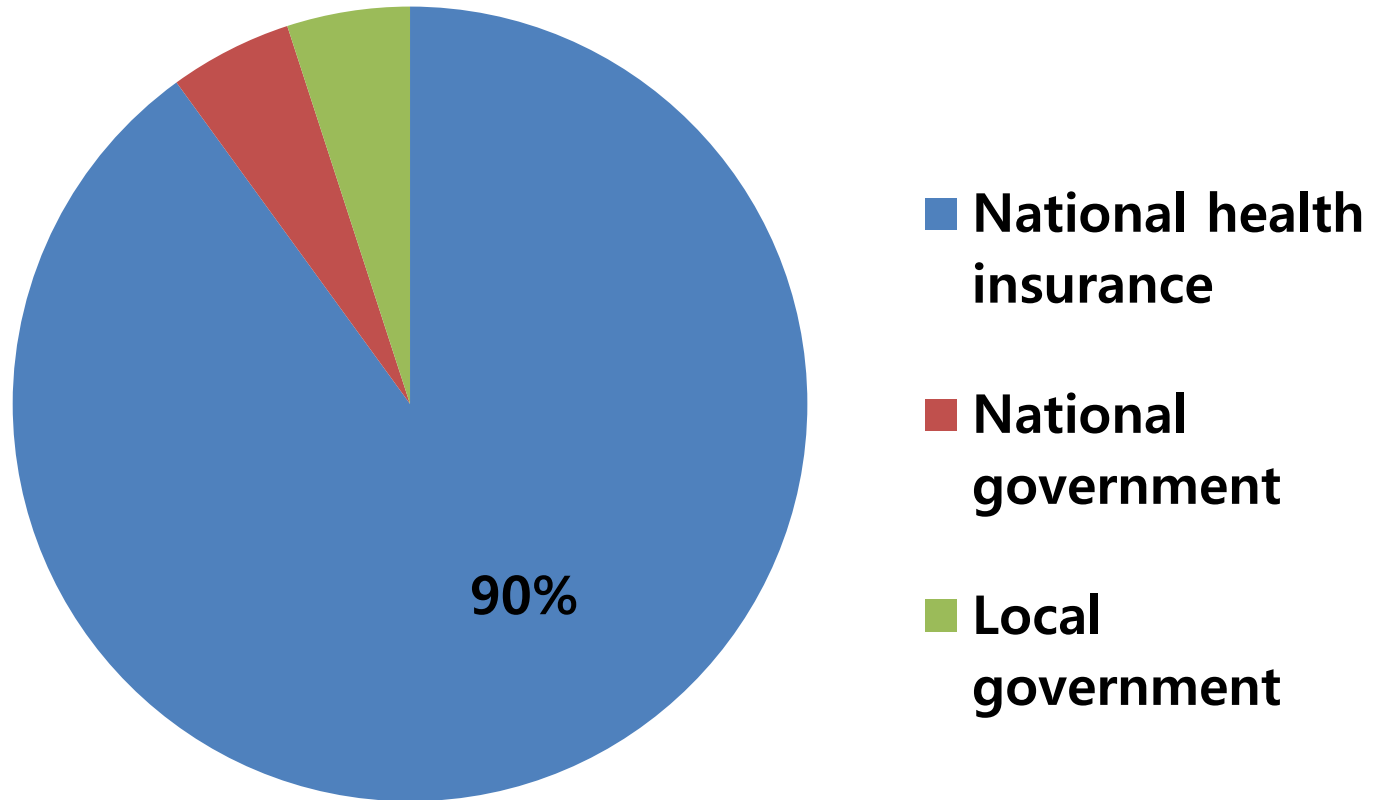
Brief history of Korean Caner Screening Program

Year	
1996	First term of 10-Year Plan of Cancer Control was launched.
1999	The National Cancer Screening Program launched for stomach, breast, cervical cancer free of charge. Target population was Medical Aids (lowest 10% income group).
2003	Liver cancer screening program added
2004	Colon cancer screening program added
2005	Target population expanded to the lower 50% of National Health Insurance beneficiaries (Free of charge)
2006	Screening for upper 50% income group (20% self payment)
2010	Self payment of upper 50% income group lowered to 10%

Payment by the population: 0-10%

Income level
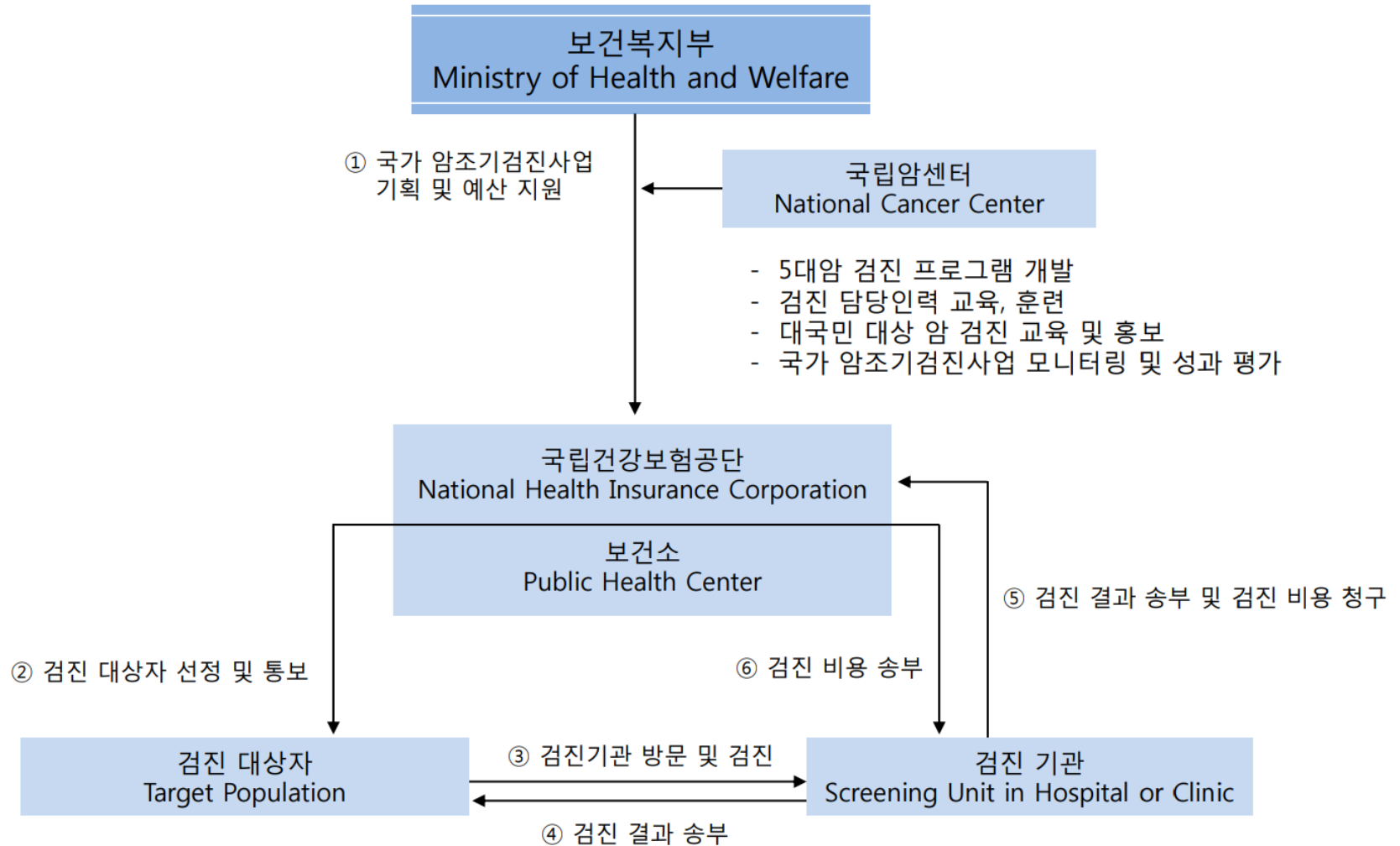
100%

NHI Cancer Screening
- 10% charge

50%

National Cancer Screening
- Free of charge

10%
Medical Aid

Structure of the budget

90%

National health insurance

National government

Local government

Governance structure

Cancer screening program (2018)

Stomach

Liver

Colorectal

Breast

Cervix

암종		검진대상	검진주기	검진방법
	위암	만 40세 이상 남녀	2년	기본검사 : 위내시경검사 (단, 위내시경검사를 실시하기 어려운 경우 위장조영검사를 선택적으로 시행)
	간암	만 40세 이상 성인 고위험군 (간경변증이나 B형 간염 바이러스 항원 또는 C형 간염바이러스 항체 양성으로 확인된 자)	6개월	간초음파검사 + 혈청알파태아단백검사
	대장암	만 50세 이상 남녀	1년	분변잠혈반응검사(FOBT) : 이상소견시 대장내시경검사(단, 대장내시경을 실시하기 어려운 경우 대장이중조영검사 선택적 시행)
	유방암	만 40세 이상 여성	2년	유방촬영술
	자궁 경부암	만 20세 이상 여성	2년	자궁경부세포검사(Pap smear)

http://www.ncc.re.kr (accessed: 2018-6-20)

Gastric cancer screening program (2018)

Choice 1
(Standard)

