

Upsurge of Breast Cancer in Young Asian Women: Trend and Its Determinants

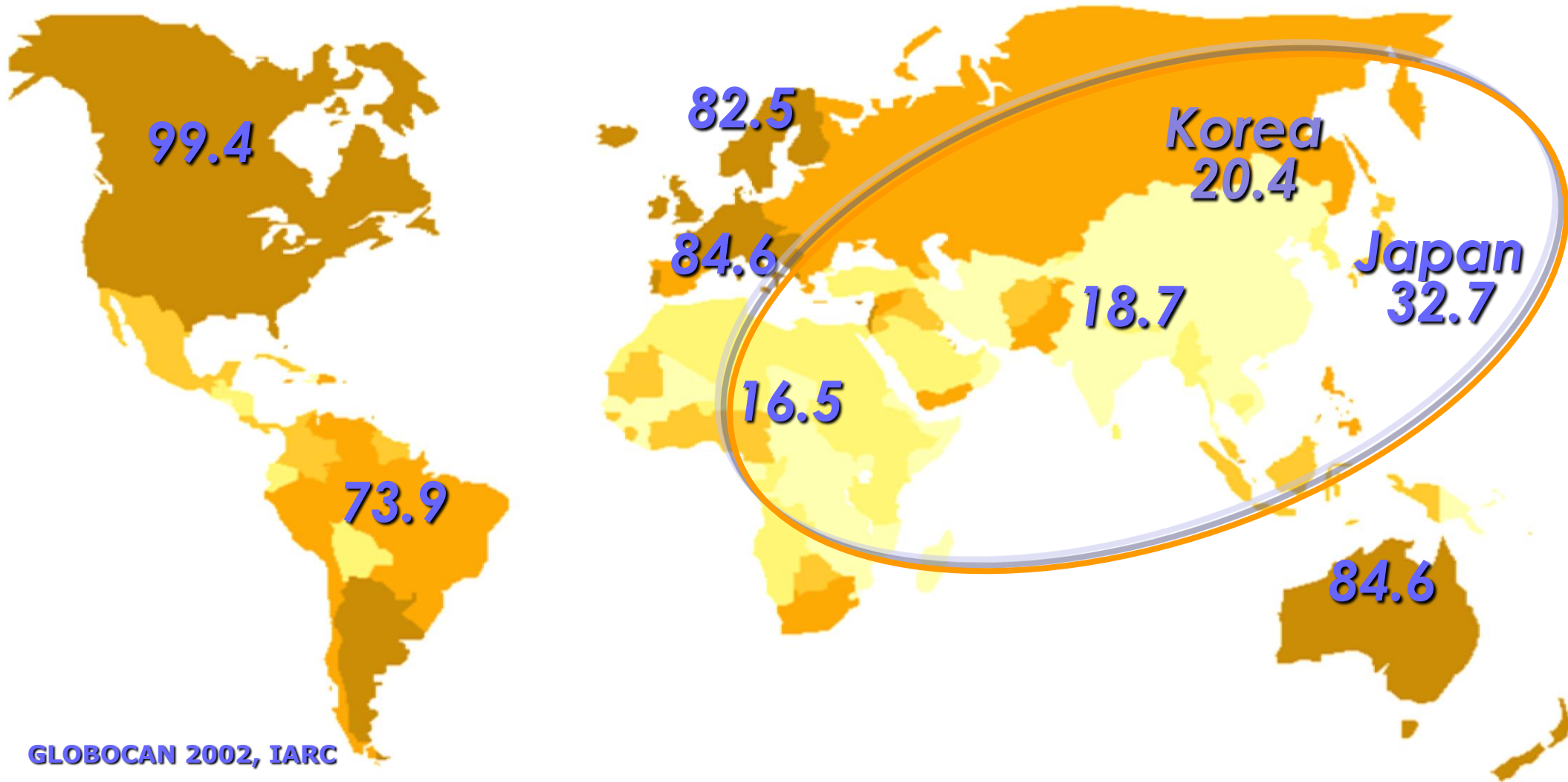
**Seoul National University College of Medicine
Asian Pacific Organization for Cancer Prevention**

Keun-Young Yoo

**+82-2-740-8324
kyyoo@snu.ac.kr**

Global Distribution of Breast Cancer (2002)

Age-standardized Incidence Rate per 100,000

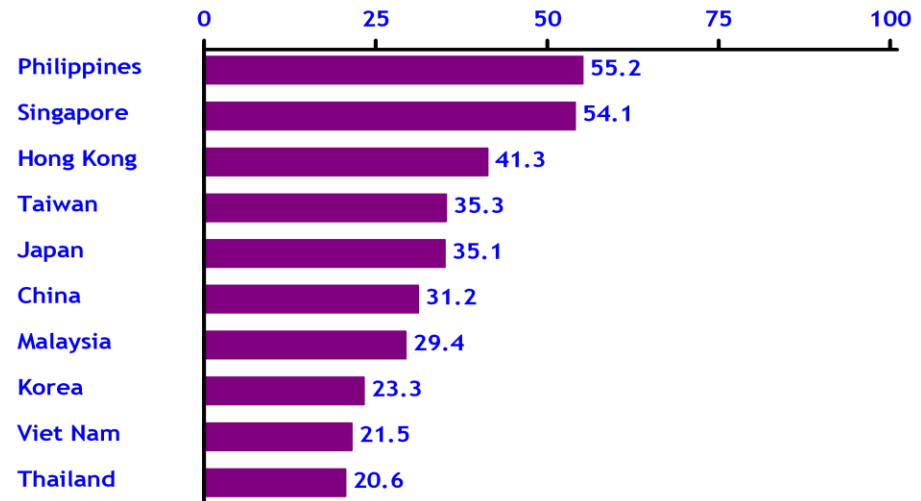


GLOBOCAN 2002, IARC

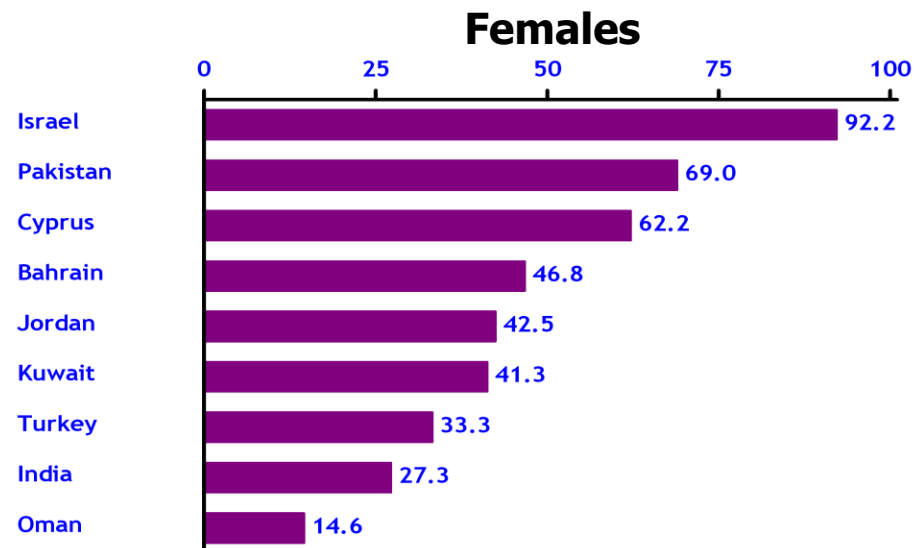
< 19.5 < 25.9 < 34.2 < 52.2 < 101.1

Incidence of Breast Cancer in Asia

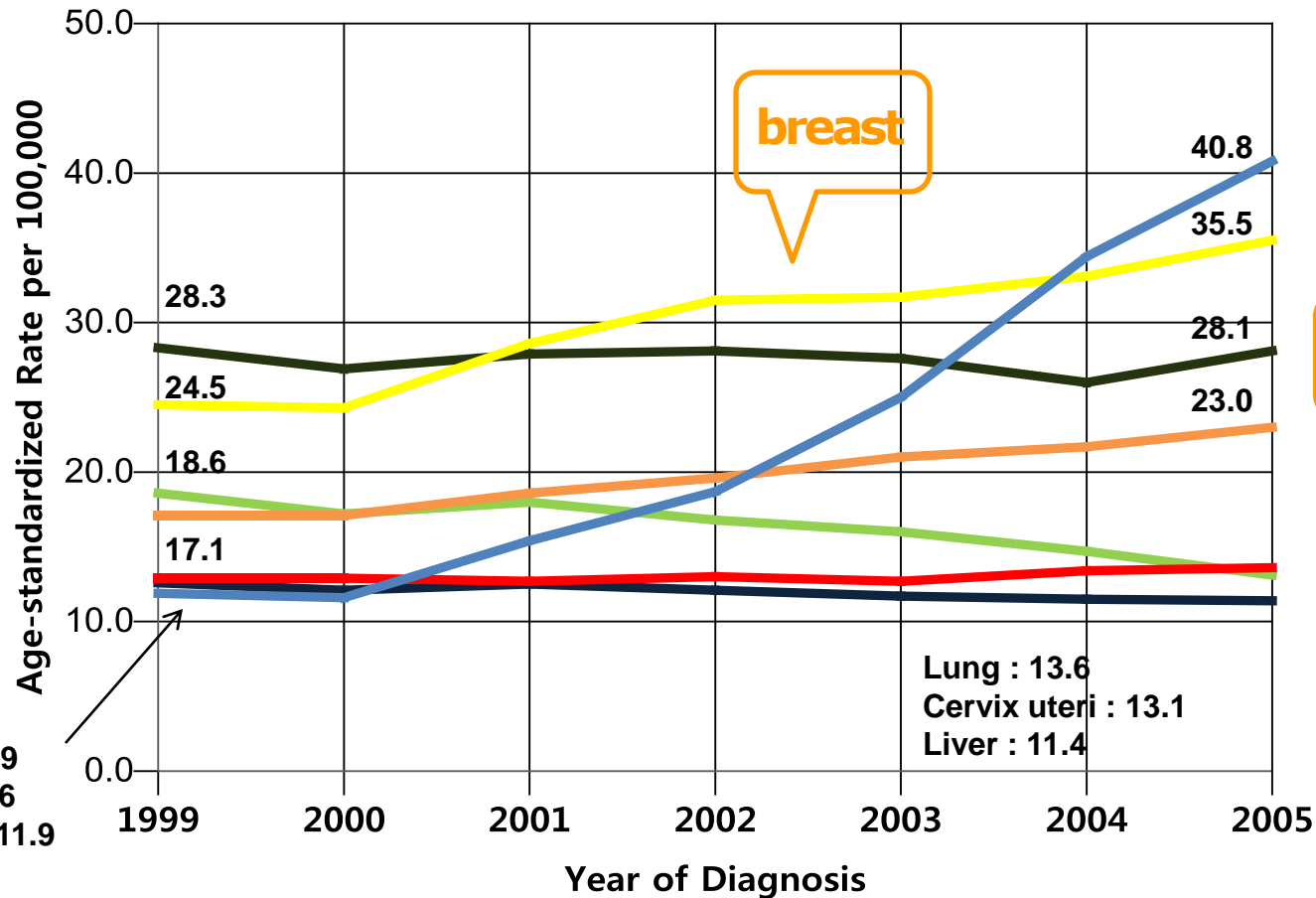
Eastern Asia



Western Asia



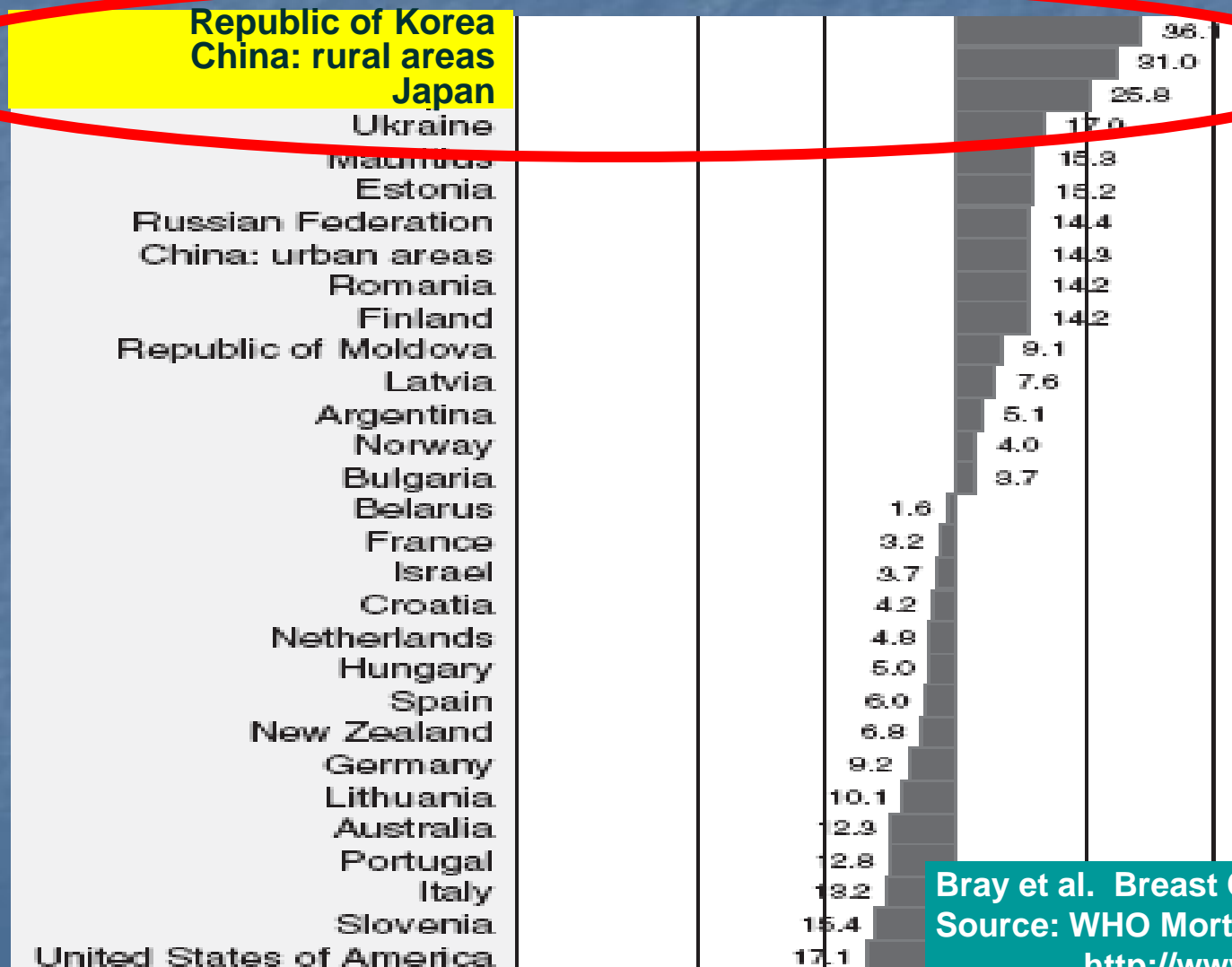
Trend of Age-standardized Incidence Rate by Site Female, 1999-2005, Korea



Site	Annual Percent Change (%)
Thyroid	25.5
Breast	6.8
Stomach	-0.4
Colorectum	5.5
Lung	0.8
Cervix uteri	-5.2
Liver	-1.7

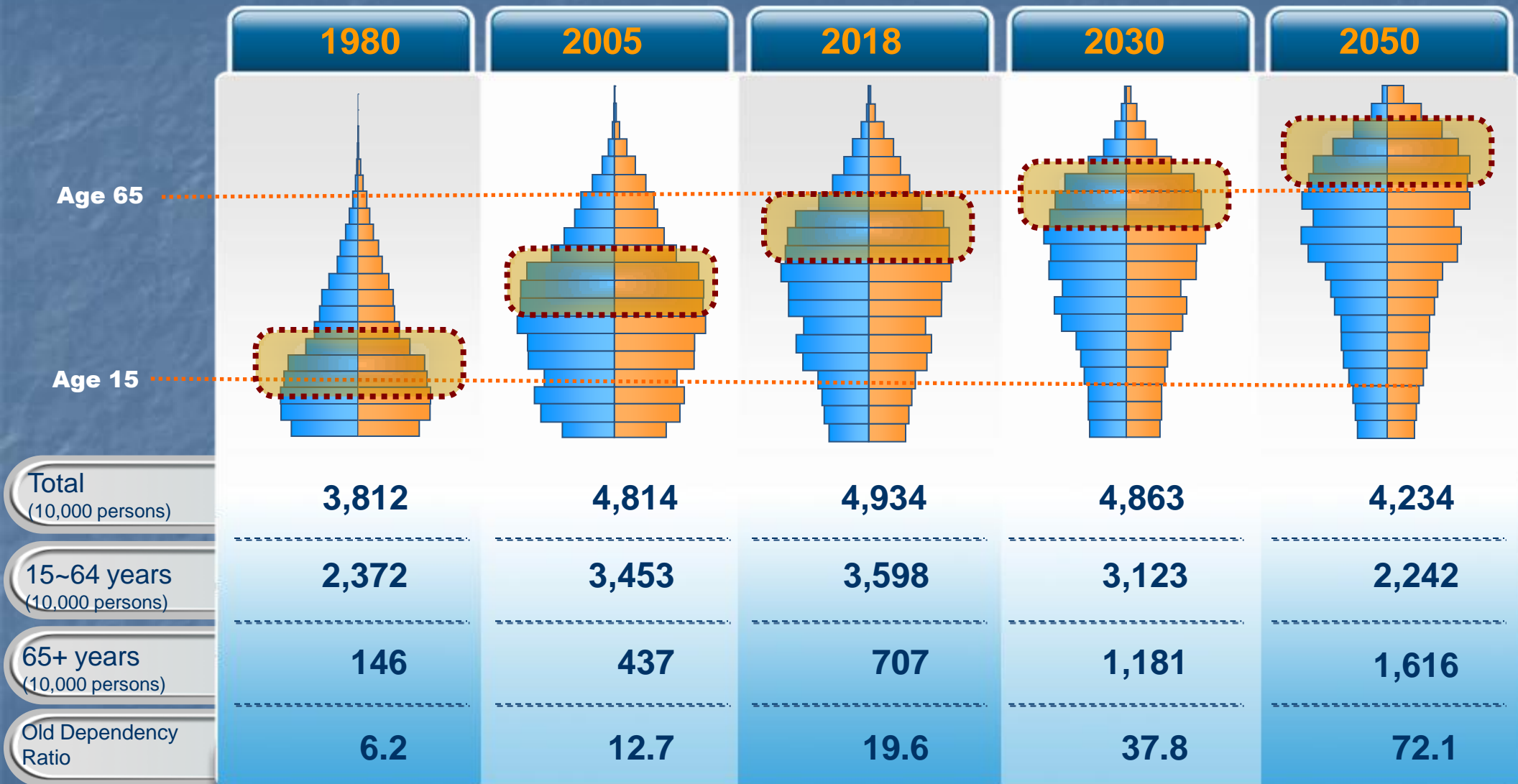
Change in Breast Cancer Mortality

Ages 25-49, % Change during 1985-87 to 1995-97



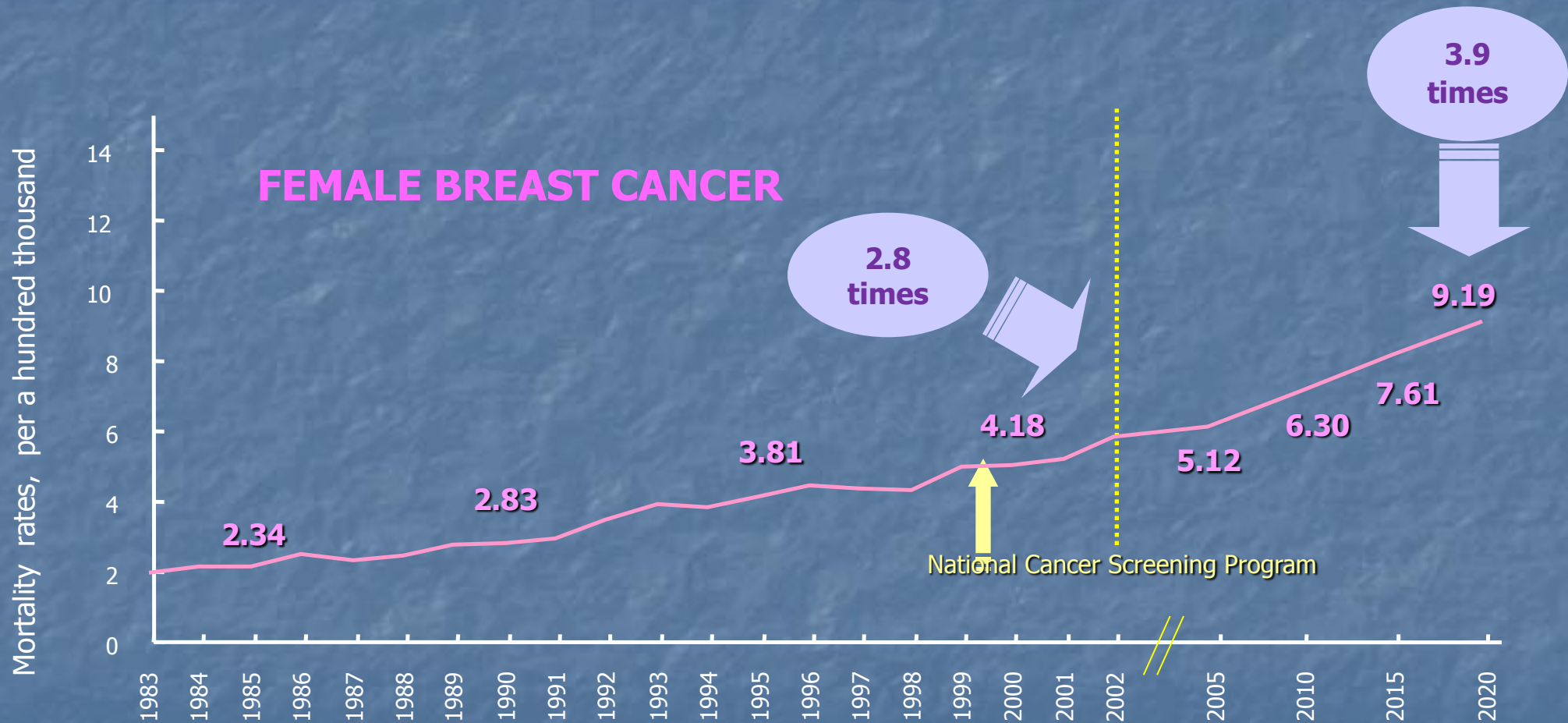
Bray et al. Breast Cancer Res 2004
 Source: WHO Mortality database
<http://www-depdb.iarc.fr/>

Age Tsunami: Baby Boomer born 1953-1958



Projection of Breast Cancer Mortality

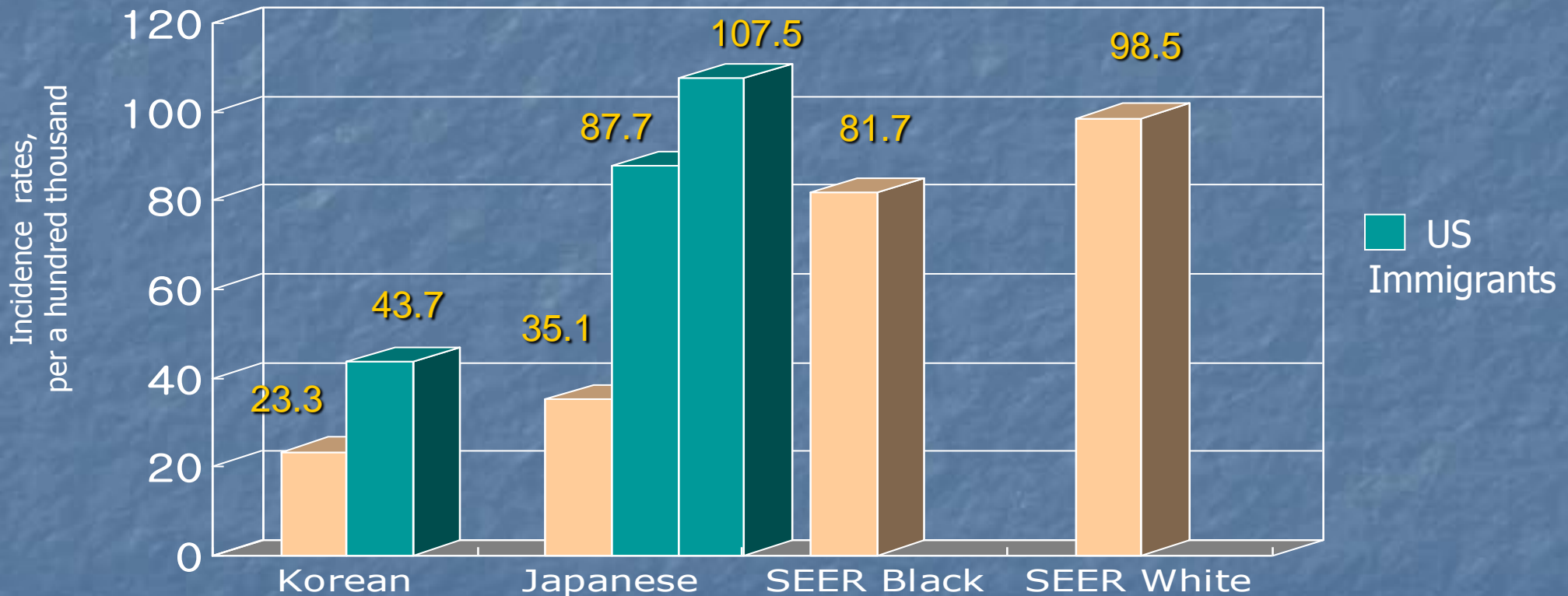
Korea, all ages, 2005-2020



Source : *National Statistical Office* 2002
Choi et al. *Asian Pacific J Cancer Prev* 2005

— based on Poisson regression model

ASR of Breast Cancer of Korean and Japanese Immigrants

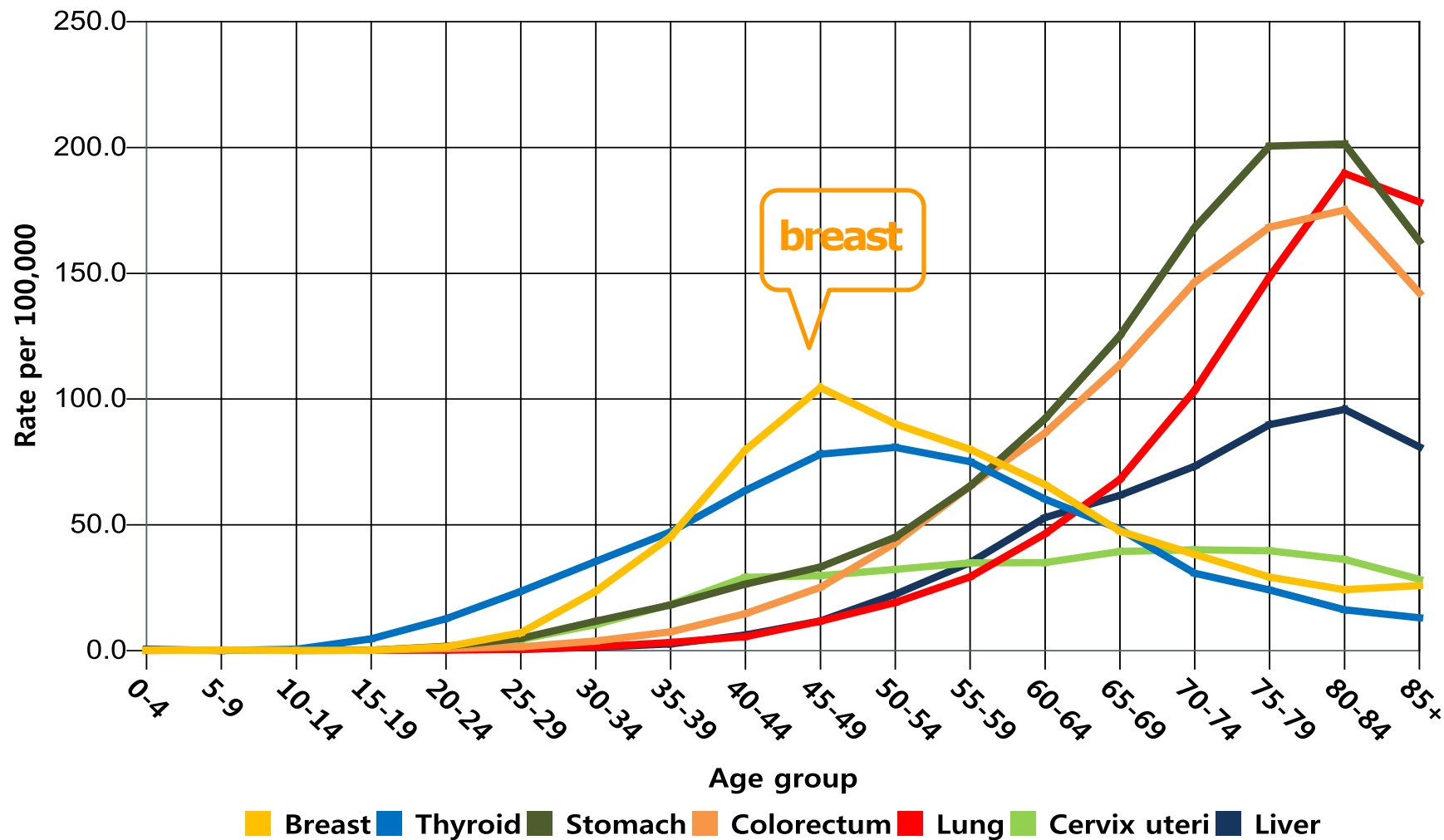


Source: Curado et al. Cancer Incidence in Five Continents Vol IX. 2007

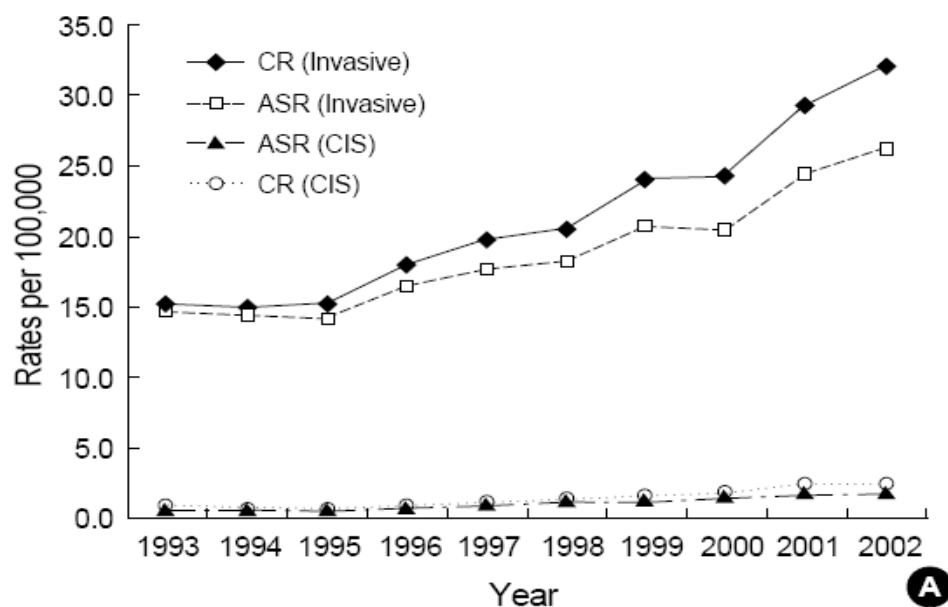
Age Incidence Curve

Age-specific Incidence Rates of Major Sites

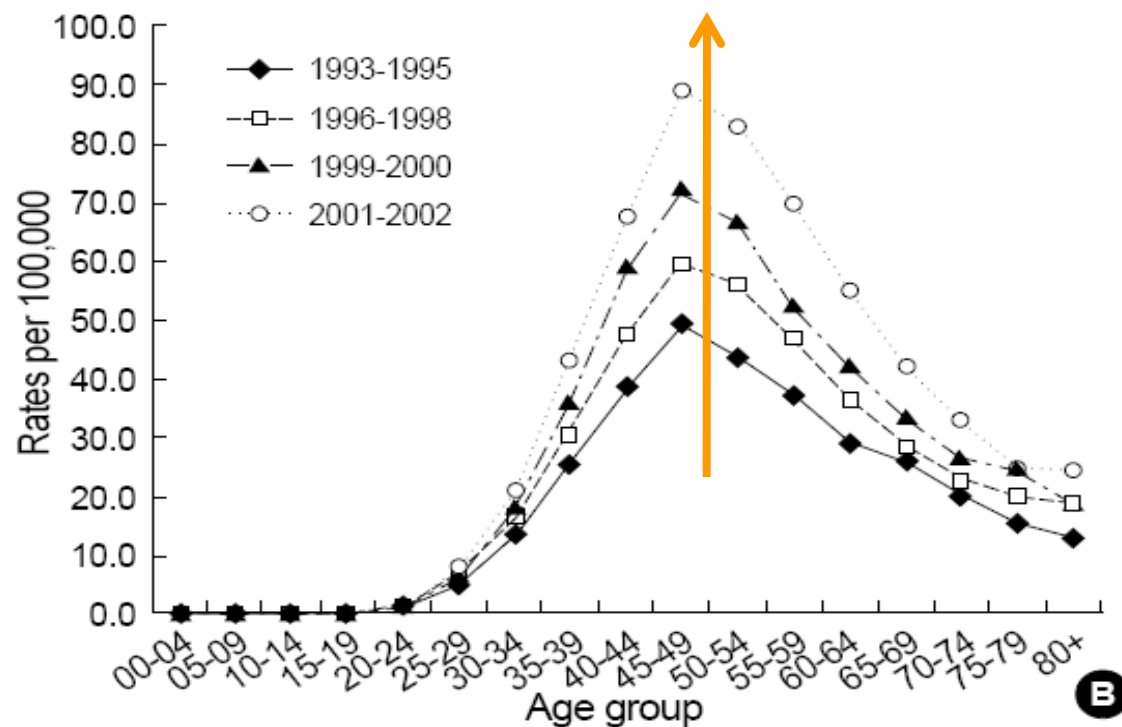
Korean Female, 2003~2005



Incidence trends of female breast cancer in 1993-2002, Korea

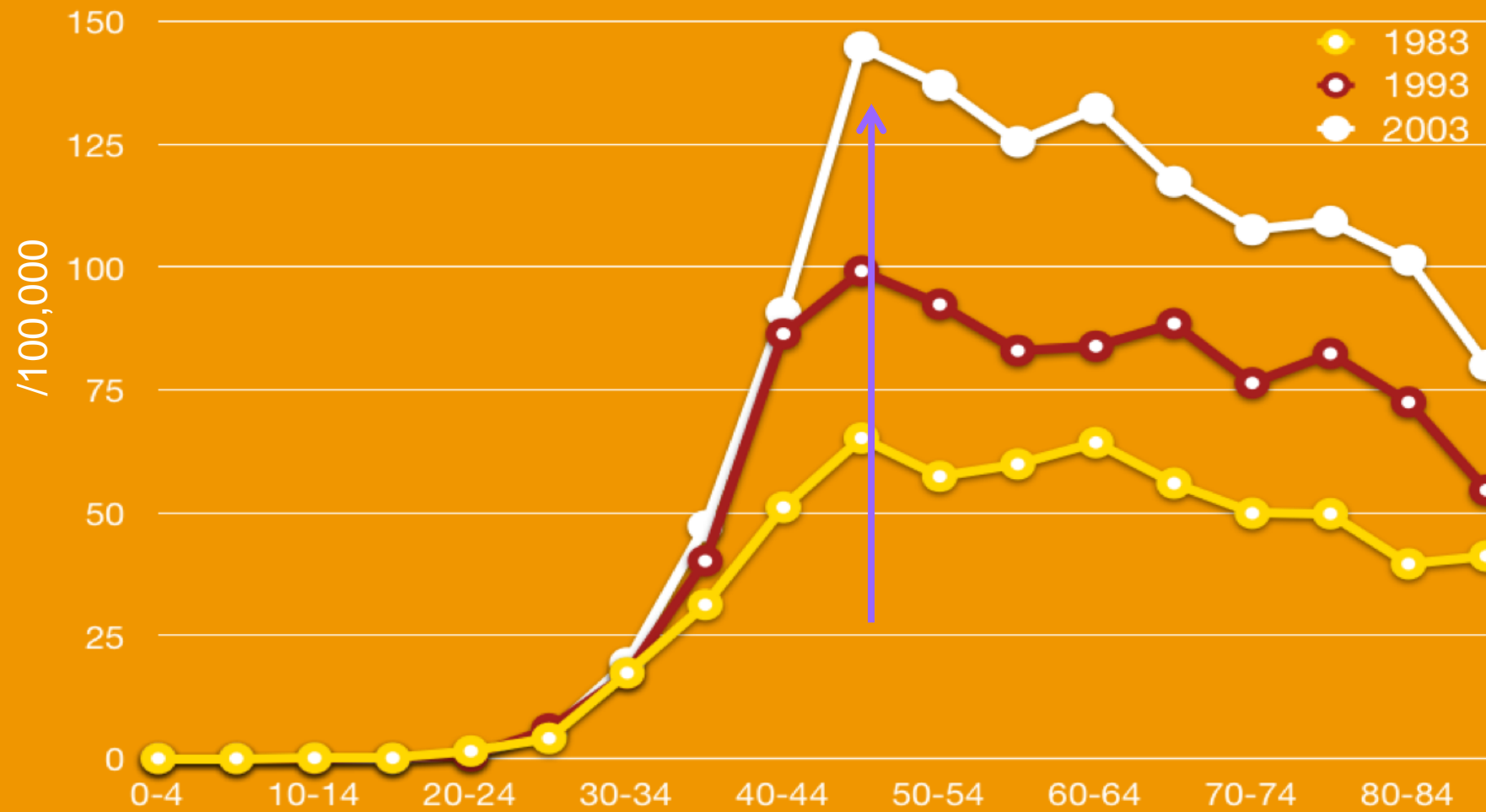


(A) Incidence trends of female invasive breast cancer and CIS by year of diagnosis