Endoscopy

If necessary

Biopsy

Participant
Every 2 yrs

Aged 40+

If suspicious

UGI

Choice 2
(If endoscopy is not available)
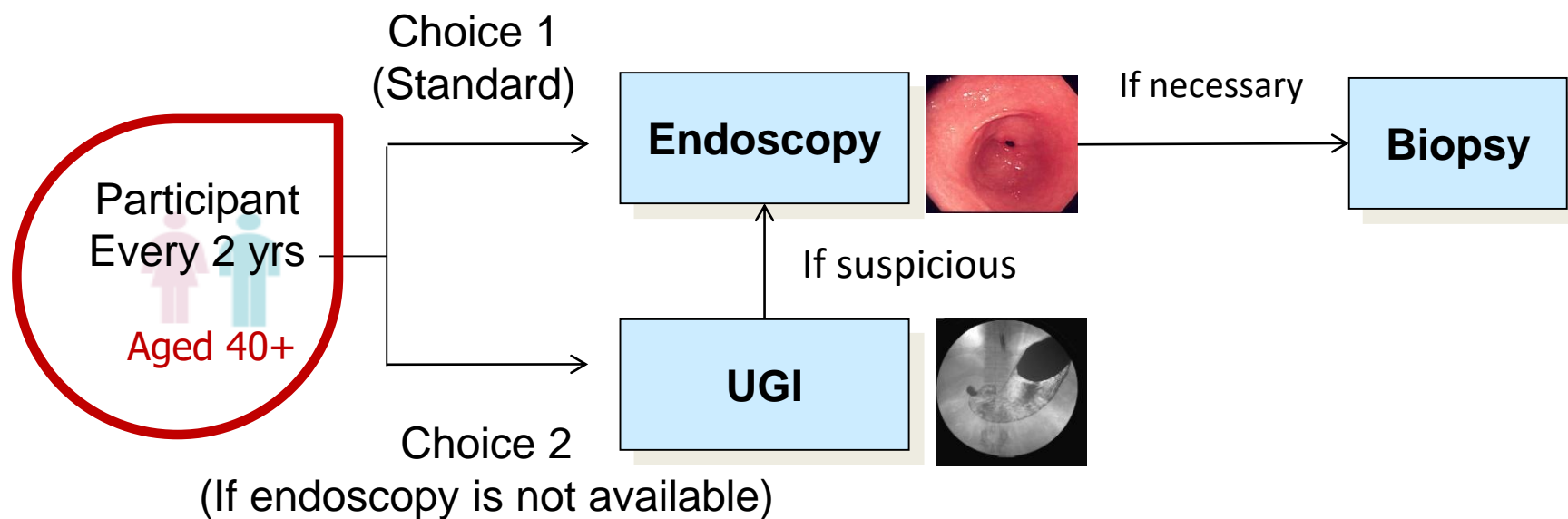
Issue 1. Screening interval
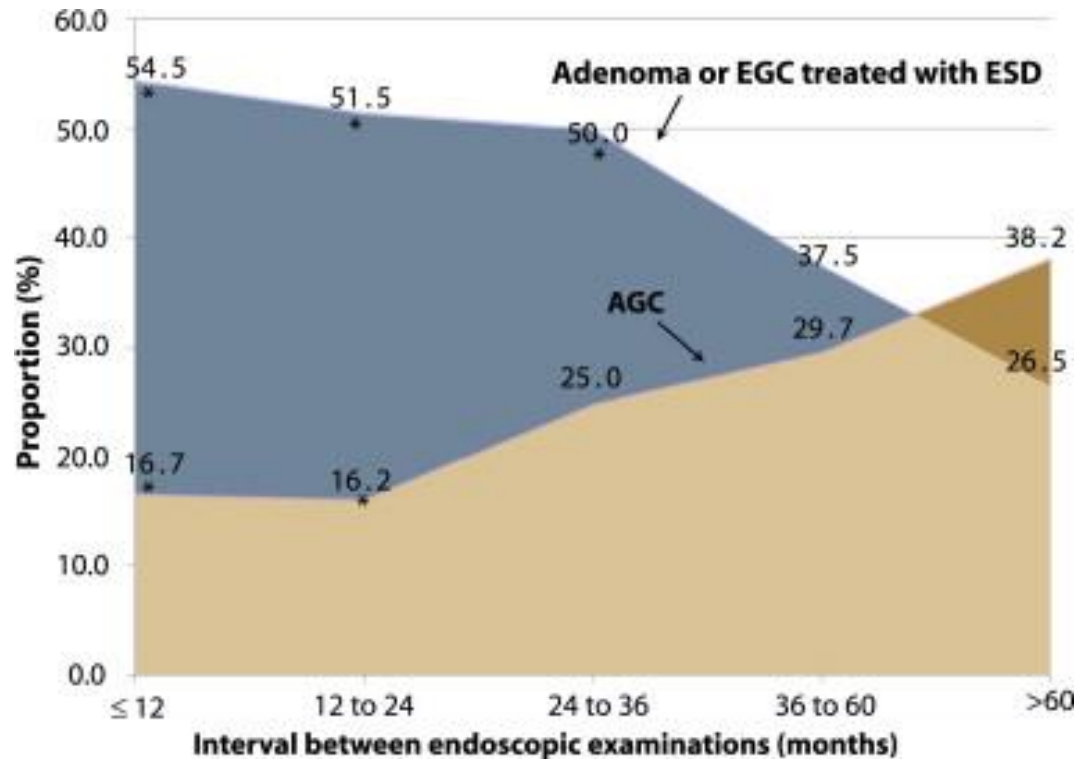
One retrospective study from Yonsei University showed no difference in the portion of endoscopically treatable gastric neoplasms between 1 and 2 years.

Park. Gastroinest Endosc 2014:80:253-259

Issue 2. Age limitations

Academic guideline	• 40-74 years old • endoscopy (optionally gastrography)
NCSP guideline	• >40 years old • endoscopy or gastrography

Medical institutions for national gastric cancer screening program

	Institutions		Number of examinations	
General Hospitals	332	6.79%	808,078	25.17%
Small Hospitals	793	16.23%	637,127	19.84%
Primary Clinics	3,734	76.41%	1,339,675	41.73%
Screening institutions	28	0.57%	425,741	13.26%

Two types of cancer screening

Organized screening

- National program (public)
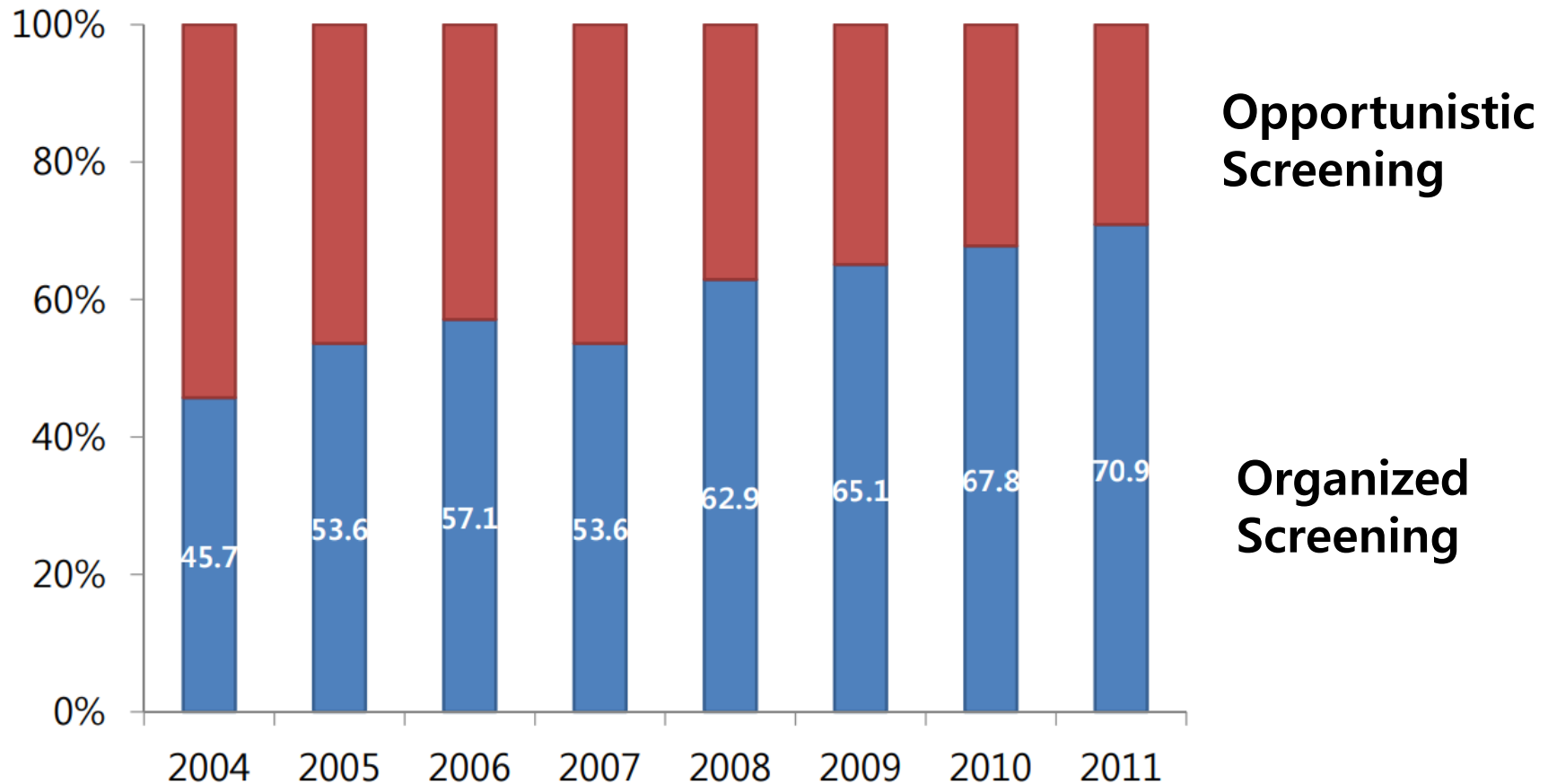- Most budget comes from national or public fund
- Standard