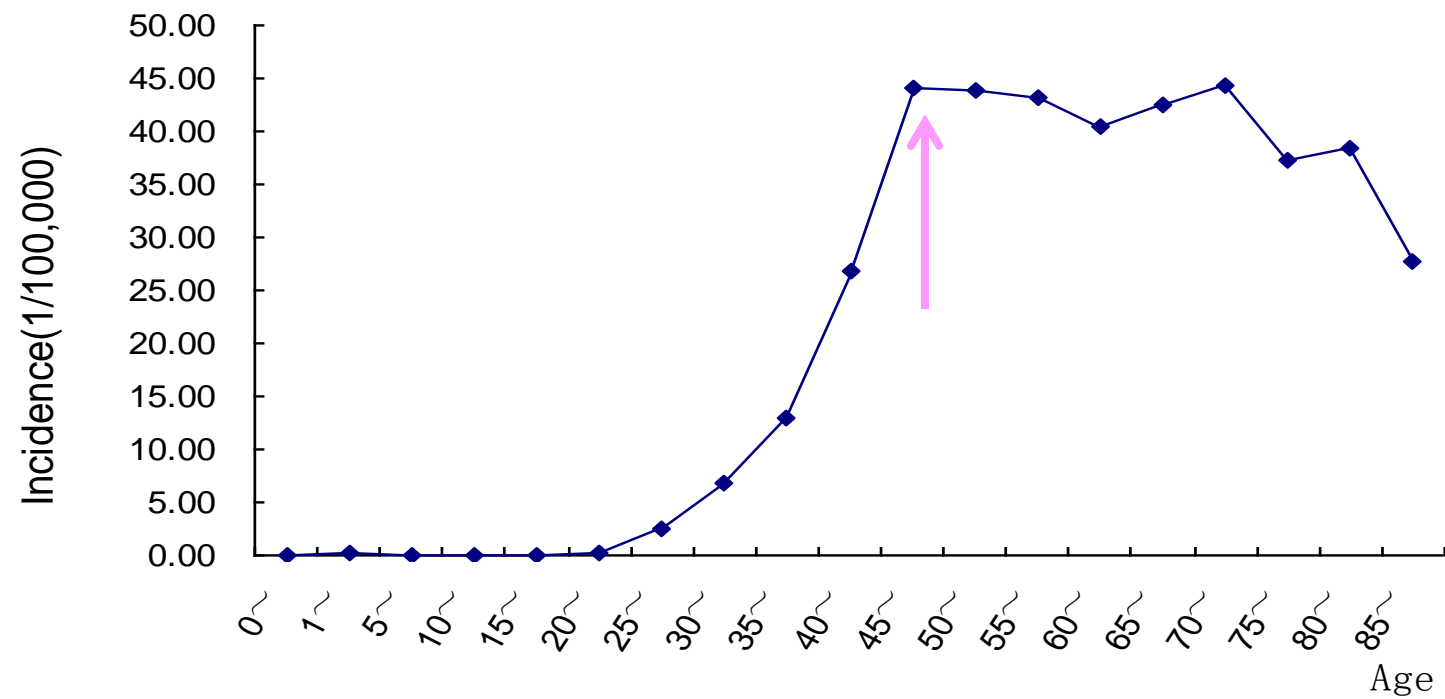


(B) Age-specific incidence rates of female invasive breast cancer by time period of diagnosis

Age-specific Incidence of Breast Cancer in Japan



from National Cancer Center Cancer Information Service, Japan



Age-specific Incidence of Breast Cancer in China 2004

Epidemiology of BC in Karachi, Pakistan

1/3 of all female cancers

ASIR = 53.8 / 100,000

60% of newly diagnosed BC were women below 50 years

ductal cell carcinoma: 92%

regional LN(+): 56%

higher in non-Muslim

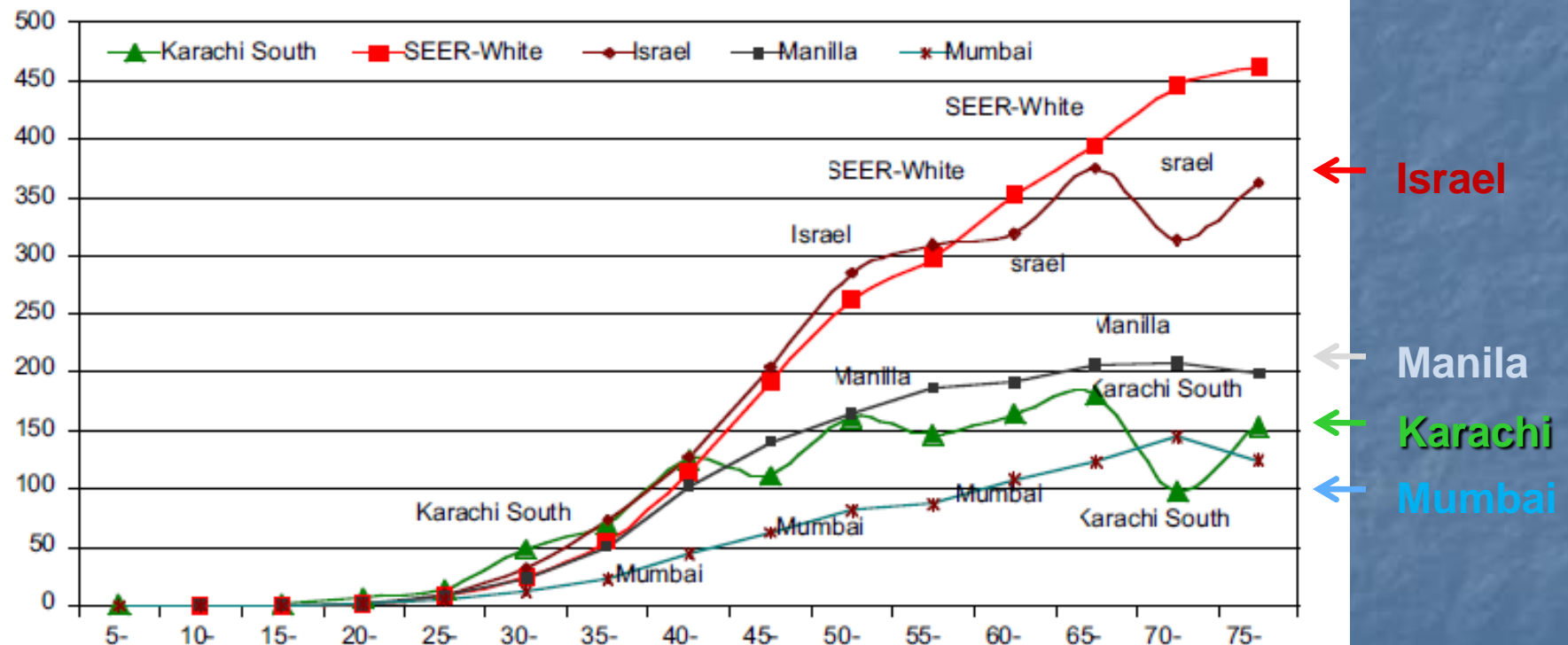


Figure 1. Comparison of Age-dependent Breast Cancer Incidences in Different Registries

Epidemiology of BC in Malaysia

the most common
1 in 20 women develop BC in lifetime
ASIR = 46.2 / 100,000
higher in **Chinese > Indians > Malays**
commonest in 40-49 years
over 50% of BC under age 50 years

ER(+): 55.7%
stages I-II: 60-70%
survival worse in Malays

similar lifestyle factors

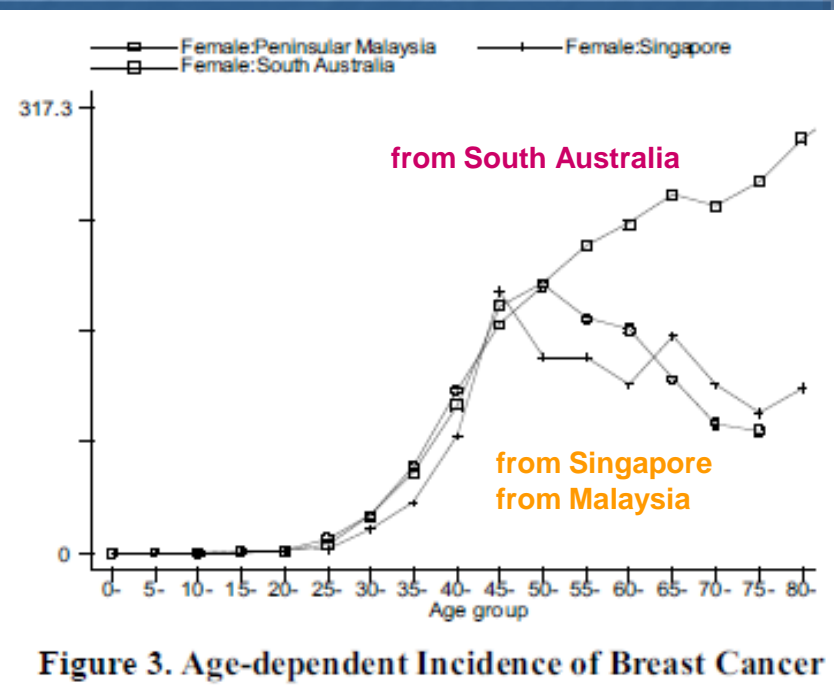
less exercise, high fat diet
parity, breastfeeding

Kamarudin et al. Asian Pacific J Cancer Prev 2006

Table 2. Female Breast Cancer Age Incidence in Malaysia (NCR Report)

Age	No	%	CR
0-9	2	0.1	0.1
10-19	5	0.1	0.3
20-29	39	1.0	2.5
30-39	457	12.2	34.1
40-49	1255	33.6	111.9
50-59	1141	30.5	159.8
60-69	571	15.3	137.7
70+	268	7.2	97.9

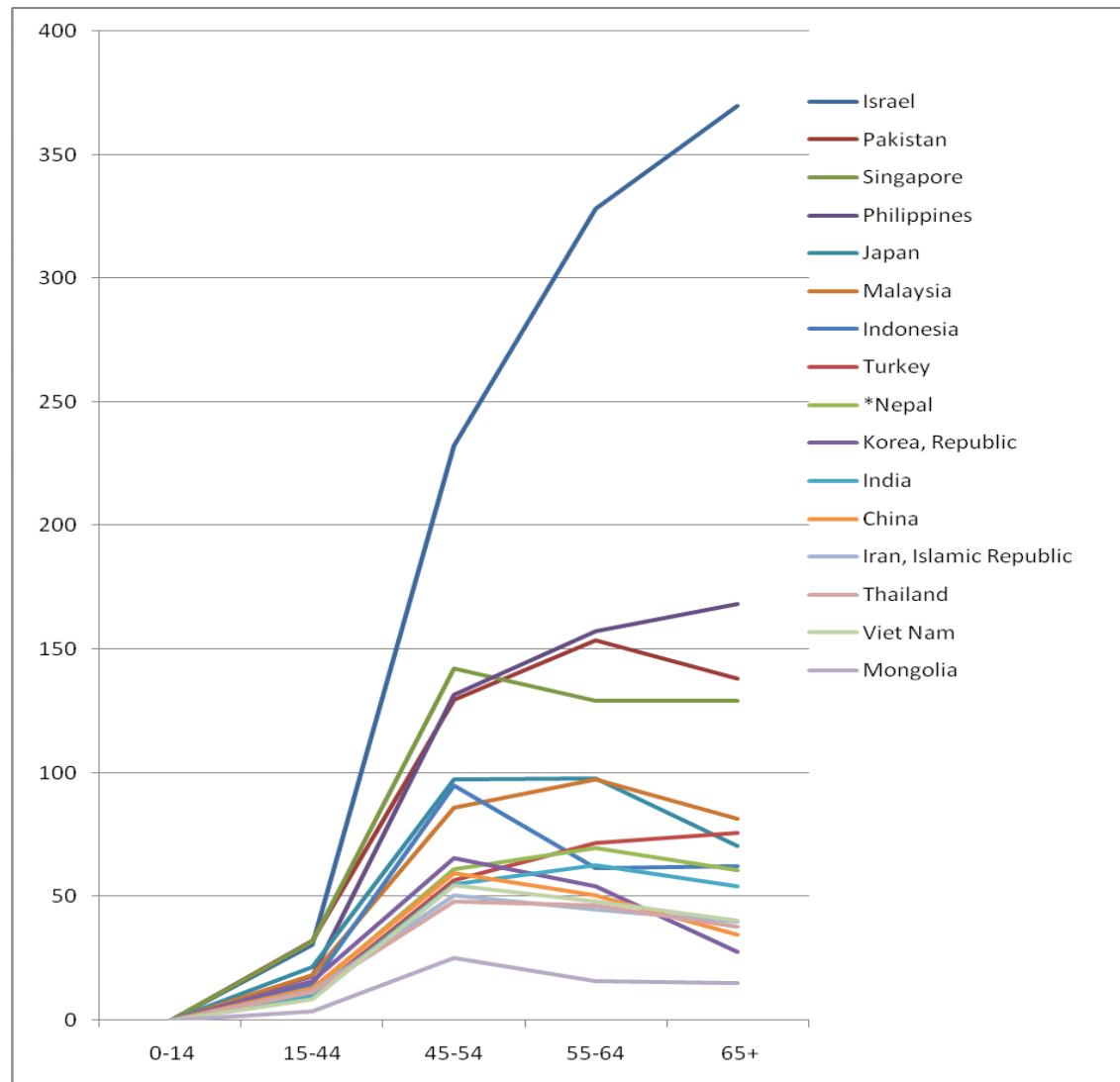
CR, cancer incidence rate/100,000



Yip et al. Asian Pacific J Cancer Prev 2006

Age-Incidence Curves of Breast Cancer in selected Asian Countries

Countries	All ages	ASR (World)
Pakistan	35.6	50.1
Singapore	58.9	48.7
Philippines	33.5	46.6
Japan	49.6	32.7
Malaysia	26.2	30.8
Indonesia	23.3	26.1
Turkey	19.9	22.0
Nepal	15.6	21.8
Korea	23.5	20.4
India	16.5	19.1
China	20.1	18.7
Iran	13.4	17.1
Thailand	16.3	16.6
Viet Nam	13.1	16.2
Mongolia	4.9	6.6

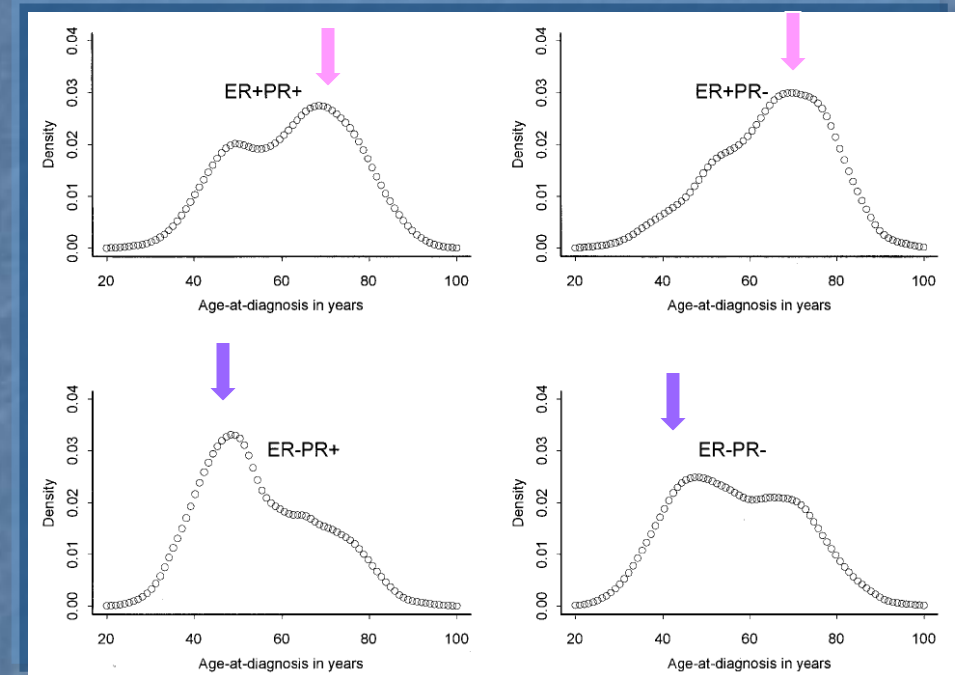


Source: Globocan 2002

ER/PR Status in US by Ethnic Group

Unit: %

Ethnic Groups	ER+PR+	ER+PR-	ER-PR+	ER-PR-
White	63.9	12.8	3.6	19.8
Blacks	48.3	11.8	5.1	34.8
Hispanic	56.7	12.0	4.6	26.7
Japanese	65.6	12.5	4.8	17.1
Chinese	60.6	11.7	5.1	22.6
Korean*	46.5	12.8	4.7	36.1
Filipino	60.2	11.6	4.9	23.3



Age frequency density plot

Chu et al. Cancer 2001;92:37-45

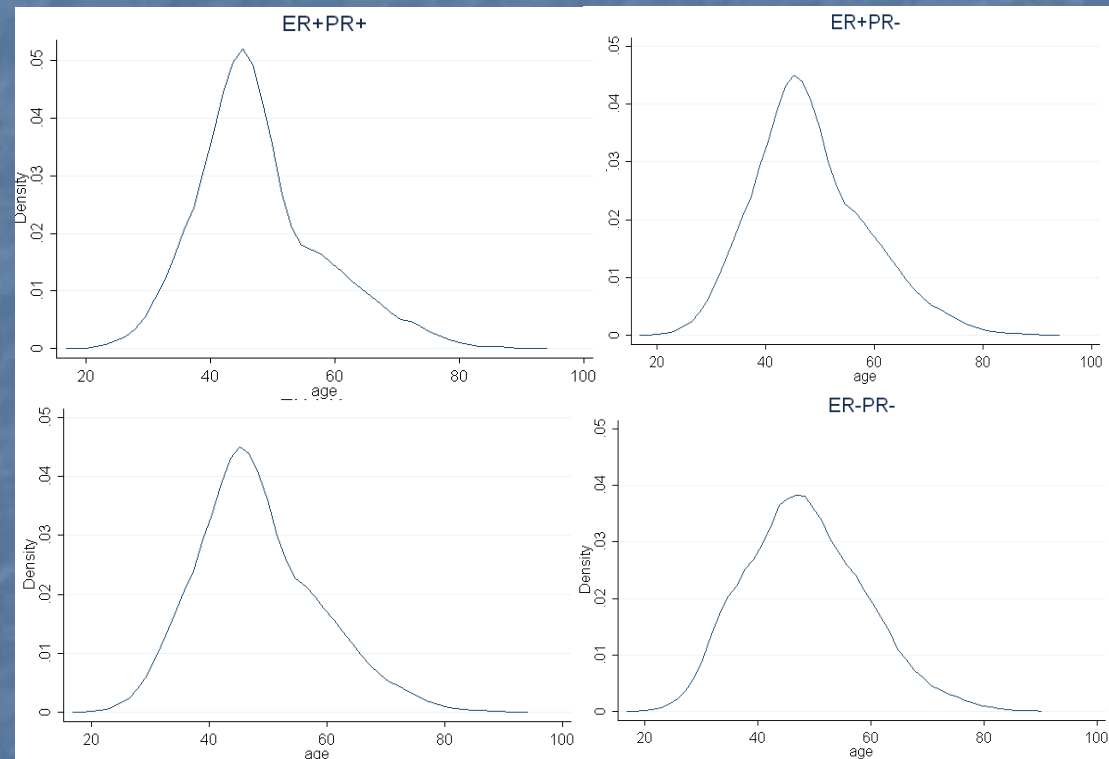
*Li et al. Cancer Epidemiol Biomarkers Prev 2002;11:601-7

Figure from Anderson et al. JCO 2001;19:18-27

ER/PR Status

28,210 Korea Breast Cancer Society, 1992-2006

ER/PR	ER+	ER-	Total
PR+	46.2%	7.3%	53.5%
PR-	12.5%	34.0%	46.5%
Total	58.7%	41.3%	100%

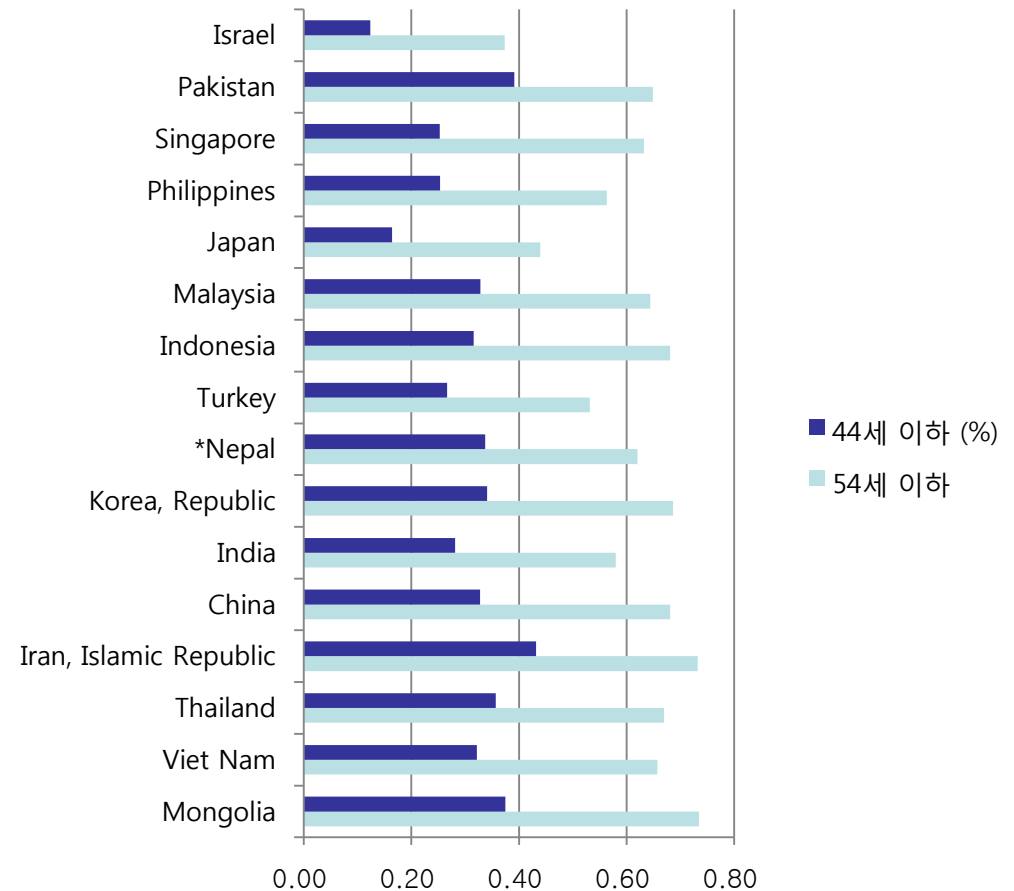


Age frequency density plot

Breast Cancer in Younger Women in Asia

% of breast cancer under 54 / 44 years old

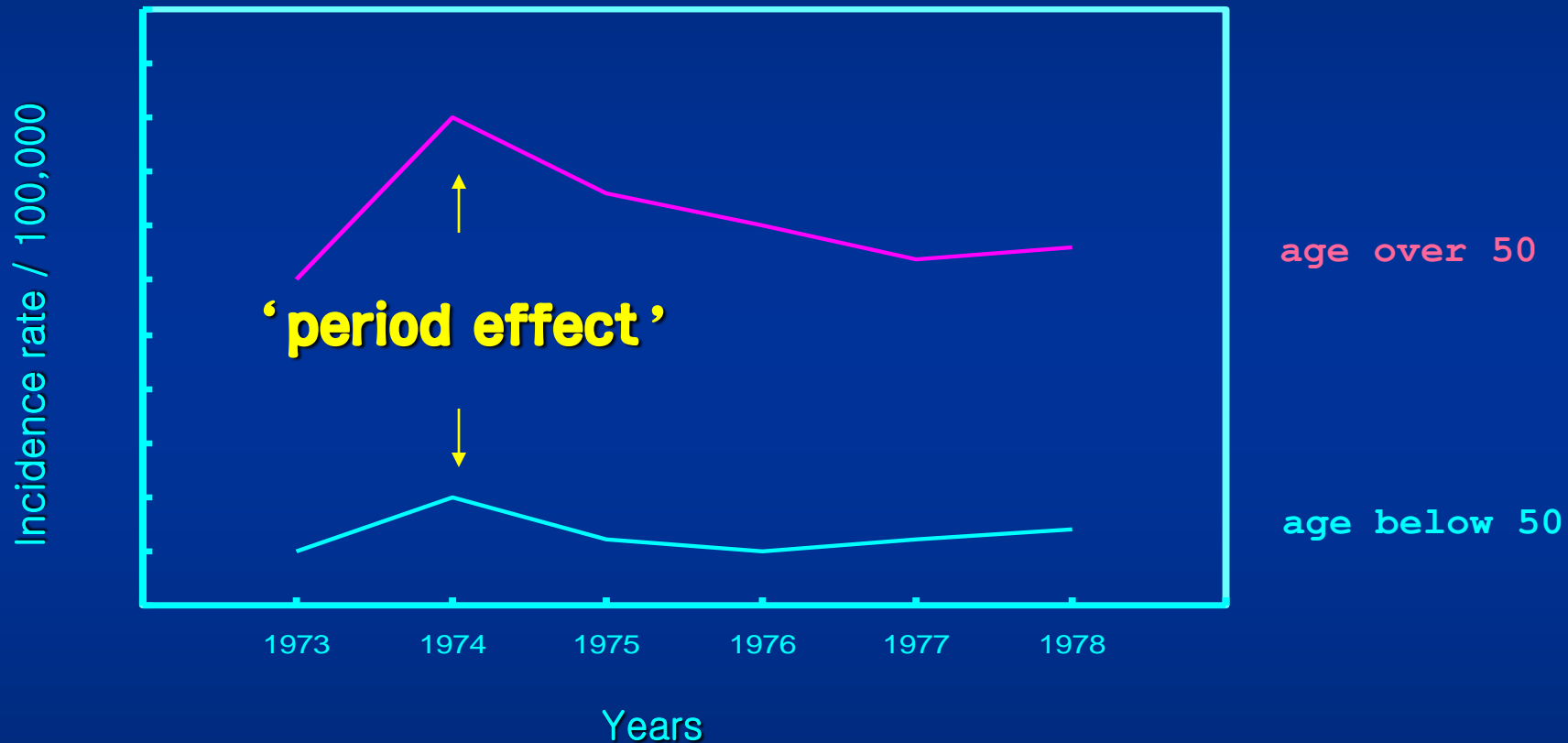
Breast Incidence case	ASR (World)	under 54 yrs	Under 44 yrs
Israel	90.8	0.37	0.12
Pakistan	50.1	0.65	0.39
Singapore	48.7	0.63	0.25
Philippines	46.6	0.56	0.25
Japan	32.7	0.44	0.16
Malaysia	30.8	0.64	0.33
Indonesia	26.1	0.68	0.32
Turkey	22.0	0.53	0.27
Nepal	21.8	0.62	0.34
Korea, Republic	20.4	0.69	0.34
India	19.1	0.58	0.28
China	18.7	0.68	0.33
Iran	17.1	0.73	0.43
Thailand	16.6	0.67	0.36
Viet Nam	16.2	0.66	0.32
Mongolia	6.6	0.73	0.38



Breast Cancer in Young Women

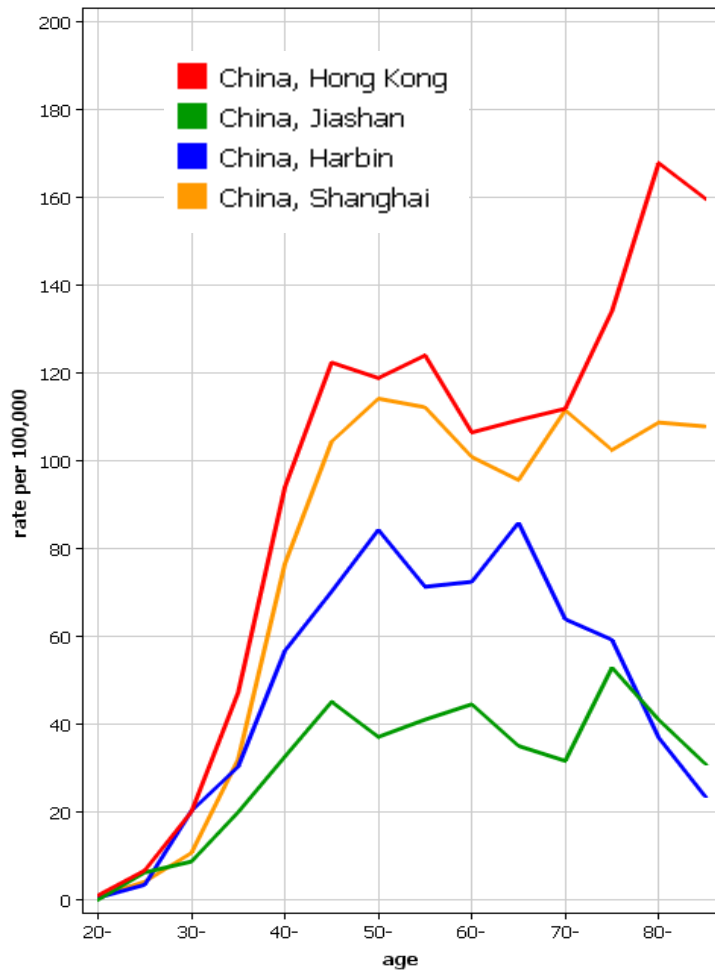
Period Effect?

Impact of Betty Ford's Breast Cancer Diagnosis on Incidence

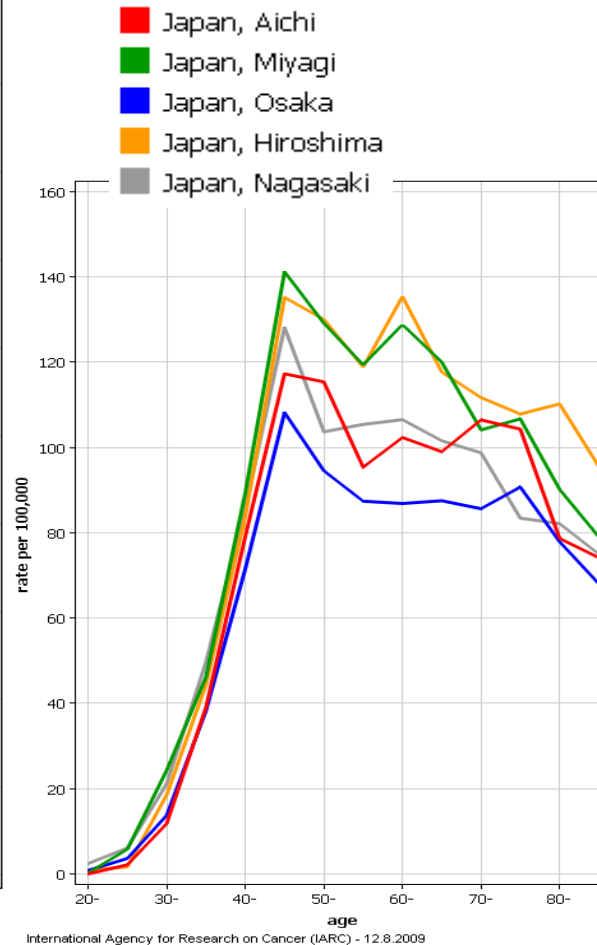


SEER Registries

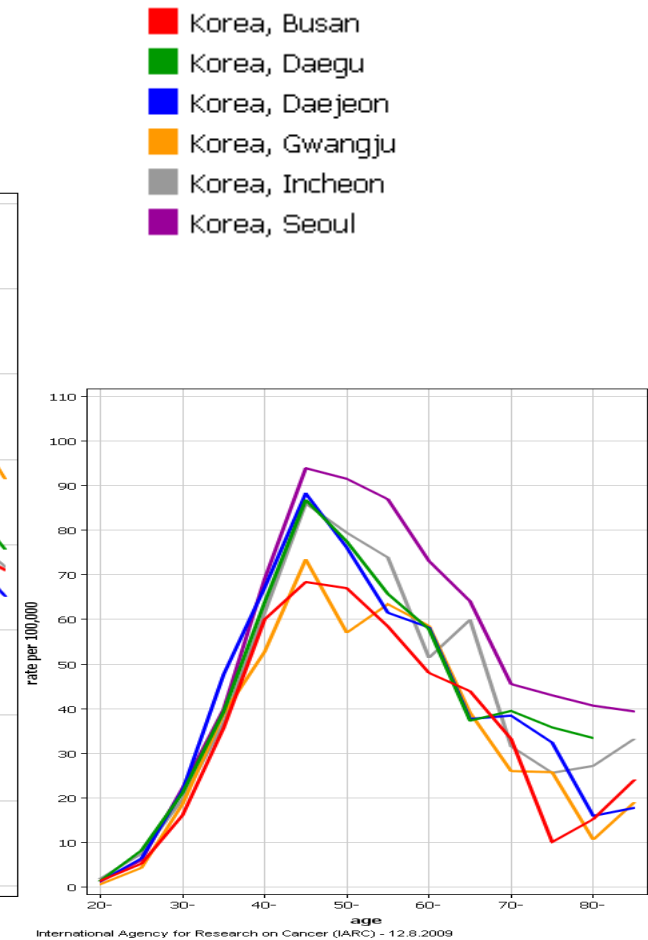
China



Japan

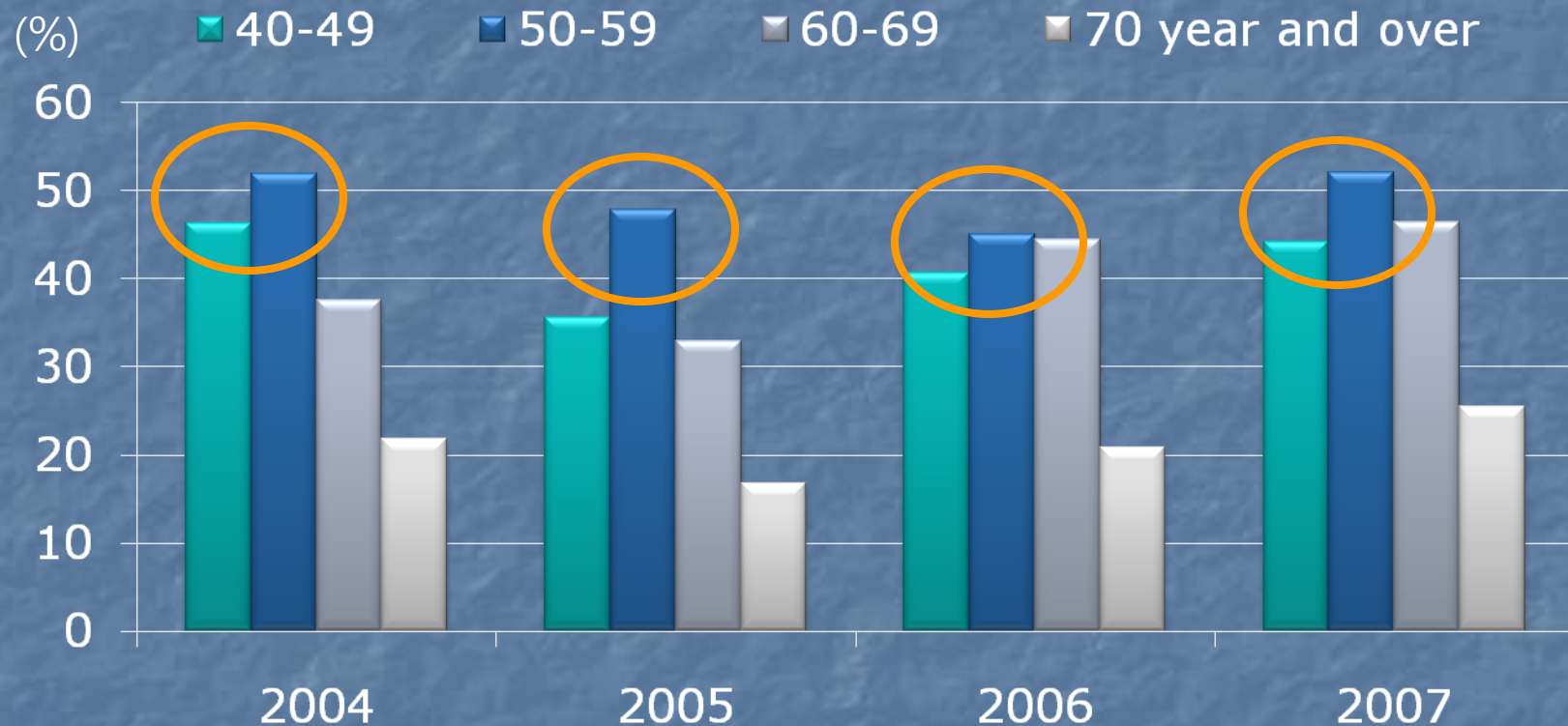


Korea



Breast Cancer Screening Rates

Age Groups, Nationwide Korea, 2004-2007



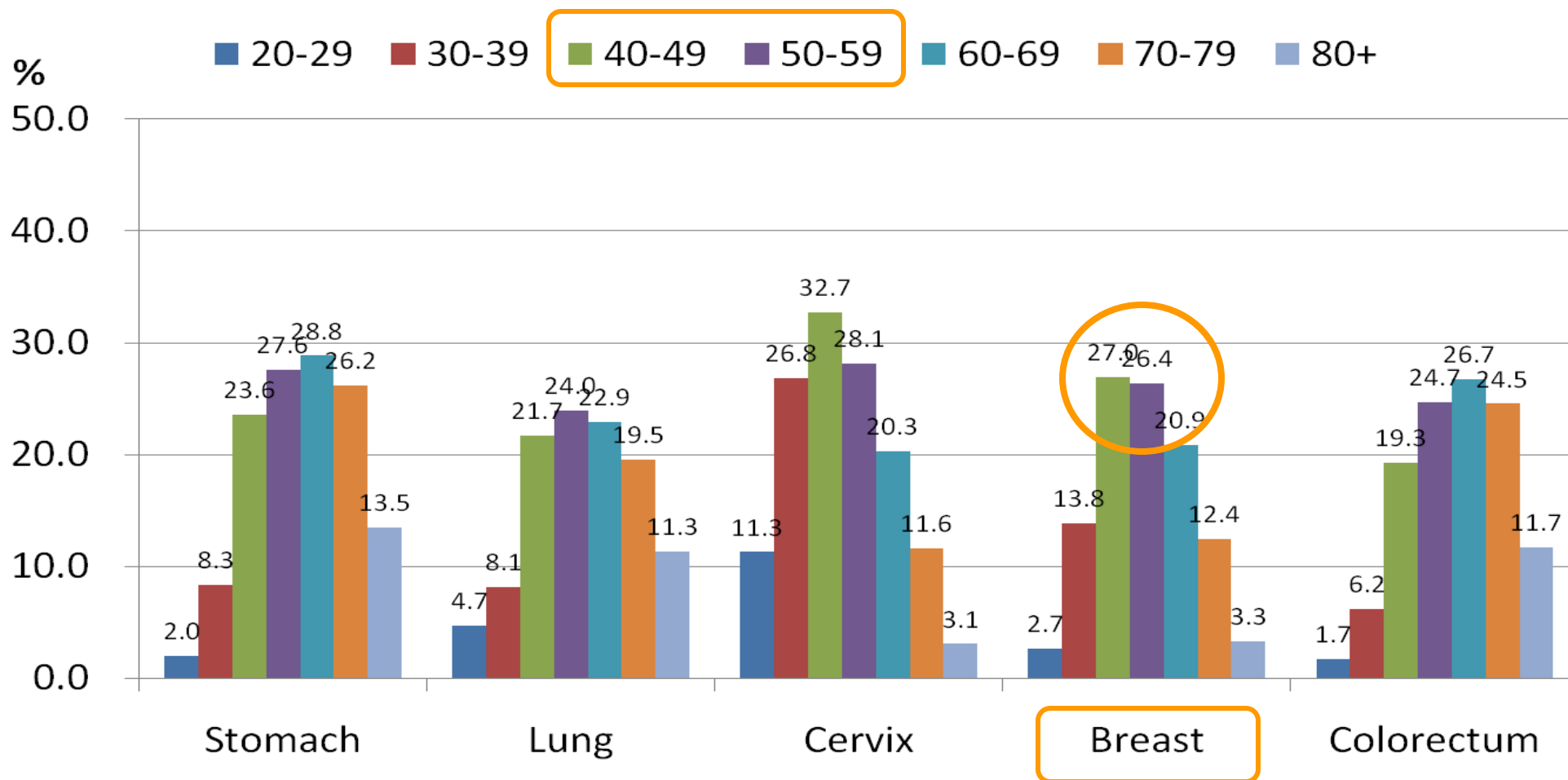
Source: National Cancer Screening Behavior Survey, 2004-2007, National Cancer Center