Opportunistic screening
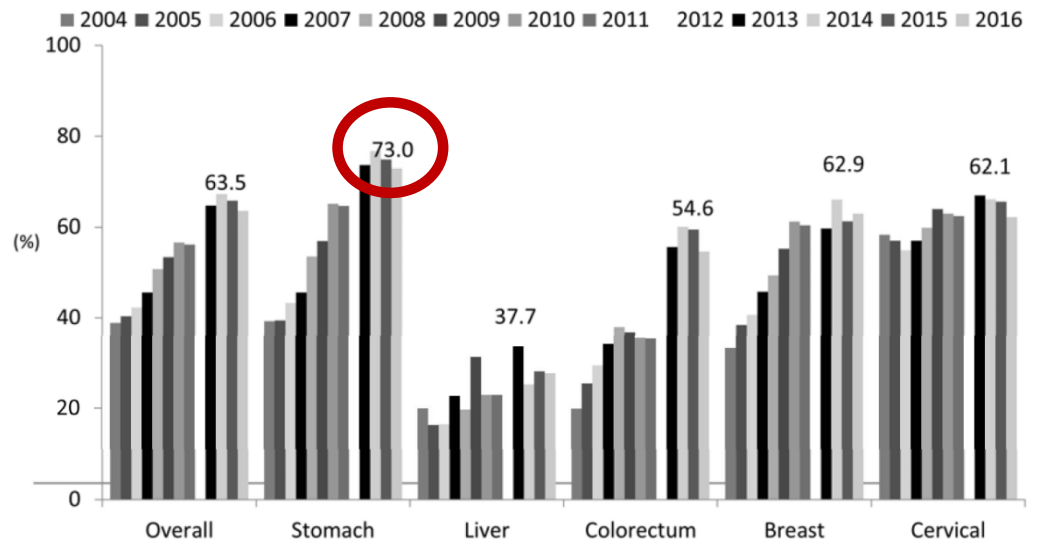
- Personal program (private)
- Payment by individuals
- Expansive

Two types of cancer screening

Screening participation rate

Organized national program
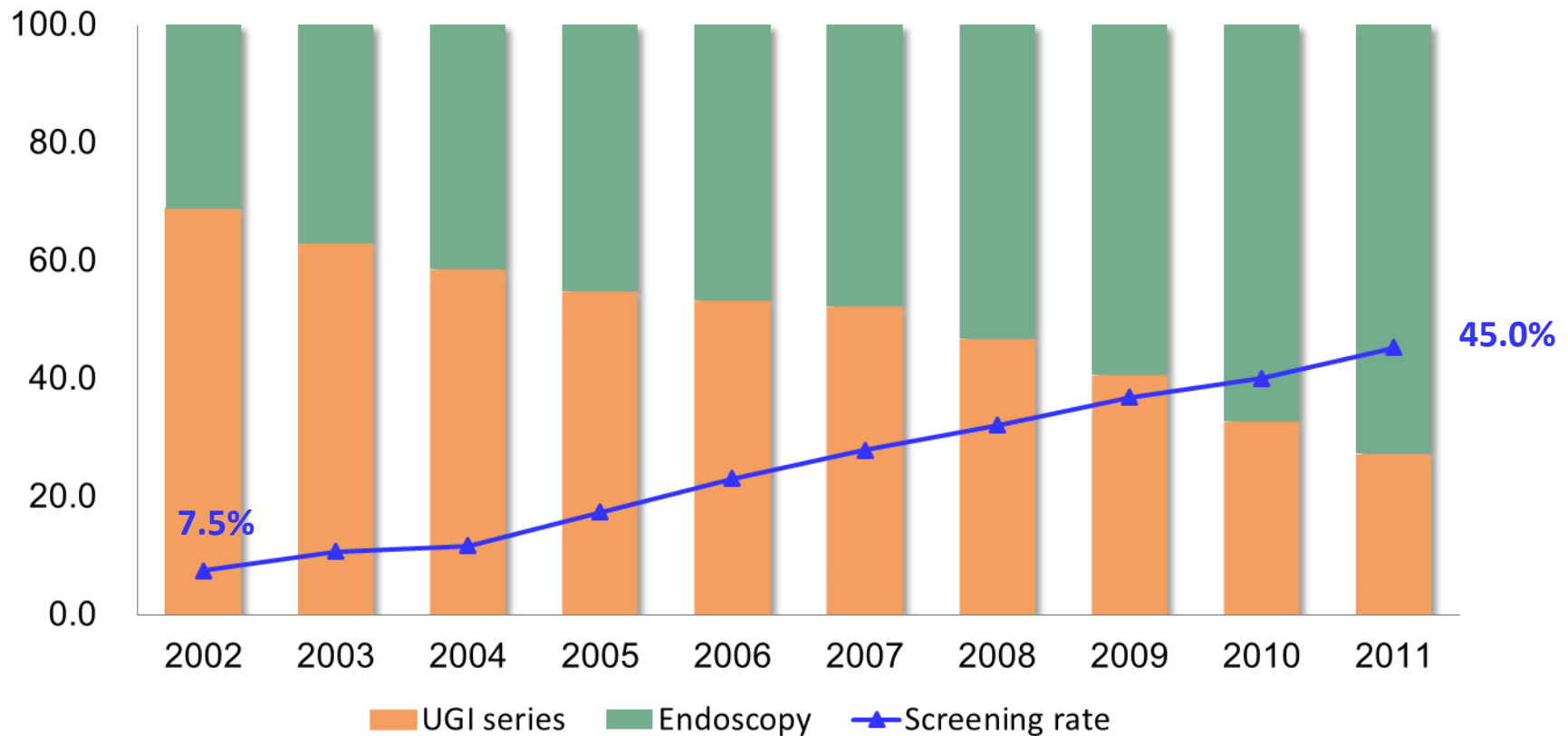
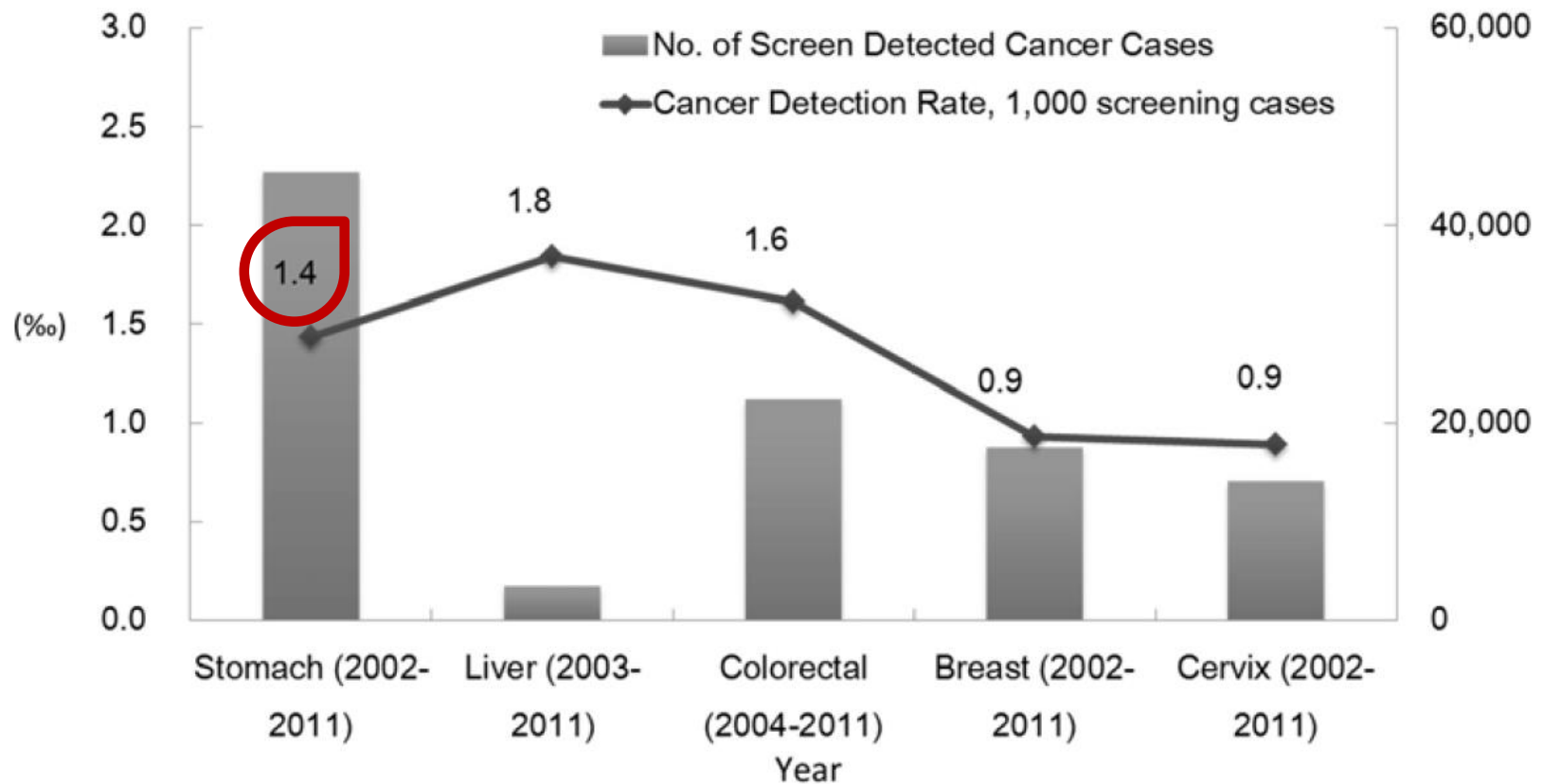**Organized national program + opportunistic private screening program**

Proportion of endoscopy
- National gastric cancer screening program (2001-2011)

Cancer detection rate by national cancer screening program by EGD or UGIS

Gastric cancer detection rate by EGD

Table 1. Characteristics of the participating subjects (n = 25 536)

Variable category		Study population (%)	Background population in Korea, 2005 (%)*
Gender	Male:female	15 180:10 356 (59:41)	24 191 000:23 947 000 (50:495)
Age (years; mean ± s.d.: 46.7 ± 11.1)	16–19	57 (0.2)	313 000 (7)
	20–29	1235 (5)	7 606 000 (16)
	30–39	5684 (22)	8 520 500 (18)
	40–49	8885 (35)	8 184 000 (17)
	50–59	6126 (24)	5 151 000 (11)
	60–69	2936 (12)	361 000 (8)
	≥70	613 (2)	270 000 (6)
NSAID history for more than 1 month		1616 (6)	
Antibiotics history for ≥1 month		253 (1)	
Endoscopic findings			
Benign gastric ulcer (active or healing)		832 (3)	
Duodenal ulcer (active or healing)		524 (2)	
Gastric cancer (histologically confirmed)		65 (0.3)	
	EGC:AGC	47 :18 (3:1)	