Voluntary Breast Cancer Screening



Participation for Cancer Screening by Age

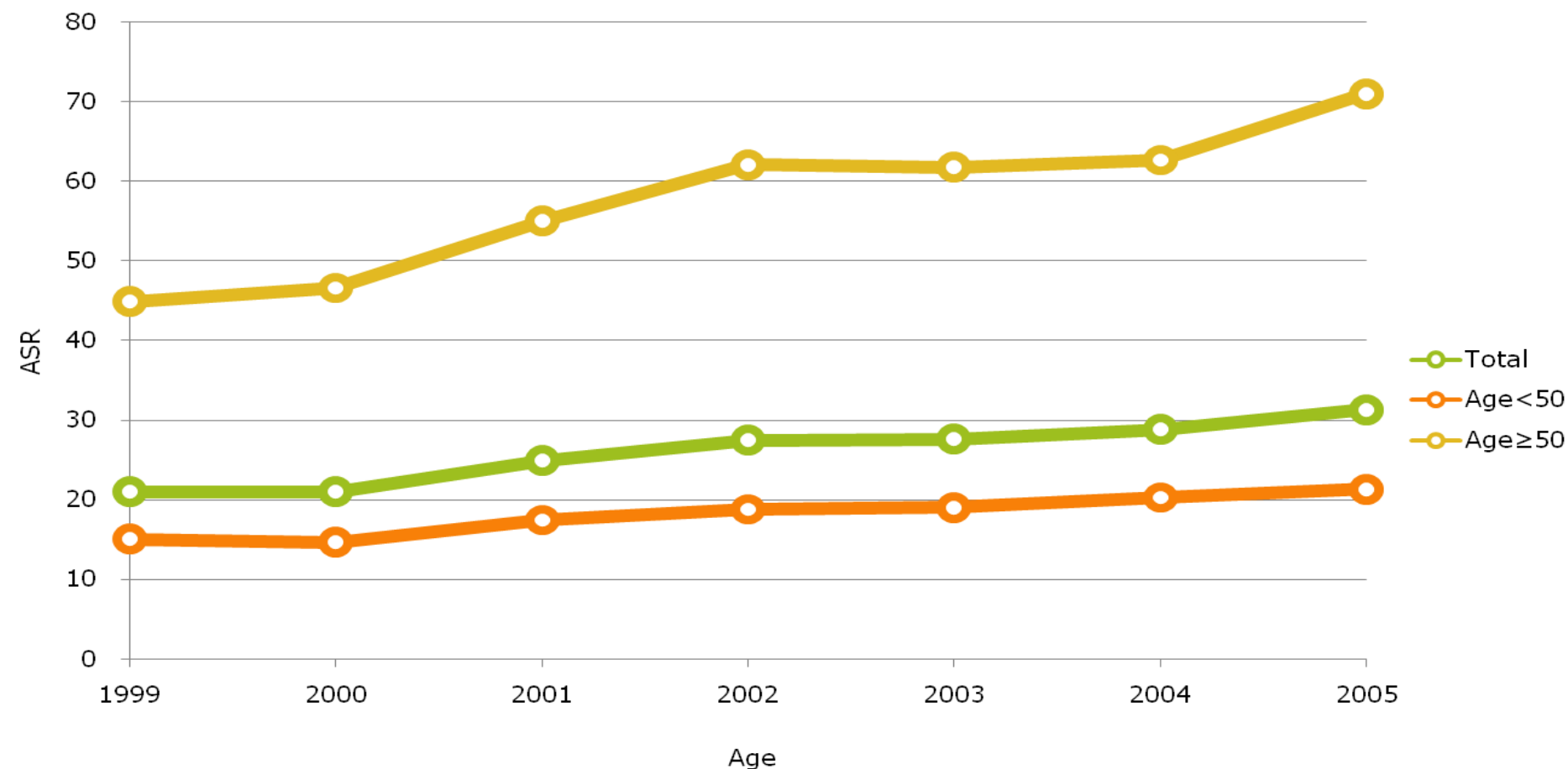
National Livelihood Survey, Japan, 2007



Breast Cancer in Young Women

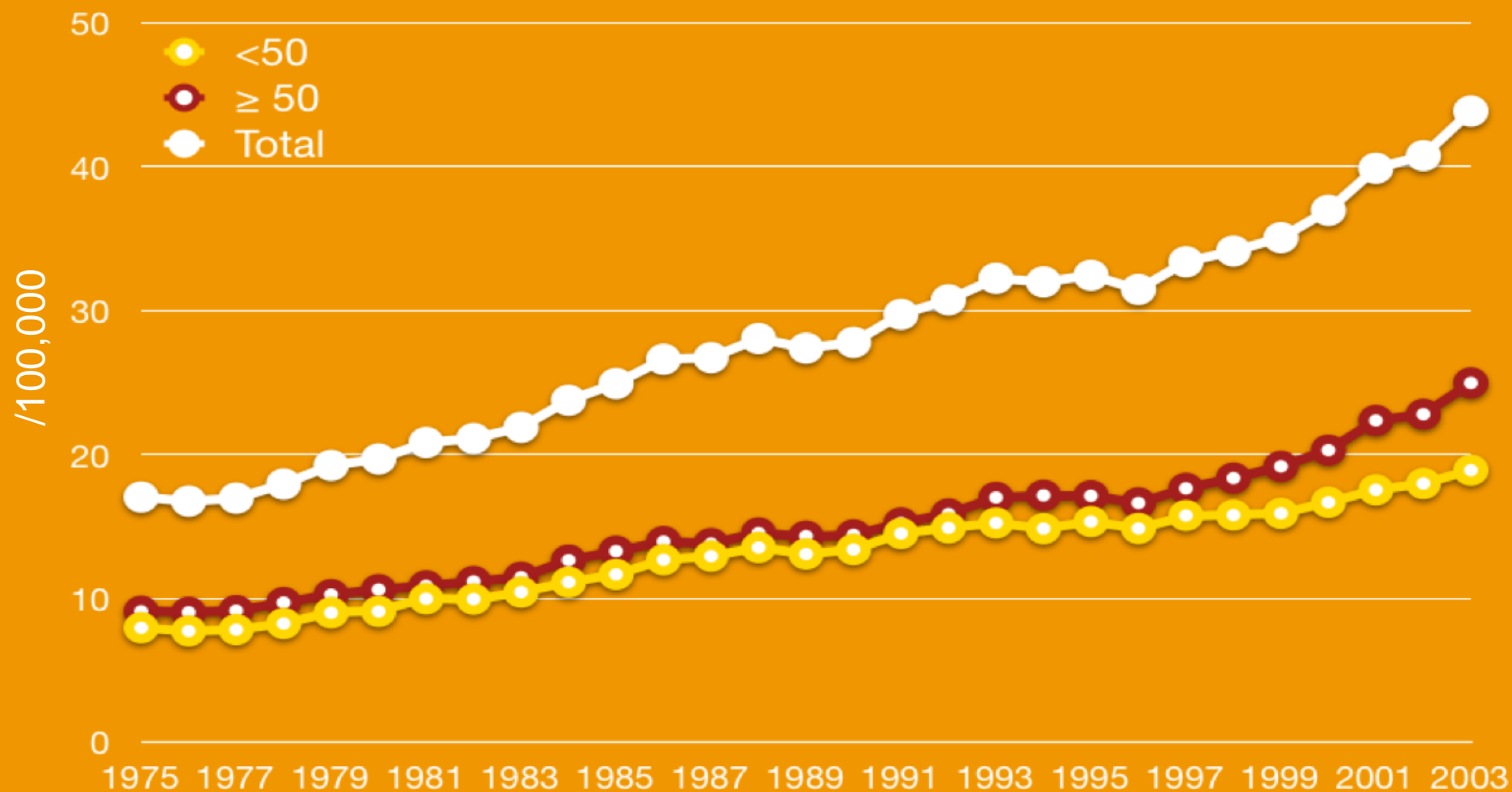
Age-Cohort Effect?

Age-adjusted Incidence of Breast Cancer in Korea



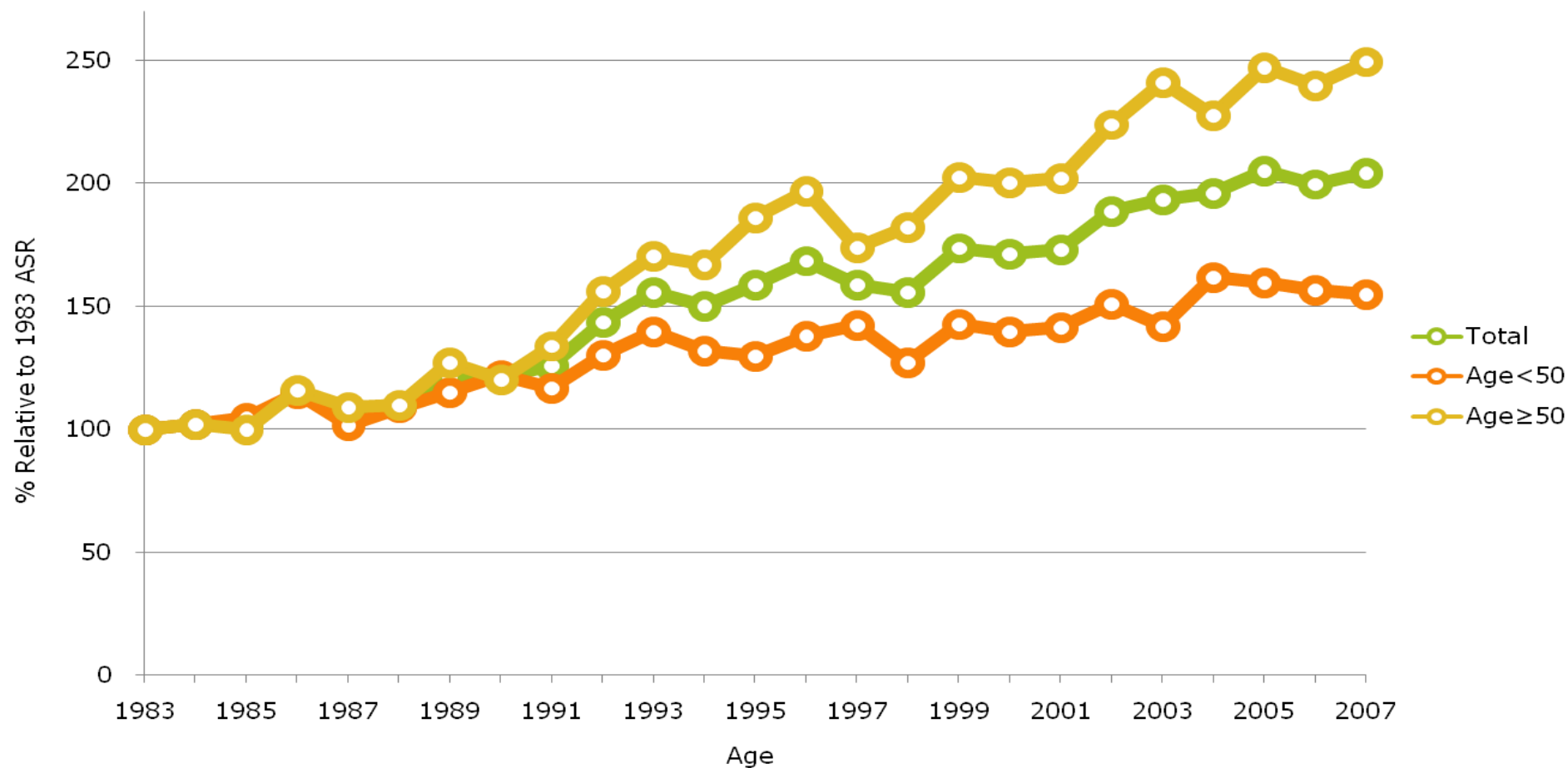
Incidence Data Source: The Korea Central Cancer Registry, 2008

Age-adjusted Incidence of Breast Cancer in Japan



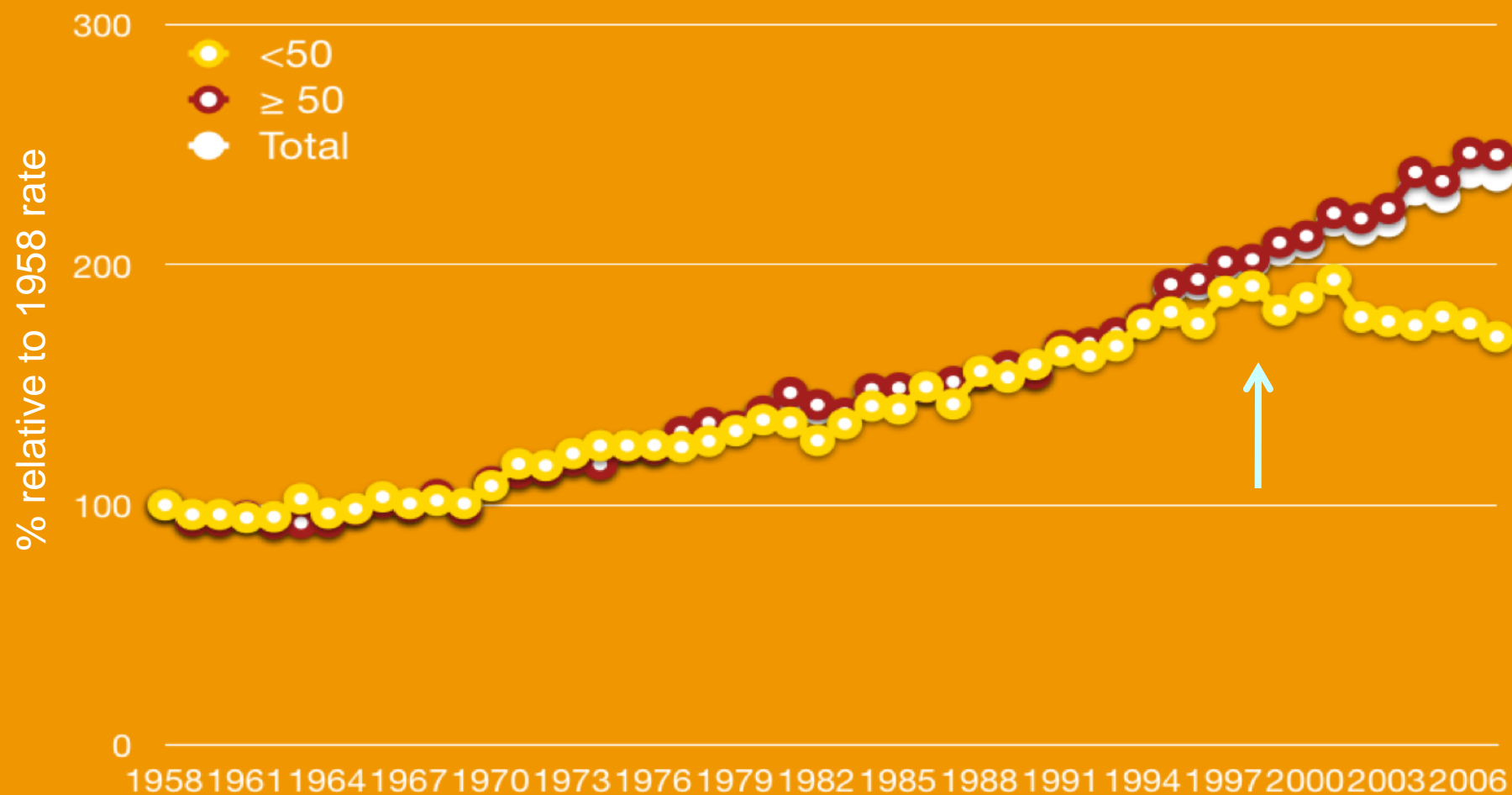
estimated by data from National Cancer Center Cancer Information Service, Japan