Kim. Aliment Pharmacol Ther

Gastric cancer detection rate by EGD

- SMC health promotion center (a big private program)
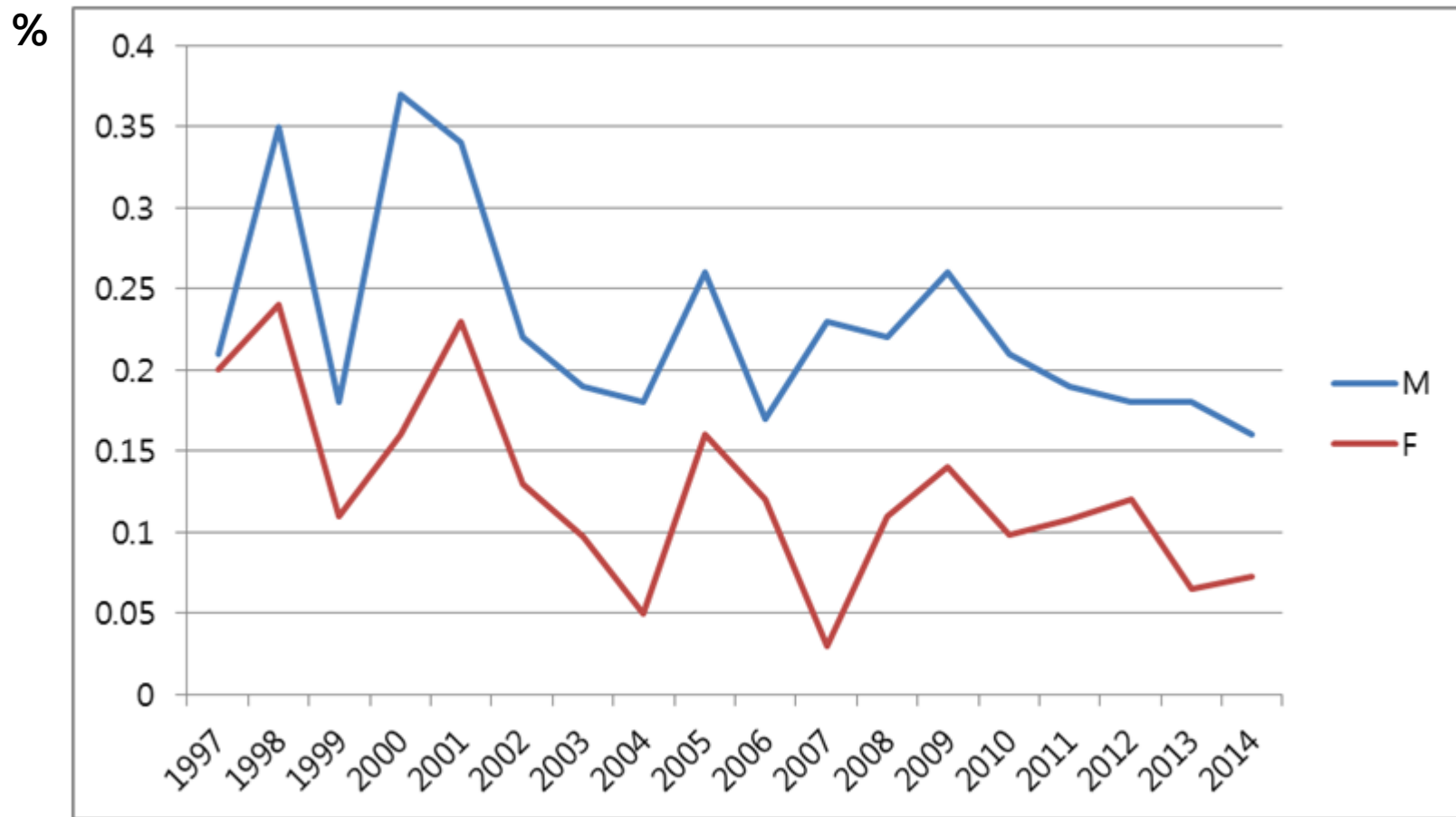
Quality improvement program

- Development of guidelines

- Education
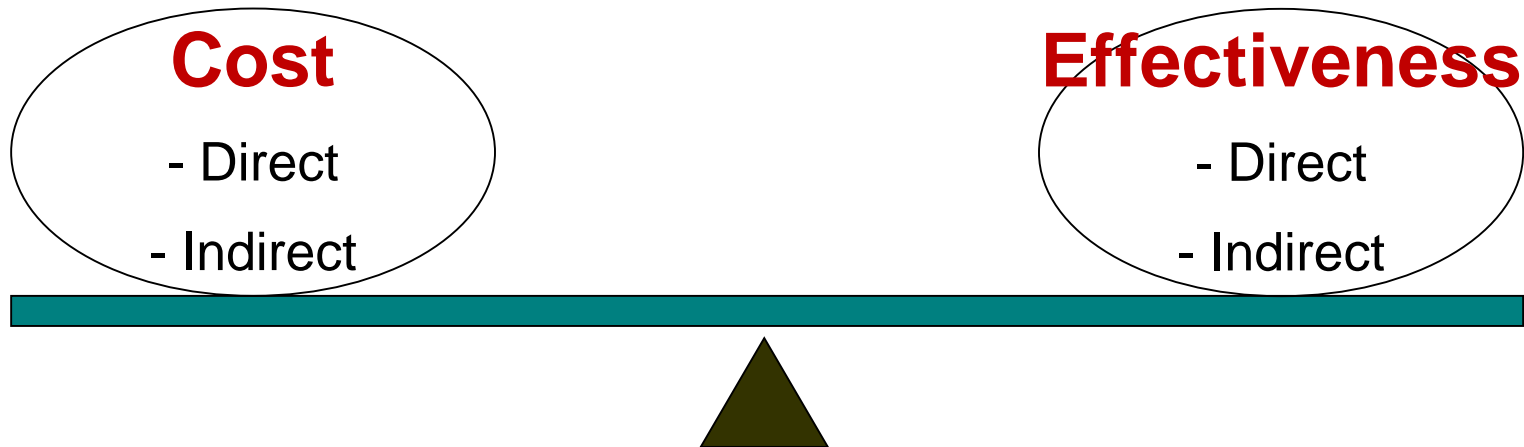
- Evaluation

Biases of cancer screening

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Cancer screening

- Detect cancers as early as possible

- Treat cancer completely

- Live longer (or forever)

Cost
- Direct
- Indirect

Effectiveness
- Direct
- Indirect
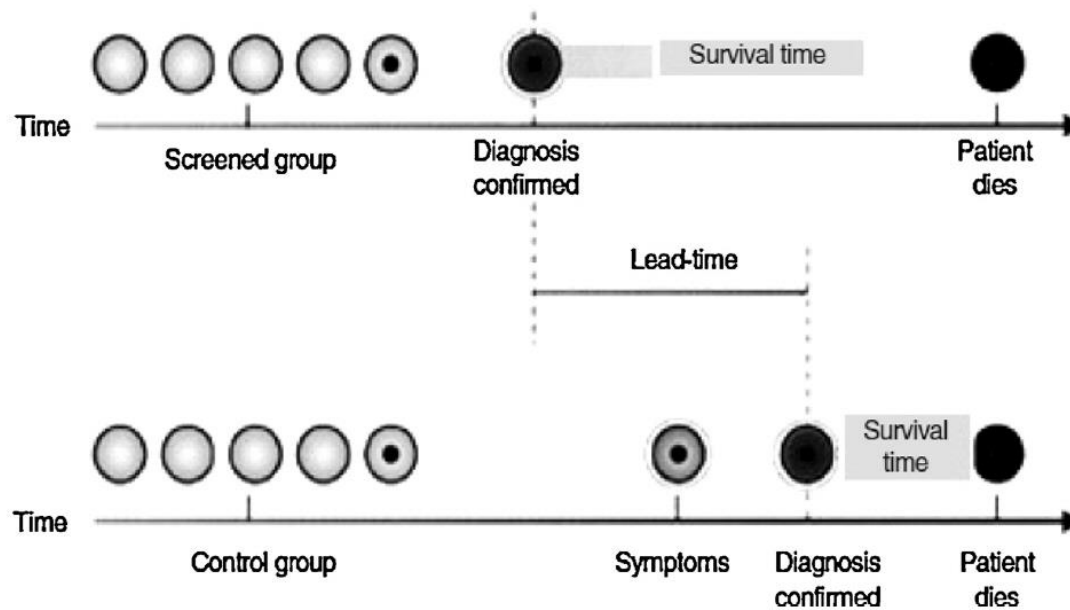
Lead time bias

Fig. 1. Conceptual idea of lead-time bias. Note: The diagnosis of disease is made earlier in the screened group, resulting in an apparent increase in the survival time, although the time of death is the same in both groups.
Source: National Cancer Center of Korea, 2010.

Health Policy (2014) http://dx.doi.org/10.1016/j.healthpol.2014.08.012

Length-time bias
- **Cancers detected in the screening program is less aggressive.**

Disease progression

Aggressive disease

Less aggressive disease

Screening

Time (years)
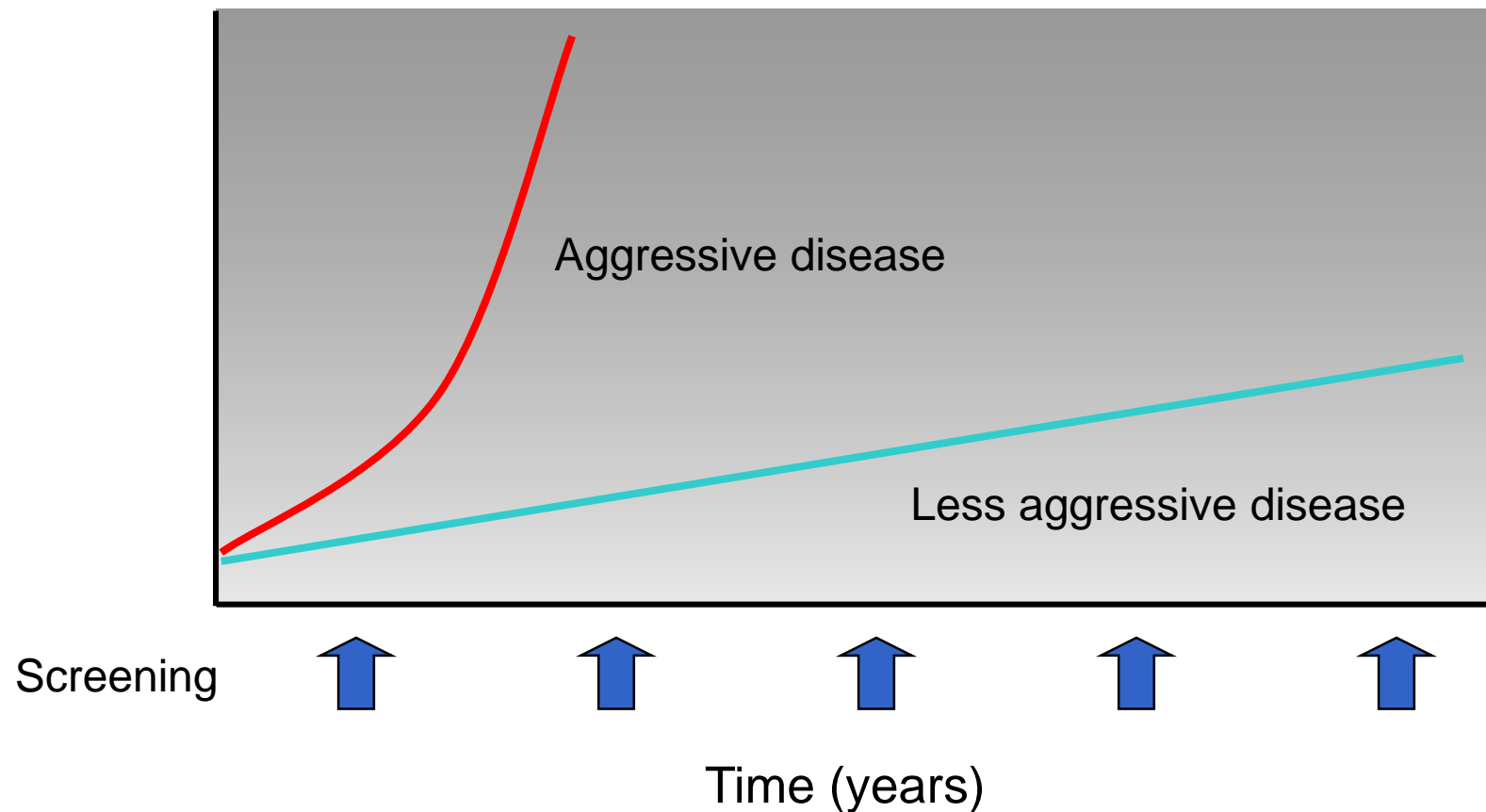
Scenario 1: advanced ↓, early ↑
- *The total number was not changed.*
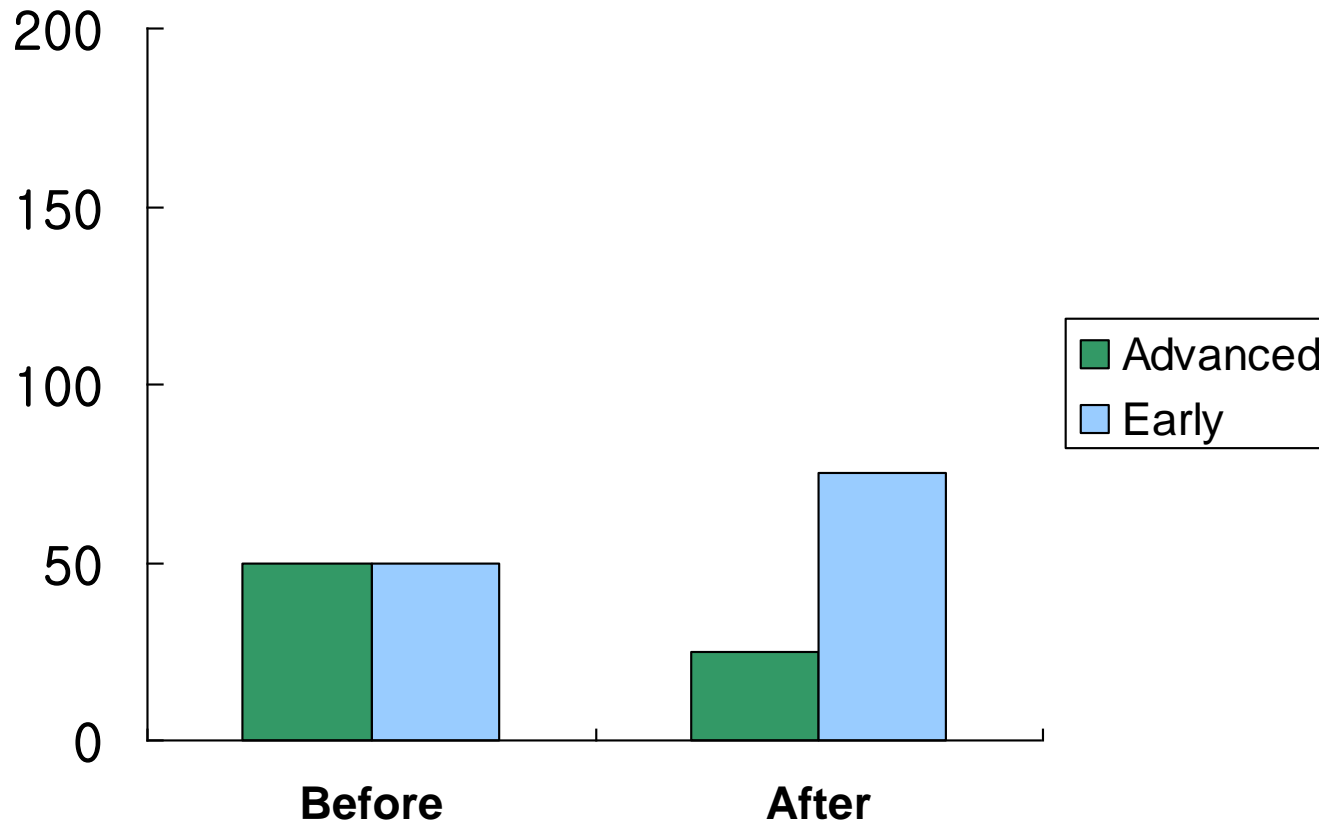
Scenario 2: advanced ↓, early ↑ ↑
- *The total number was increased.*
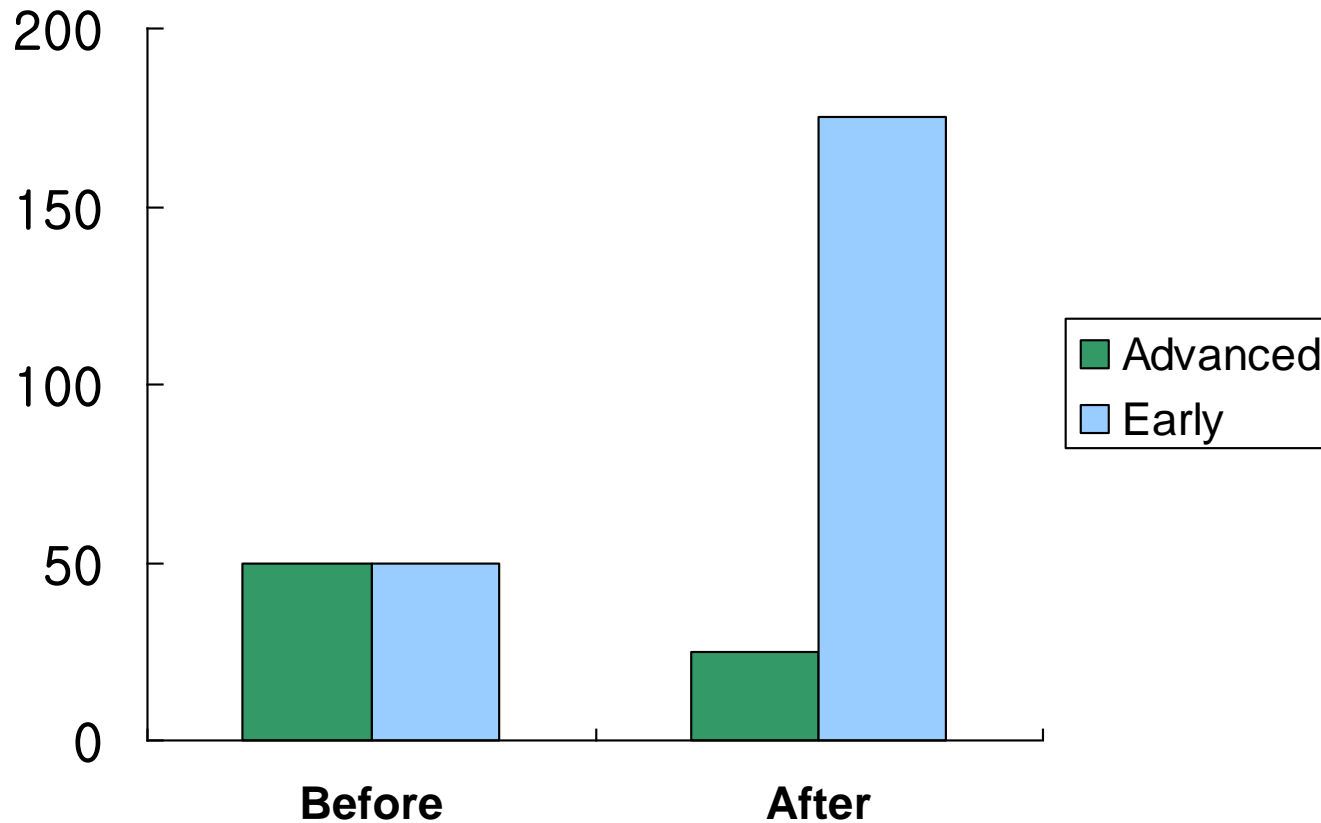
Scenario 3: early ↑↑, advanced →
- *The total number was increased.*
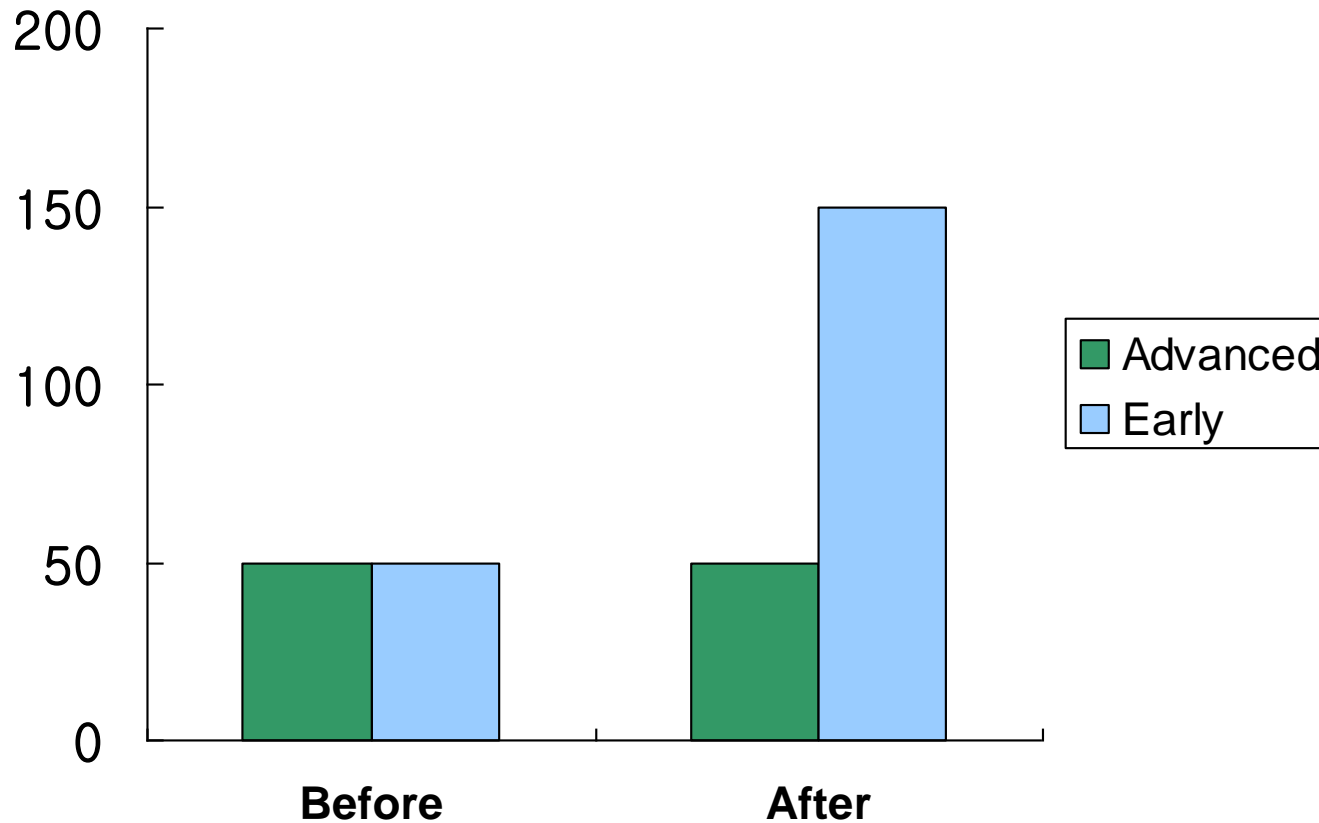
Box summary