Period Trends in Breast Cancer Mortality: Korea



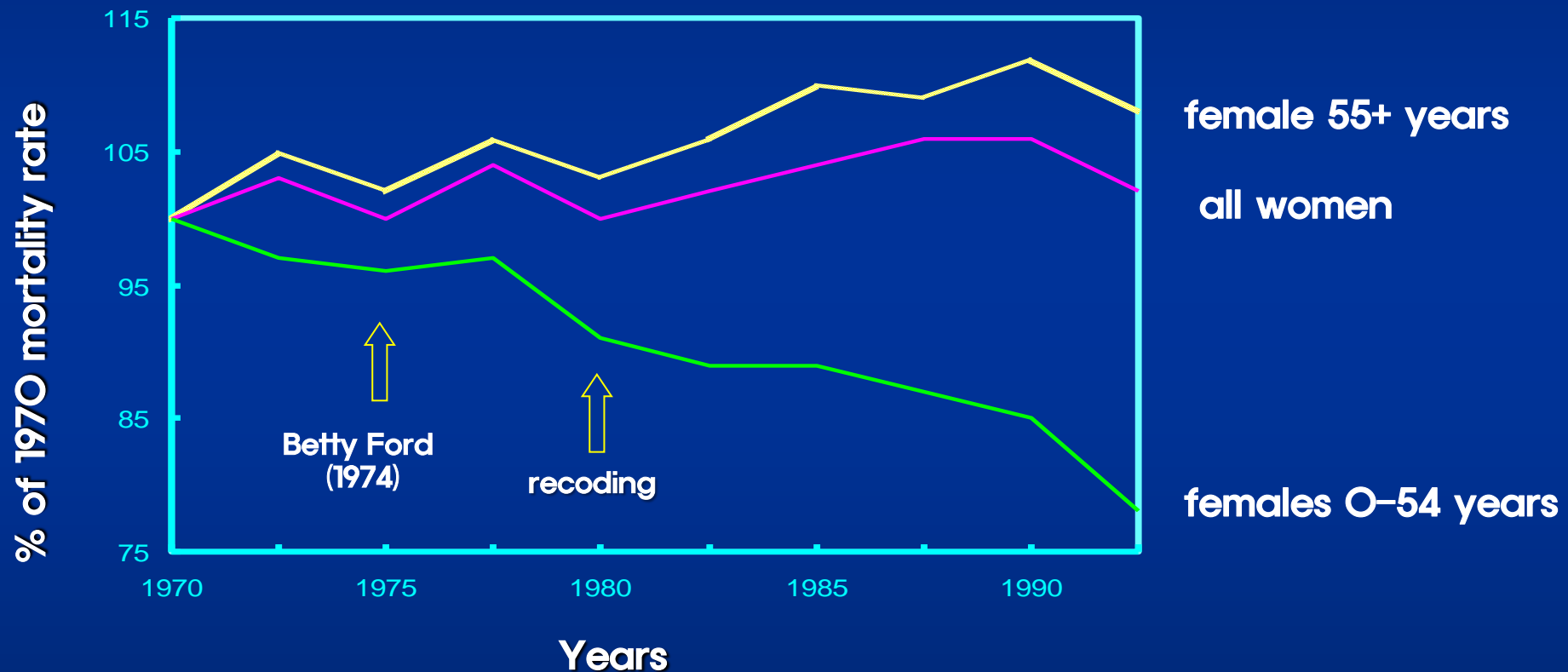
Mortality Data Source: Korea National Statistical Office, 2008

Period Trends in Breast Cancer Mortality: Japan

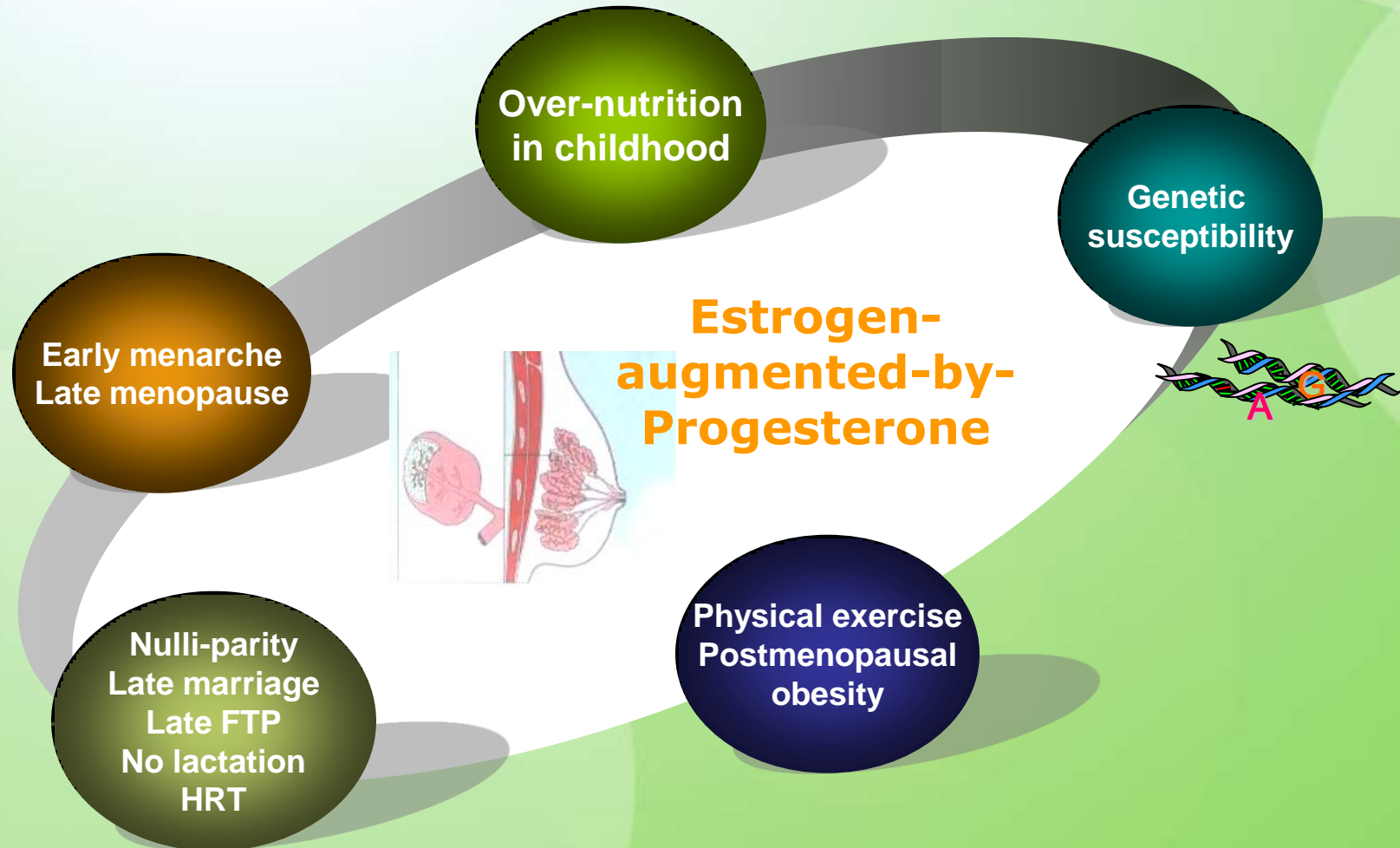


estimated by data from National Cancer Center Cancer Information Service, Japan

Breast Cancer Mortality 1970–1993, by Age Group

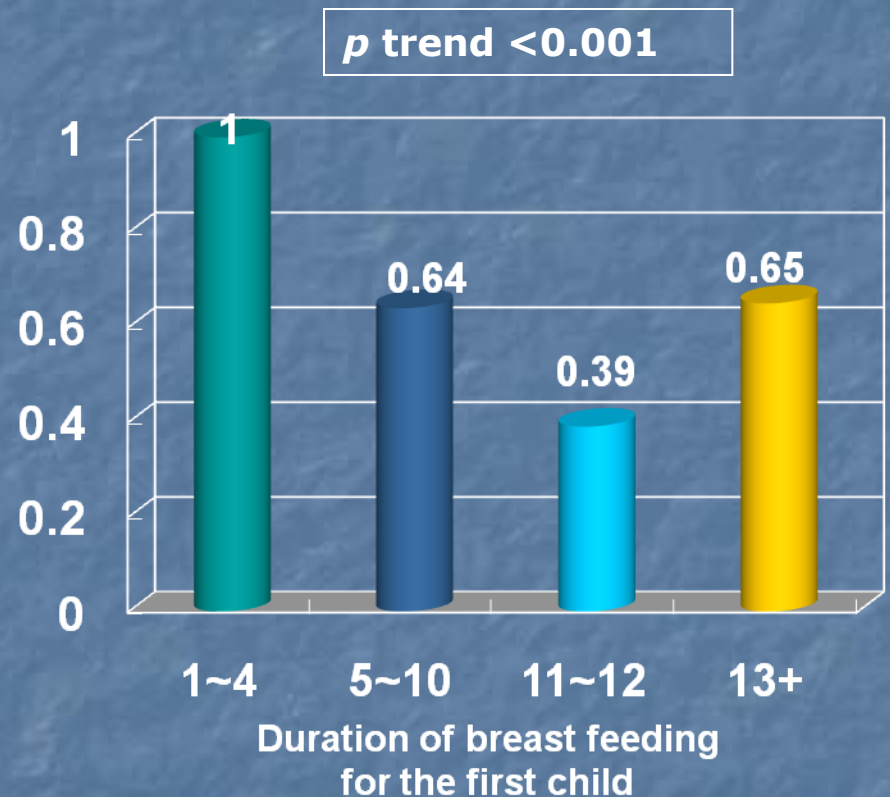
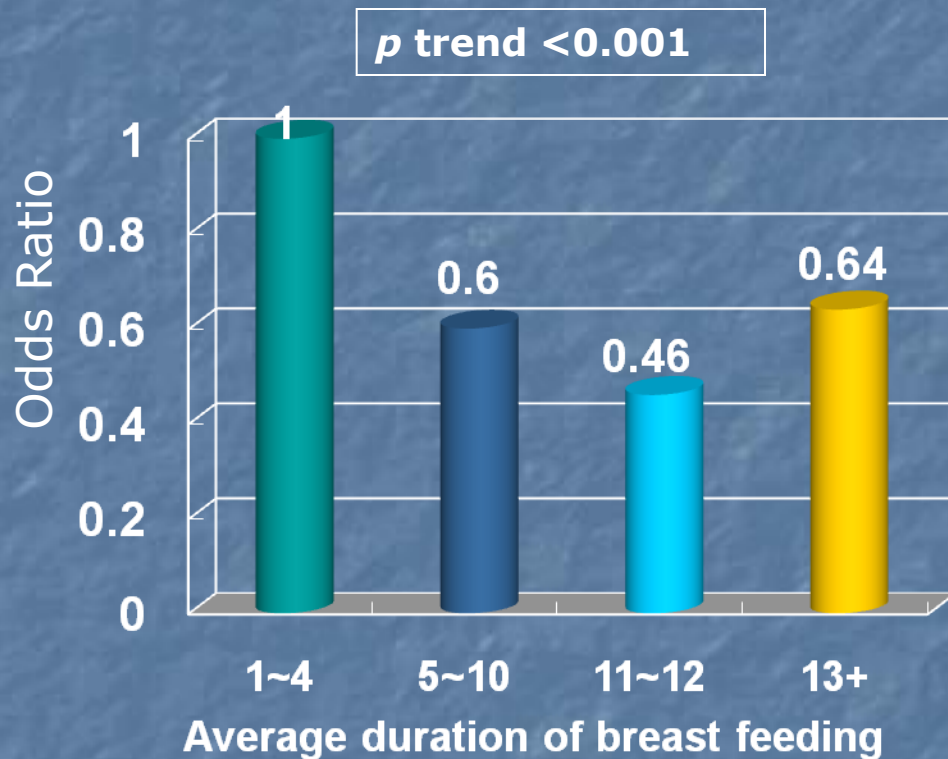


Life-time Risk of Breast Cancer



Breast Feeding

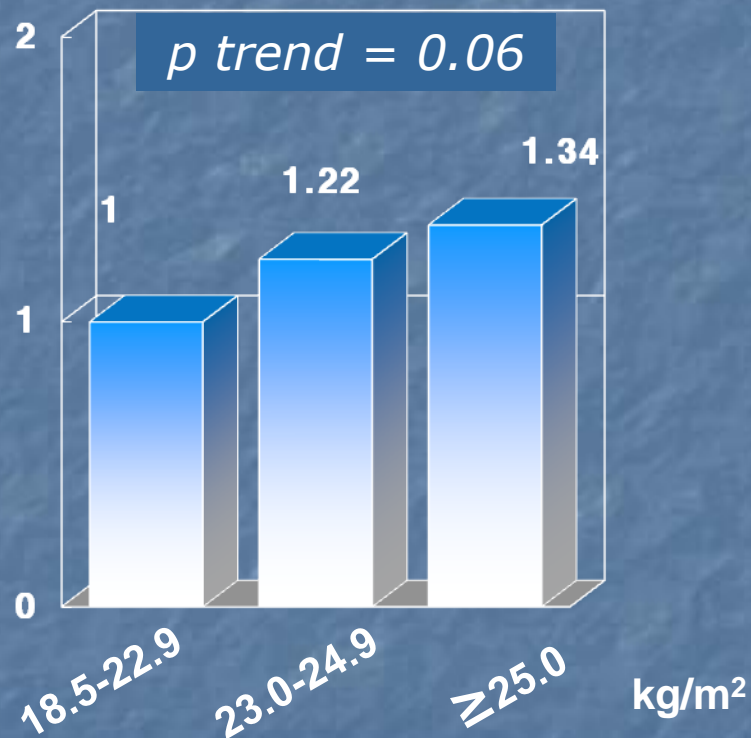
Case-control study, Korea, 1997-2003



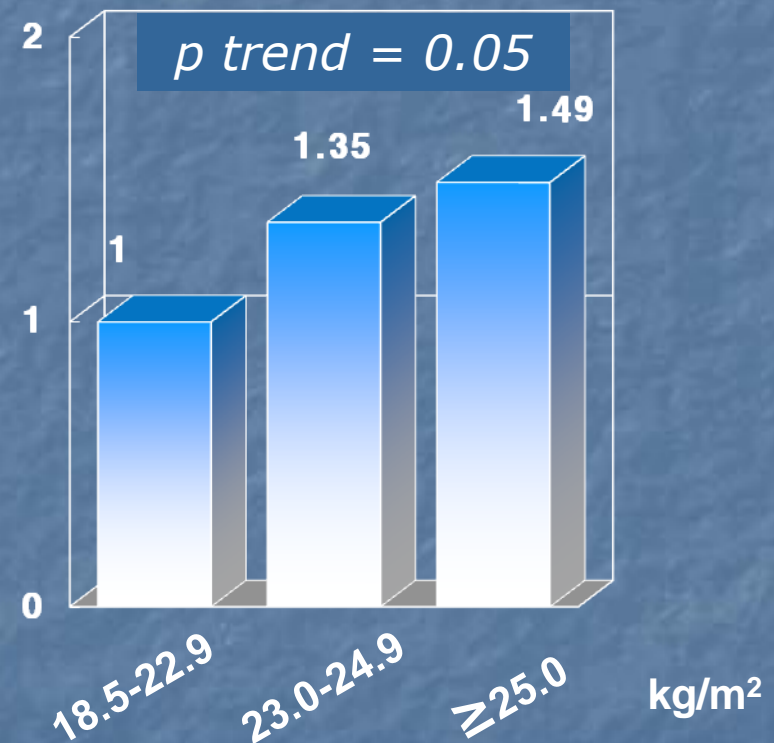
Adjusted for age, hospital, family history of breast cancer, BMI, menopausal status, age at menarche, number of live-birth, age at full-term pregnancy

Body Mass Index and Breast Cancer Korea, 2004-2005

OR Premenopausal



OR Postmenopausal



adjusted for age, hospital, family history of breast cancer, age at menarche, age at first full-term pregnancy, number of full-term pregnancy, history of hormone replacement therapy

Increase in High Fat Diet Correlates with Upsurge of Breast Cancer in Korea

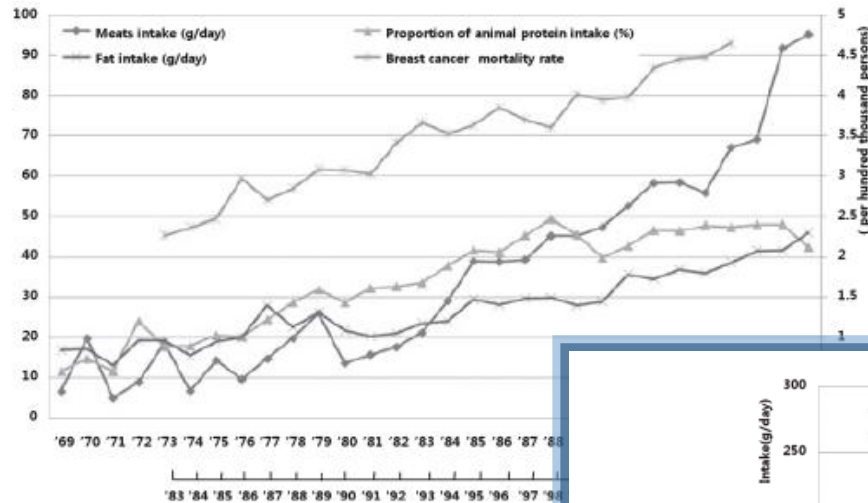


Figure 1. Trends of meat, fat, and animal protein intake, and age-standardized breast cancer mortality rate in Korea. The data were analyzed for a 10-year time lag. KNHANES: Korean National Health and Nutrition Examination Survey, KNSO: Korea National Statistical Office.

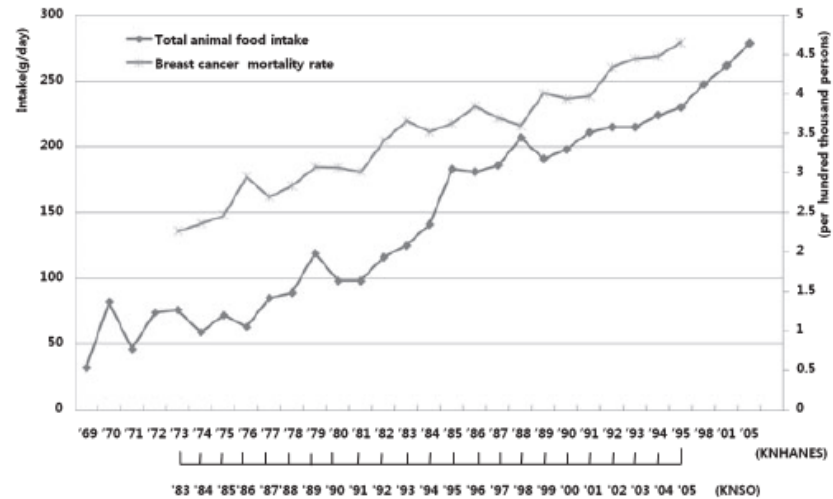


Figure 2. Trends in total animal food intake and age-standardized mortality rates of breast cancer in Korea. The data were analyzed for a 10-year time lag. KNHANES: Korean National Health and Nutrition Examination Survey, KNSO: Korea National Statistical Office.