- For the establishment of a cancer screening program, we need to consider not only benefits but also cost and biases at the same time.

- Strong scientific support for the screening program should be provided by good outcome data.

Outcome of Korean National Gastric Cancer Screening

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Evaluating effectiveness of NCSP

Target population of the NCSP, 2002-2003 (n = 16,902,631)

Excluded due to:
- Incomplete ID (n = 1,997)
- Prevalent cancer cases (n = 316,351)

NCSP cohort for gastric cancer (n = 16,584,283)

Ascertainment of incident gastric cancer, 2004-2009 (n = 127,288)

Died during 2004-2002[a, b] (n = 54,418)

Alive on the date of death of the corresponding cases

1:4 matched case-control[c] (n = 54,418 pairs)
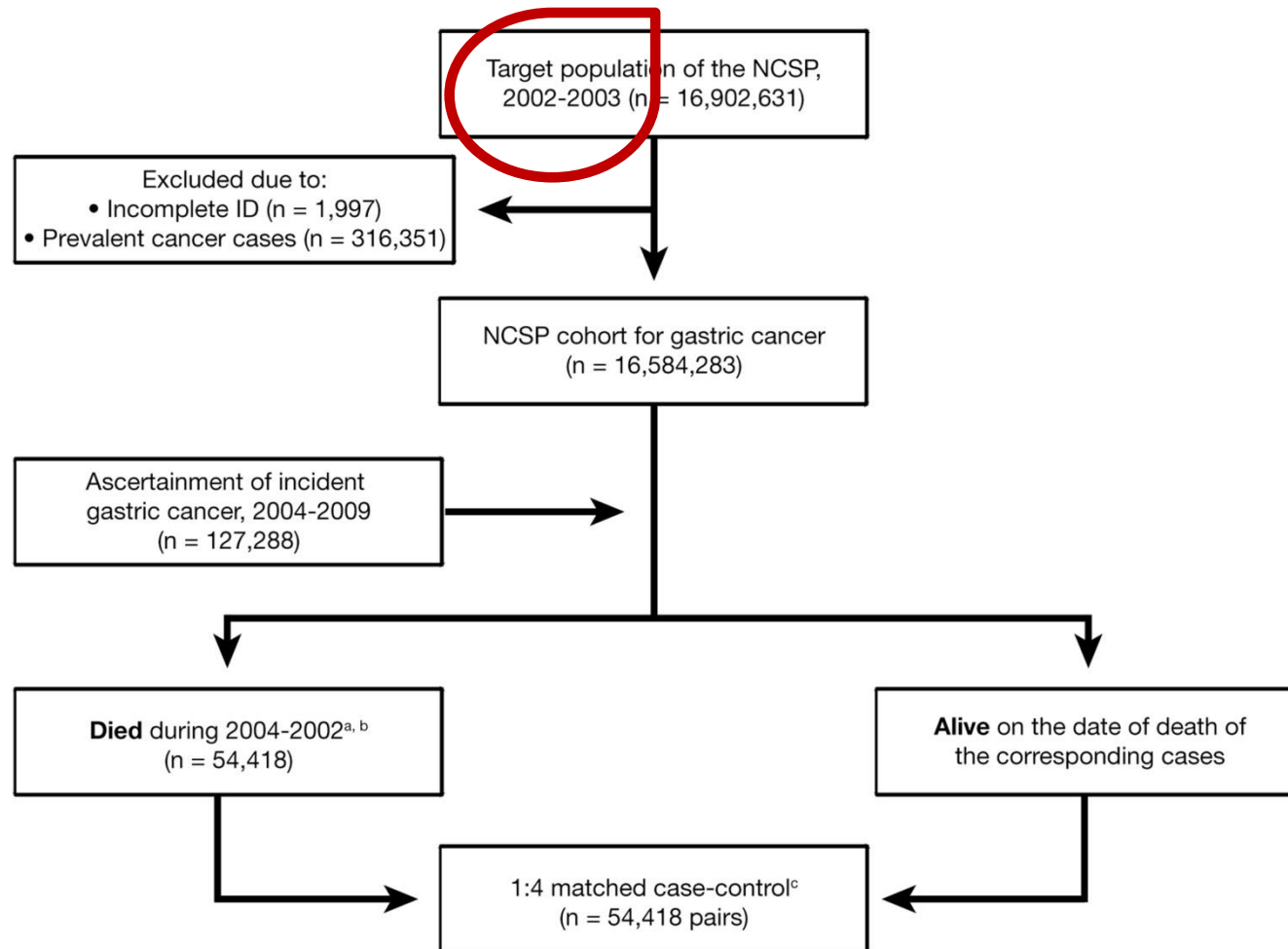
Effectiveness of the Korean National Cancer Screening Program in Reducing Gastric Cancer Mortality

Table 1. Association Between Receipt of Gastric Cancer Screening and Cause of Mortality: Number of Pairs and Proportions of the Screened Case Subjects and Matched Controls, as Well as ORs and 95% CIs Compared With Never-Screened Individuals

| | All-cause mortality | | | | | GC-specific mortality | | | | | All-cause mortality except from GC | | | | |
| | | Screened, % | | | | | Screened, % | | | | | Screened, % | | | |
	Pairs, n	Case	Control	OR	95% CI	Pairs, n	Case	Control	OR	95% CI	Pairs, n	Case	Control	OR	95% CI
Overall	54,418	25.7	28.9	0.83	0.81–0.85	44,095	24.7	28.8	0.79	0.77–0.81	10,323	29.9	29.4	1.03	0.98–1.08
Year of entry															
2002	31,111	26.1	29.4	0.83	0.81–0.86	25,157	25.2	29.3	0.79	0.76–0.81	5954	30.3	29.5	1.04	0.97–1.11
2003	23,307	25.1	28.2	0.83	0.80–0.86	18,938	24.1	28.0	0.79	0.76–0.82	4369	29.4	29.3	1.01	0.93–1.09
Sex															
Male	37,739	26.7	29.8	0.84	0.82–0.86	29,783	25.4	29.6	0.79	0.77–0.81	7956	31.4	30.6	1.05	0.99–1.11
Female	16,679	23.5	26.9	0.81	0.78–0.84	14,312	23.3	27.1	0.79	0.75–0.83	2367	24.6	25.5	0.95	0.85–1.06
Age group, y															
40–44	3396	19.8	24.1	0.76	0.69–0.84	3100	20.1	24.4	0.77	0.69–0.85	296	16.6	20.9	0.74	0.52–1.05
45–49	3324	20.8	27.3	0.67	0.61–0.74	2969	20.7	27.4	0.67	0.60–0.74	355	21.1	27.1	0.71	0.53–0.94
50–54	5074	24.4	31.8	0.67	0.62–0.72	4309	23.0	31.9	0.61	0.57–0.67	765	32.3	31.8	1.02	0.86–1.22
55–59	4510	28.4	35.3	0.70	0.65–0.76	3746	27.6	35.4	0.67	0.61–0.73	764	32.2	34.8	0.88	0.74–1.05
60–64	9538	31.8	37.0	0.77	0.73–0.81	7486	30.5	36.8	0.73	0.69–0.77	2052	36.2	37.7	0.93	0.84–1.04
65–69	8411	31.4	35.0	0.83	0.79–0.88	6469	30.3	35.1	0.78	0.73–0.83	1942	35.0	34.5	1.02	0.92–1.14
70–74	10,695	26.9	27.5	0.96	0.92–1.01	8320	26.1	27.5	0.92	0.87–0.97	2375	29.7	27.6	1.13	1.01–1.25
75–79	5212	20.2	18.6	1.13	1.04–1.22	4230	19.3	18.2	1.09	1.00–1.19	982	24.0	20.2	1.29	1.08–1.55
80–84	3557	12.8	10.5	1.28	1.14–1.44	2908	12.5	10.5	1.23	1.08–1.40	649	14.3	10.3	1.53	1.17–2.01
≥85	701	7.1	4.1	1.82	1.28–2.59	558	7.2	4.2	1.80	1.22–2.67	143	7.0	3.9	1.91	0.87–4.19
Socioeconomic status															
NHI, high	16,104	26.4	29.2	0.85	0.82–0.89	12,637	25.7	29.7	0.80	0.76–0.84	3467	28.7	27.5	1.07	0.98–1.17
NHI, middle	15,656	18.2	21.2	0.80	0.76–0.84	13,098	17.5	20.9	0.78	0.74–0.82	2558	21.4	23.0	0.89	0.80–1.00
NHI, low	18,243	30.0	34.0	0.82	0.79–0.85	14,876	28.6	33.7	0.77	0.74–0.80	3367	36.0	34.9	1.05	0.97–1.15
MAP	4415	32.3	33.9	0.92	0.85–0.99	3484	31.5	33.9	0.88	0.81–0.96	931	35.5	34.2	1.06	0.91–1.24
Total, 40–74		0.89	0.84–0.94	0.56	0.52–0.61	<.001	0.87	0.82–0.92	0.53	0.48–0.58	<.001	0.99	0.86–1.14	0.84	0.68–1.05	.252

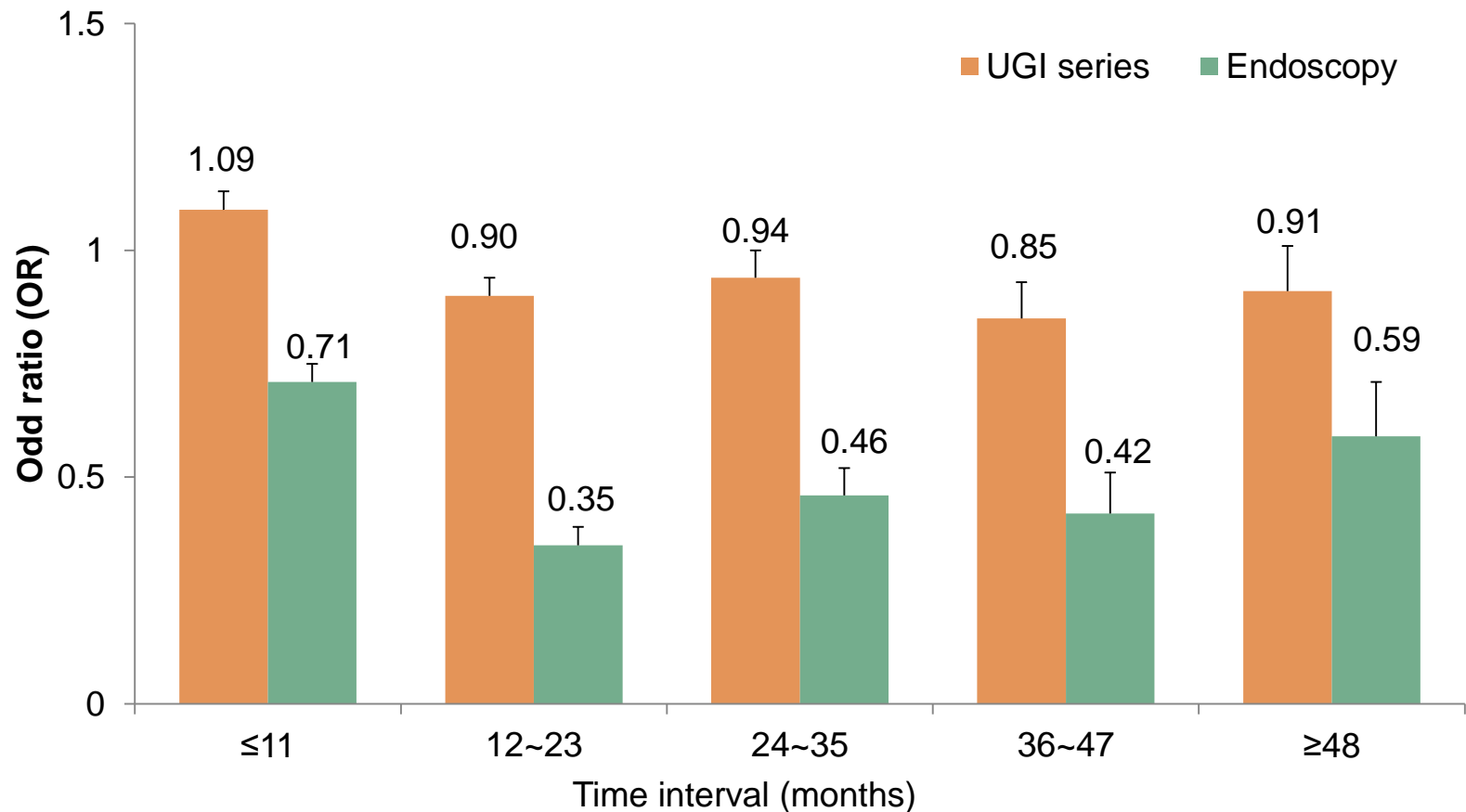**GC specific mortality reduction**

Overall — 21%

Age 40-74 — 47%

Methods and frequency matters.
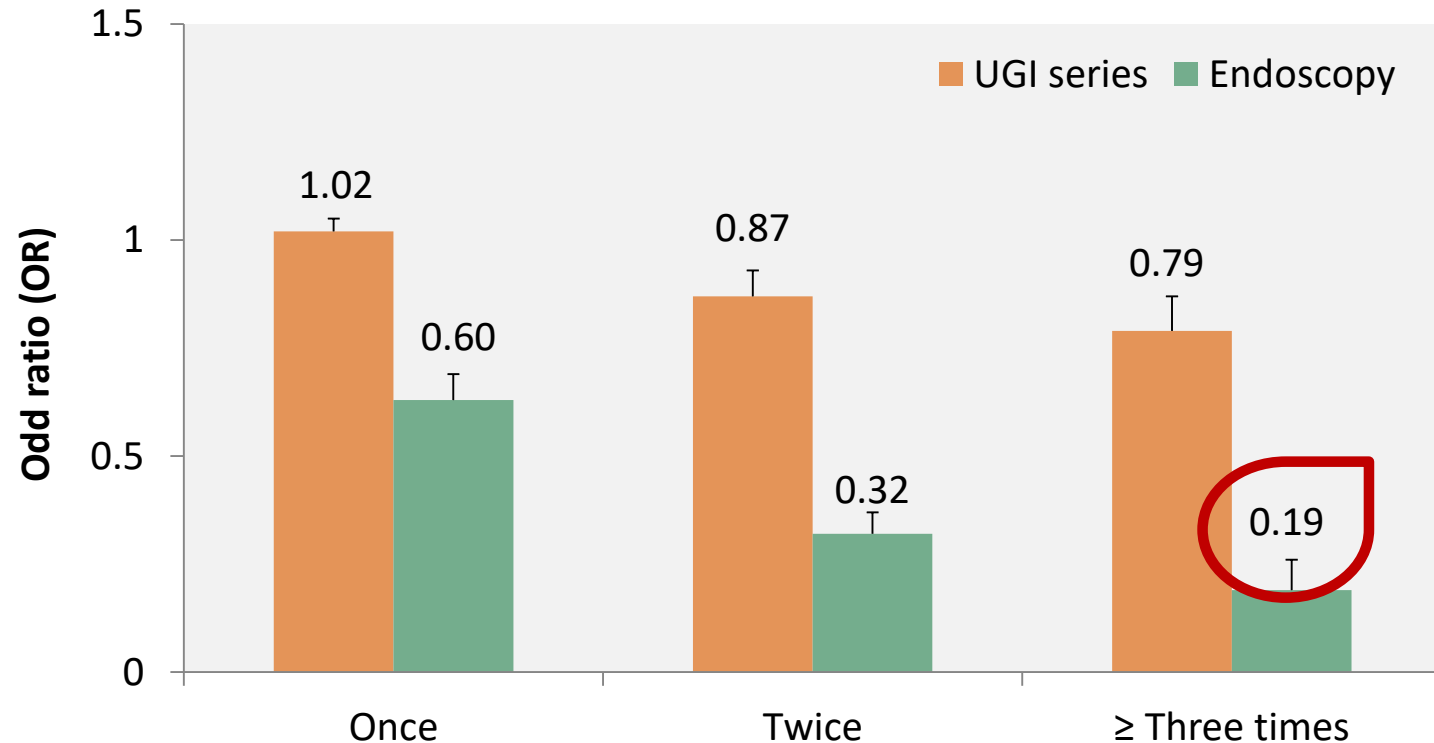
- Endoscopy: 81% mortality reduction for ≥ 3 times
- UGIS: 21% mortality reduction for ≥ 3 times

By endoscopy, the effect of mortality reduction remained by 48 months from the cancer diagnosis to the last screening.