Determinants of Age at Menarche

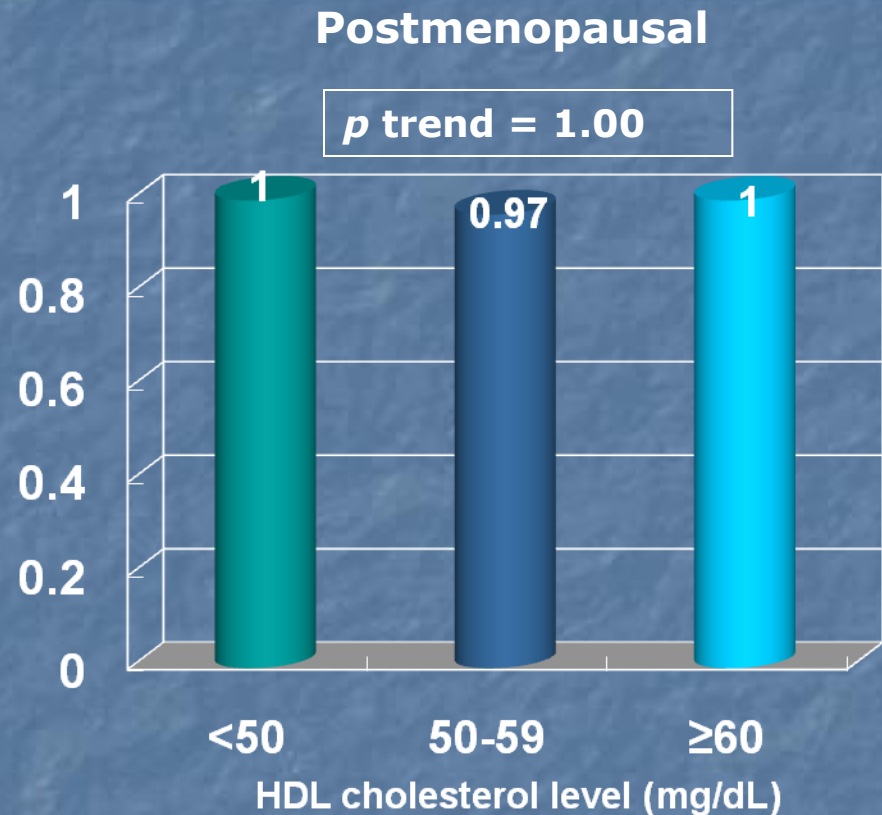
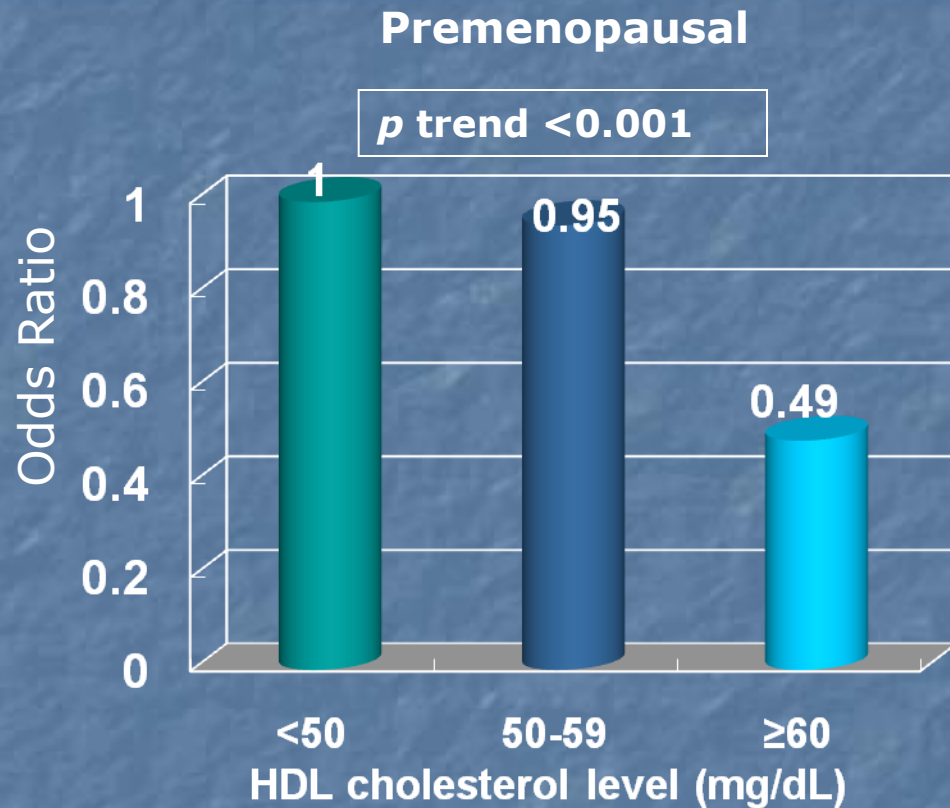
Community Survey in Yonchon County, Korea, n = 1,407

Determinants	Estimates*	S.E.	p
Height, current	-0.007	0.010	ns
Weight, current	-0.013	0.006	0.03
A.C., current	-0.014	0.004	0.00
H.C., current	-0.014	0.005	0.00
Weight, 20 years in age	-0.023	0.010	0.02
Weight, lifetime maximum	-0.015	0.007	0.02

* based on general linear model

HDL cholesterol and breast cancer

Case-control study, Korea, 2004-2005



Adjusted for age, family history of breast cancer, BMI, age at menarche, age at full-term pregnancy, and total cholesterol

Risk and Protective Factors of Breast Cancer in Korean Women

■ established

- early menarche
- late menopause
- nulli-parity
- later FFTP
- family history
- obesity (postmenopausal)
- alcohol drinking
- breast feeding
- HRT

■ probable

- smoking
- physical activity
- NSAID use
- oral contraceptives
- ionizing radiation

Yoo et al.	Am J Epidemiol 1992
Yoo et al.	CCC 1993
Suh et al.	J Korean Med Sci 1996
Yoo et al.	Am J Epidemiol 1997
Yoo et al.	J Korean Med Sci 2002
Choi et al.	BMC Cancer 2005
Kim et al.	Eur J Cancer Prev 2007

KOJACH: KOrea / JApan / CHina

Workshop of KOJACH-I, II Cooperative Studies on Cancer

Risk and Protective Factors for Breast and Colorectal Cancer⁺



Beijing Guangxi Hotel,⁺
Beijing, China⁺
October 10th, 2008⁺

Supported by ⁺
Grant-in-Aid for Scientific Research on
Special Priority Area, MEXT, Japan,
2000-2009⁺

General information of KOJACH-I, II cooperative studies ⁺

Chairperson: Yoon-OK Ahn (Korea)⁺

Progress report of KOJACH Study

K Tajima⁺

KOJACH-I Study ⁺

Chairperson: K-YYoo (Korea), C-M Gao (China)⁺

Risk factors for colorectal cancer in Japan

T Kawase & K Matsuo⁺

Risk factors for colorectal cancer in Korea

D-H Kim & Y-O Ahn⁺

Risk factors for colorectal cancer in Chongqing

Z-Y Zhou & J Cao⁺

KOJACH-II Study ⁺

Chairperson: H Tanaka (Japan), J Cao (China)⁺

Risk factors for breast cancer in Japan

K Matsuo & H Tanaka⁺

Risk factors for breast cancer in Korea

S-K Park, Y-J Kim & K-YYoo⁺

Risk factors for breast & colorectal cancer in Nanjing

J-H Ding & C-M Gao⁺

Business Meeting

Chairperson: K Tajima (Japan)⁺

Determinants of Upsurge of Breast Cancer in Young Asian Women

Korean women

early menarche	(moderate - strong)
postmenopausal obesity	(moderate)
breast feeding	(strong)
high fat diet	(strong)

Yoo et al. Earlier onset of age at menarche may be determined by body weight at age 20, and might be initiated by weight gain in her childhood.

Seoul J Med 1995

.....

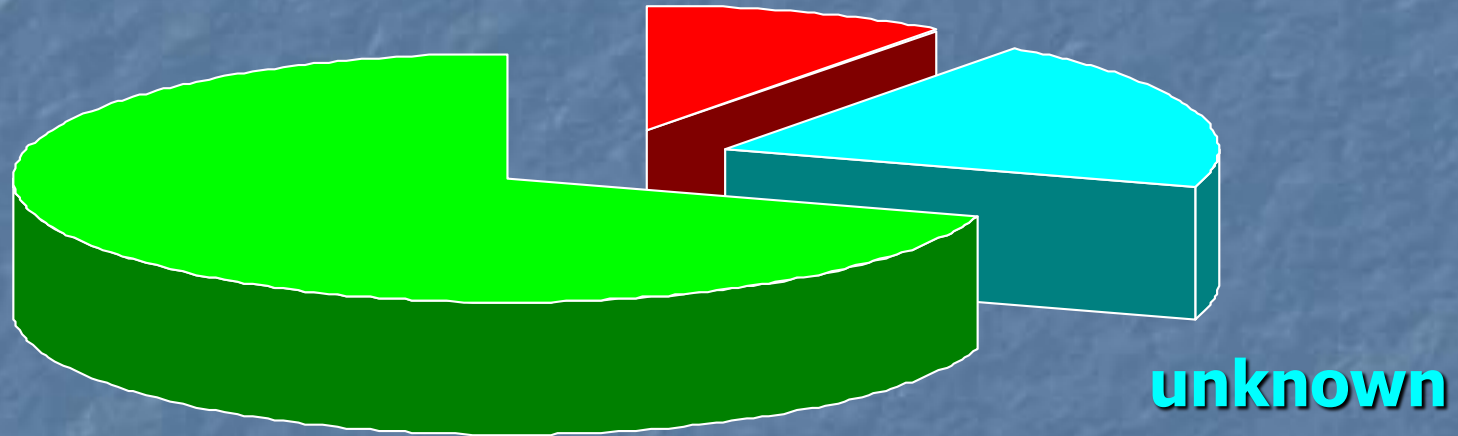
Terry et al. Infant weight gain, in addition to childhood weight gain, may be associated with earlier age at menarche. *Am J Epidemiol 2009*

How much is explained about breast cancer?

environmental

45-50%

inherited 5~10%(?)



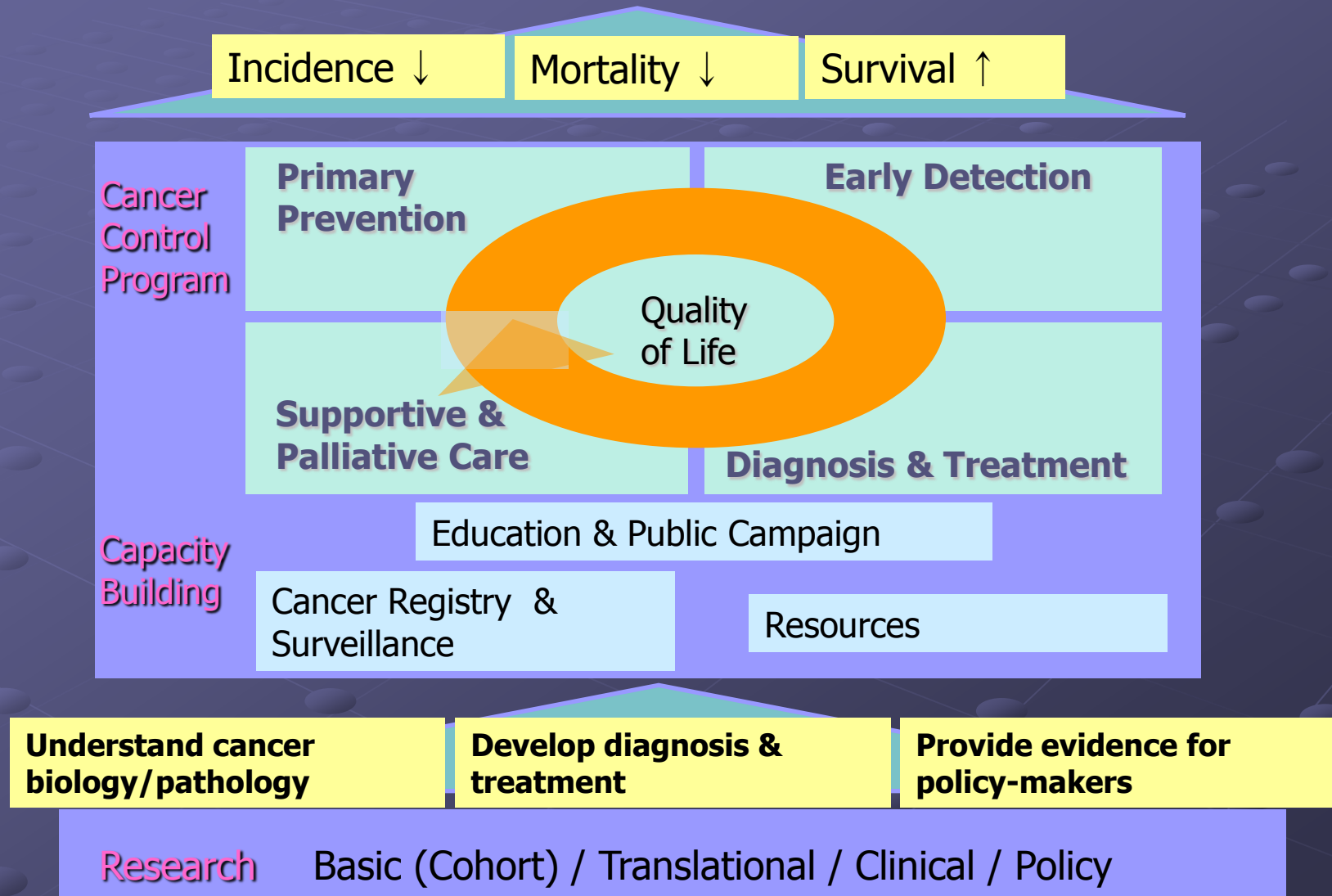
Genome Epidemiologic Studies on Breast Cancer at Seoul National University (since 2000)

GST M1/T1 & alcohol	Pharmacogenetics (2000)
COMT	Pharmacogenetics (2001)
XRCC1/3	Pharmacogenetics (2002), Breast Cancer Res Tr (2007)
GST & reproductive Factors	Breast Cancer Res Tr (2002)
CYP2E1/ALDH2	Pharmacogenetics (2003)
hOGG1	Breast Cancer Res Tr (2003)
Cytochrome P450-19/1B1/1Aa	Br J Cancer (2003), Exp Mol Med (2006)
ER-alpha	Breast Cancer Res Tr (2003)
TGF- β 1 & TNF- β	Breast Cancer Res Tr (2005)
ATM	CEBP (2005)
SULT1A1 & SULT1E1	CEBP (2005)
ERCC2 / ERCC4	Exp Mol Med (2005)
IL-1 β & IL-1RN	Breast Cancer Res Tr (2006)
eNOS, hormone receptor	Breast Cancer Res Tr (2006)
HIF 1-A	Clinica Chimica Acta (2008)
DNA repair genes	Asian Pacific J Cancer Prev (2008)
Innate immunity genes	Carcinogenesis (2009)
common SNiPs	J Natl Cancer Inst (2006)
CASP8	Nature Genetics (2007)
Genome-wide Association	Nature (2007)
XRCC3 Thr241Met	Breast Cancer Res Tr (2007)
Five SNiPs	CEBP (2008)

**Breast
Cancer
Association
Consortium**

Survivorship

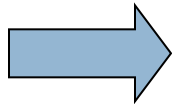
2nd Term Ten-year Plan for National Cancer Control in Korea (2006-15)



Breast cancer screening guideline



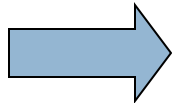
Age ≥ 40



**Mammography
Clinical breast examination**

Every 2 years

**Age
30~39**



Self breast examination

Every months

Life-time Screening Rates of Cancer

All Combined, Korea

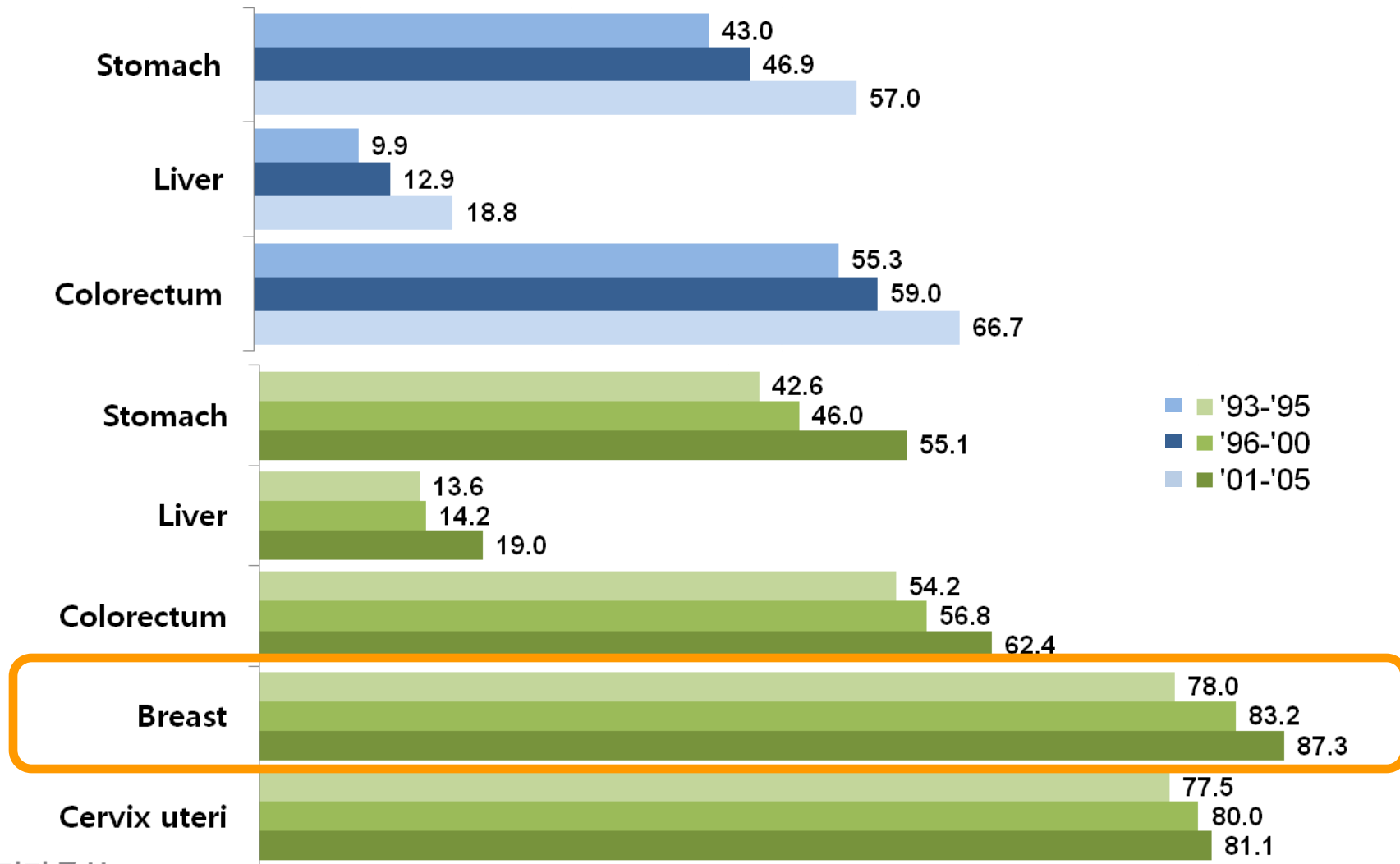
unit: %

Cancers	2004	2005	2006	2007
Stomach	52.0	48.5	53.5	55.3
Liver	31.8	47.7	58.3	57.6
Colon	25.3	27.9	34.0	40.7
Breast	55.9	57.4	60.2	66.4
U. cervix	76.8	74.0	68.0	73.6

Source: National Cancer Center. Nationwide Survey for Health Screening Performance Rate, 2004~2007