Not only screening, but also prevention by H. pylori eradication

Jun Haeng Lee, MD.

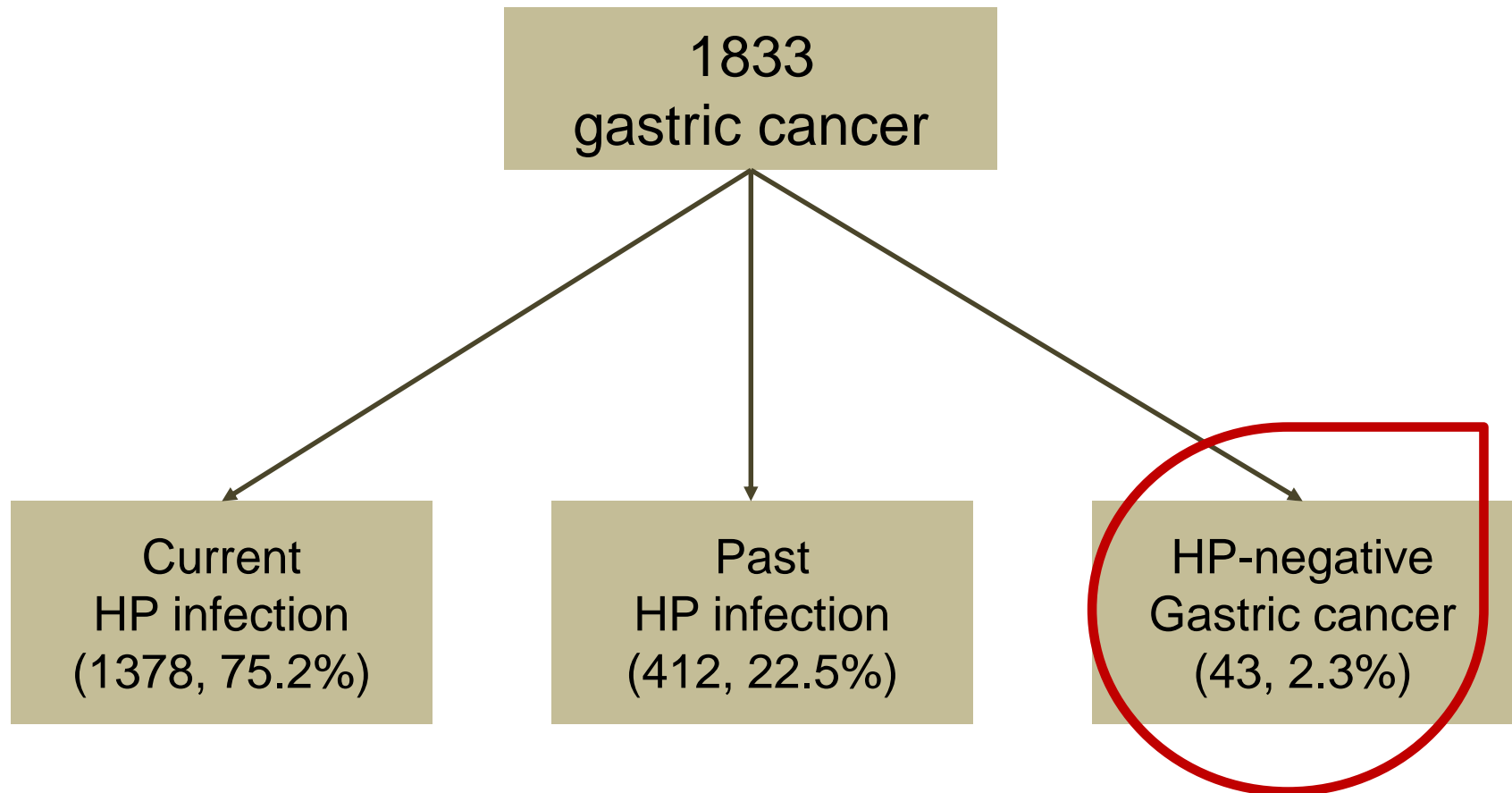**Department of Medicine, Sungkyunkwan University School of Medicine, Seoul, Korea**

Screening is not a prevention.

Screening is just early detection and prevention of gastric cancer-related death.

In order to prevent gastric cancer,
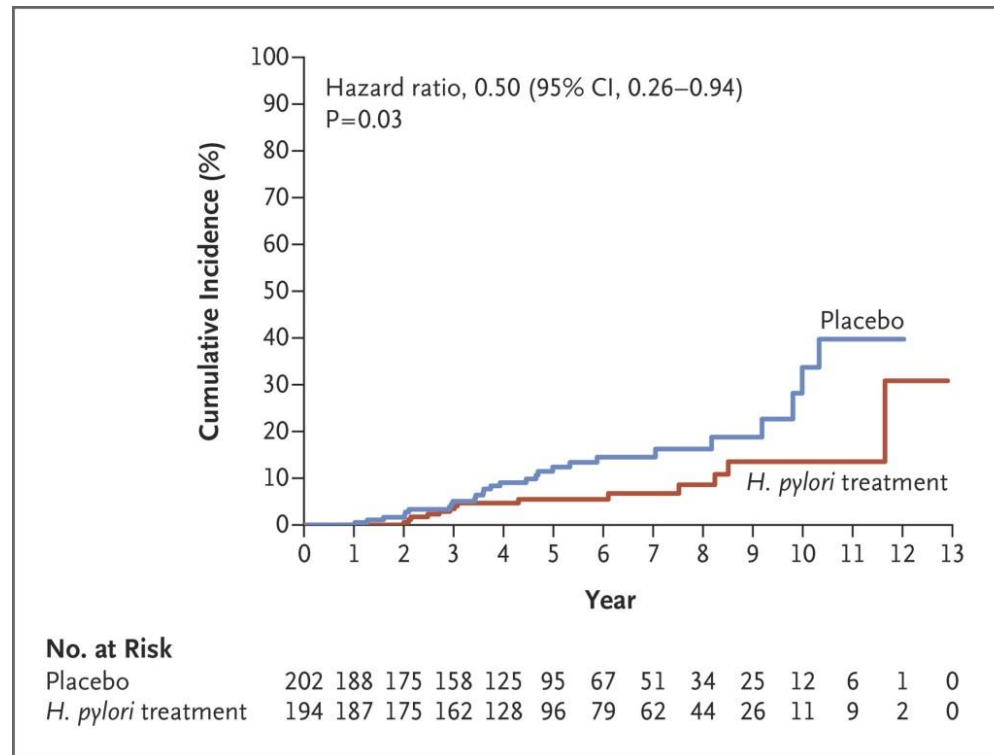*H. pylori* eradication may be the best option.

True Helicobacter (-) cancer is very rare.
- Rapid urease tests, serology examinations, and histological evaluations.

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                    ┌──────────────────┐
                    │       1833       │
                    │  gastric cancer  │
                    └──────────────────┘
           ┌───────────────┼───────────────┐
           ▼               ▼               ▼
    ┌────────────┐  ┌────────────┐  ┌────────────┐
    │  Current   │  │    Past    │  │ HP-negative│
    │HP infection│  │HP infection│  │Gastric cancer│
    │(1378, 75.2%)│ │(412, 22.5%)│  │ (43, 2.3%) │
    └────────────┘  └────────────┘  └────────────┘
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Hp eradication for the prevention of metachronous gastric cancer

Improvement of atrophy and metaplasia by Hp eradication

Table 2. Improvement from Baseline in Grade of Atrophy and Intestinal Metaplasia at 3-Year Follow-up, According to Trial Group and *H. pylori* Status.*

Variable	Trial Group		Odds Ratio (95% CI)†	P Value	*H. pylori* Infection Status		Odds Ratio (95% CI)‡	P Value
	H. pylori Treatment (N=162)	Placebo (N=165)			Eradicated (N=140)	Persistent (N=187)		
	no./total no. (%)				no./total no. (%)			
Improvement in grade of glandular atrophy								
Antrum	39/151 (25.8)	30/160 (18.8)	1.51 (0.88–2.59)	0.13	36/132 (27.3)	33/179 (18.4)	1.66 (0.97–2.84)	0.06
Corpus lesser curvature§	76/157 (48.4)	23/153 (15.0)	5.30 (3.08–9.13)	<0.001	69/135 (51.1)	30/175 (17.1)	5.05 (3.01–8.48)	<0.001
Corpus greater curvature	38/155 (24.5)	25/158 (15.8)	1.73 (0.98–3.03)	0.06	36/133 (27.1)	27/180 (15.0)	2.10 (1.20–3.68)	0.009
Improvement in grade of intestinal metaplasia								
Antrum	42/160 (26.3)	38/164 (23.2)	1.18 (0.71–1.96)	0.52	39/139 (28.1)	41/185 (22.2)	1.37 (0.83–2.28)	0.22
Corpus lesser curvature	59/161 (36.6)	30/164 (18.3)	2.58 (1.55–4.30)	<0.001	55/139 (39.6)	34/186 (18.3)	2.93 (1.77–4.85)	<0.001
Corpus greater curvature	14/158 (8.9)	18/161 (11.2)	0.77 (0.37–1.61)	0.49	13/136 (9.6)	19/183 (10.4)	0.91 (0.43–1.92)	0.81

Choi IJ. NEJM 2018

Expansion of Hp eradication coverage by Korean government (2018.1.1.)

Full coverage

- Peptic ulcer

- MALToma

- EGC after ESD/EMR

- ITP

Limited (100/100)

- Adenoma after ESD/EMR

- Family history of gastric cancer

- Atrophic gastritis

- Patients' wish

Conclusion

- Gastric cancer screening program was successfully established in Korea.

- At least 80% of gastric cancer-related death can be prevented by endoscopy-based screening with 2-year interval.