Note: Proportion of person who has ever taken at least a cancer screening by the given year under the screening guideline recommended by the National Cancer Center and the Ministry of Health & Welfare

Five Year Survival of Cancer Sites of National Screening Program



International Comparison of Five Year Relative survival

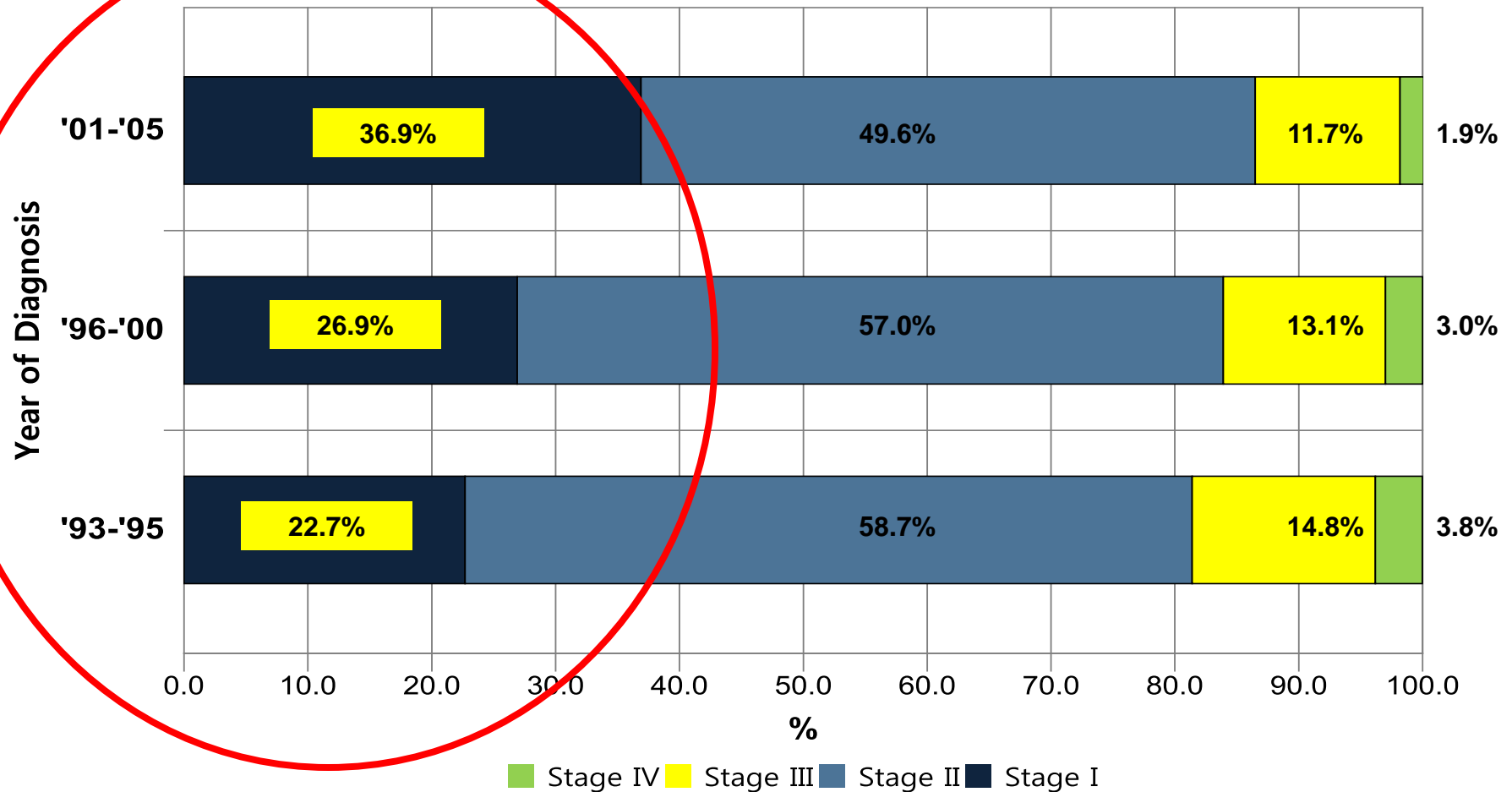
(Unit: %)

	Korea (‘01-‘05)	USA ¹⁾ (‘96-‘04)	Japan ²⁾ (‘97-‘99)	Eurocare ²⁾ (‘95-‘99)
Stomach	56.4	24.7	62.1	24.1
Lung	15.5	15.2	25.6	12.6
Colorectum	64.8	64.4	65.2	53.5
Liver	18.9	11.7	23.1	8.6
Thyroid	98.1	96.9	92.4	86.5
Breast	87.3	88.7	85.5	81.1
Cervix uteri	81.1	71.2	71.5	66.5
Prostate	76.9	98.9	75.5	77.0
All Cancers	52.2	65.3	54.3	51.9

1) Ries LAG, et al (eds). SEER Cancer Statistics Review, 1975-2005, National Cancer Institute, 2008

2) National Cancer Center in Japan. Cancer Statistics in Japan, 2008

Stage Frequency of Breast Cancer



Source: Korea Central Cancer Registry,
Korean Breast Cancer Society

Breast Cancer in Korea, Today

United States

War against Cancer, 1971

Decline in cancer mortality, 1991

Japan

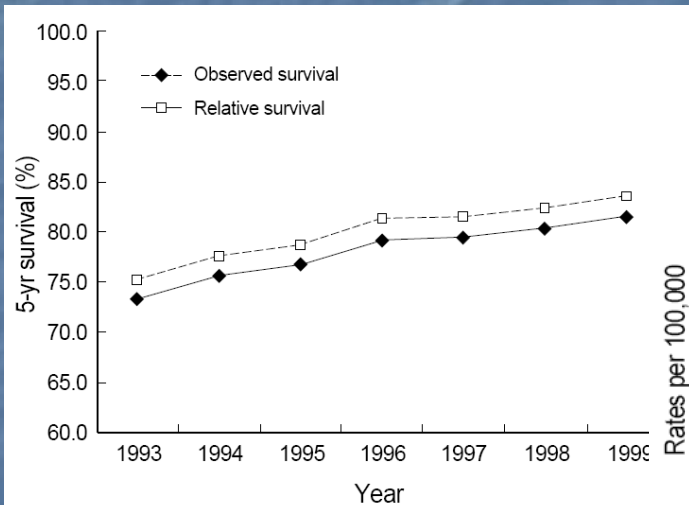
NCCP, 1965

NCSP for breast cancer, 1987

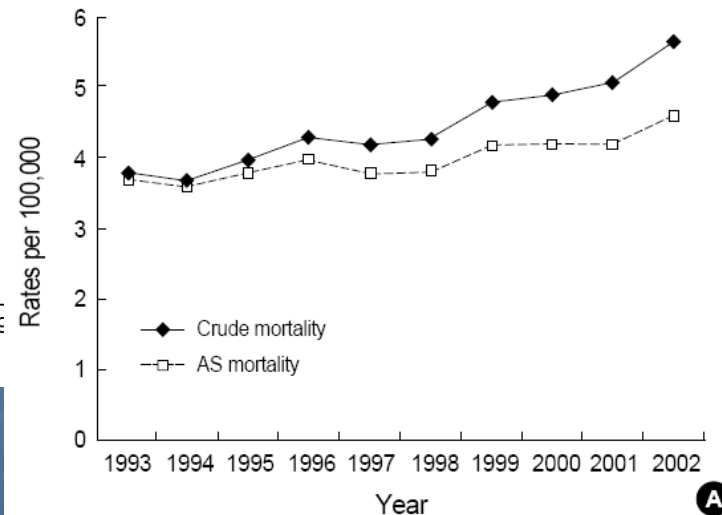
Korea

1st NCCP, 1996

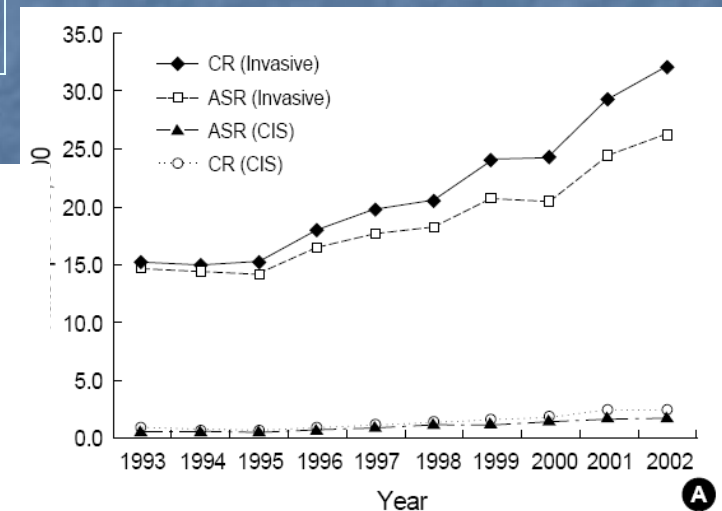
1st NCSP for BC, 1999



**5YSR, Breast Cancer,
1993-1999**



**Mortality, Breast Cancer,
1993-2002**



**Incidence, Breast Cancer,
1993-2002**

Developing Countries, Today...

- mainly poverty-related tumors (cervical, esophagus, liver)
- tumors linked to western style of life
(breast, lung, prostate, colorectal)
- lack of primary and secondary prevention
- lack of resources for treatment

Epidemiology of BC in Indonesia

BC in younger women showed aggressive phenotype
larger tumor size, more LN, higher c-erbB2 / p53
higher ER/PR expression

More common adjuvant chemotherapy,
higher recurrence, metastasis, and death

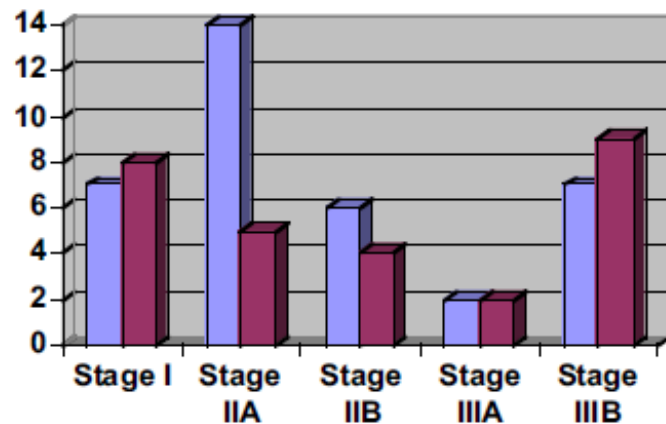


Figure 1. Clinical Stages of Breast Cancers in Patients Aged < 40 Years (left) and ≥ 60 Years Old (right)

Table 1. Characteristics of Operable Breast Cancer Cases in Patients Aged <40 years old

Variables	n	%	Total (%)	5-year survival (%)
Lymph node			36 (78.3)	
Negative	12	33.3		81.8
1-3	8	22.3		58.3
≥ 4	16	44.4		33.3
Lymph node			36 (78.3)	
Positive	24	66.7		42.2
Negative	12	33.3		81.8
Tumor size			36 (78.3)	
0-2	7	19.5		100
> 2-5	20	55.5		59.2
> 5 cm	9	25.0		16.7
Tumor size			36 (78.3)	
> 2 cm	29	80.5		44.6
0-2 cm	7	19.5		100
Grade			45 (97.8)	
Low	1	2.4		0
Intermediate	22	48.8		58.3
High	22	48.8		55.3
ER			46 (100)	
Negative	17	37.0		43.8
Positive	29	63.0		61.9
PR			45 (97.8)	
Negative	22	48.9		35.7
Positive	23	51.1		61.9
p53			42 (91.3)	
Positive	38	90.4		53.2
Negative	4	9.6		100
MIB-1 proliferation index			38 (82.6)	
Positive	38	100		56.5
Negative	-	-		-
c-erbB2			43 (93.5)	
Positive	32	74.4		52.0
Negative	11	25.6		74.1
Mitotic Index			45 (97.8)	
Low	2	4.6		50.0
Intermediate	17	37.7		90.0
High	26	57.7		34.6
Adjuvant chemotherapy			39 (84.8)	
Yes	25	64.1		47.0
No	14	35.9		72.7
Adjuvant tamoxifen			35 (76.1)	
No	4	11.5		100
Yes	31	88.5		55.0
Death			46 (100)	
Death	14	30.4		55.1
Alive	23	50.0		
Unknown	9	19.6		
Recurrence			38 (82.6)	
Yes	3	7.9		33.3
No	35	92.1		60.1
Metastasis			38 (82.6)	
Yes	11	25.0		24.2
No	27	75.0		71.1

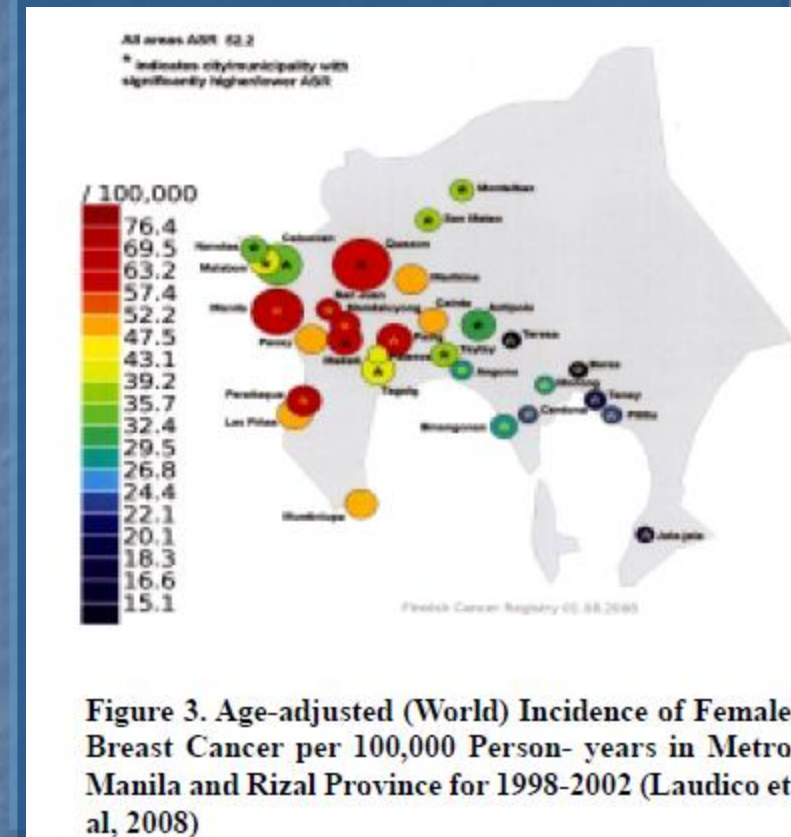
Table 2. Characteristics of Operable Breast Cancer Cases in Patients Aged ≥60 years old

Variables	n	%	Total (%)	5-year survival (%)
Lymph node			37 (77.1)	
Negative	15	40.5		87.5
1-3	15	40.5		51.3
≥ 4	7	19.0		0
Lymph node			37 (77.1)	
Positive	22	59.5		33.2
Negative	15	40.5		87.5
Tumor size			39 (81.3)	
0-2	5	12.8		75.0
> 2-5	26	66.6		63.6
> 5 cm	8	21.6		0
Tumor size			39 (81.3)	
> 2 cm	34	79.4		48.7
0-2 cm	5	12.6		75.0
Grade			43 (89.6)	
Low	2	4.6		0
Intermediate	18	41.9		81.8
High	23	53.5		47.7
ER			46 (95.8)	
Negative	23	50.0		32.6
Positive	23	50.0		73.9
PR			44 (91.7)	
Negative	24	54.5		51.2
Positive	20	45.5		64.8
p53			34 (70.8)	
Positive	4	11.8		66.7
Negative	30	88.2		56.7
MIB-1 proliferation index			33 (68.8)	
Positive	6	18.2		66.7
Negative	27	81.8		58.2
c-erbB2			38 (79.2)	
Positive	21	55.3		44.9
Negative	17	44.7		71.1
Mitotic Index			39 (81.3)	
Low	1	2.5		100
Intermediate	10	25.6		58.3
High	28	71.9		65.6
Adjuvant chemotherapy			27 (56.3)	
Yes	6	22.2		58.5
No	21	77.8		66.7
Adjuvant tamoxifen			34 (70.8)	
No	7	20.5		66.7
Yes	27	79.5		57.8
Death			48 (100)	
Death	10	20.8		56.8
Alive	24	50.0		
Unknown	14	29.2		
Recurrence			35 (72.9)	
Yes	2	5.7		0
No	33	94.3		59.7
Metastasis			35 (72.9)	
Yes	8	22.8		28.1
No	27	77.2		74.1

Epidemiology of BC in Philippines

the highest in Asia
rapid increase during 1980-2002
higher in cities than municipalities
decreasing fertility
westernization of lifestyle

AJCC I (5%) IIA(20%) IIB(18%)
5-ysr = 58.6%



Epidemiology of BC in Tehran, Iran

the 2nd most common cancer

ASIR = 17.09 / 100,000

31% of newly diagnosed BC: under 40 years old
mean age = 51.3 years

higher education

late menopause / more FTP / longer lactation

1st-degree family history

higher BMI

Table 1. Incidence rate of Breast Cancer per 100.000 Population from 1998-2001 by Age Group

Age Group	Year				Overall
	1998	1999	2000	2001	
15-19	0.00	0.00	0.18	0.00	0.09
20-24	0.84	1.04	1.45	0.82	0.99
25-29	5.40	5.08	5.88	5.00	5.27
30-34	14.45	13.66	17.95	12.09	14.53
35-39	33.96	26.62	35.41	24.19	30.11
40-44	51.81	50.54	56.90	42.99	50.43
45-49	68.36	60.22	72.76	55.99	64.44
50-54	72.63	66.24	81.03	56.46	68.87
55-59	76.35	63.52	87.39	65.49	73.18
60-64	90.50	75.33	74.72	68.89	77.30
65-69	74.06	51.48	65.65	46.29	59.30
70-74	47.54	49.13	64.83	46.45	53.32
75-79	60.91	45.36	59.99	71.38	59.46
80-84	27.56	36.50	54.30	53.84	40.87
85+	39.94	23.80	23.60	23.40	25.67
Total	18.19	15.90	19.51	14.76	17.09

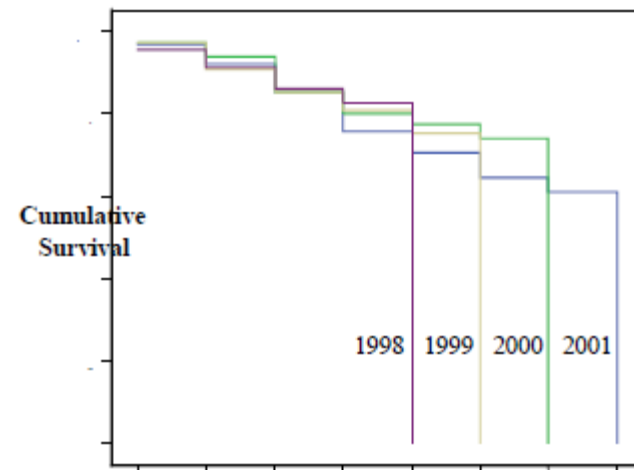


Figure 1. Survival Curves for Breast Cancer Cases in Tehran Cancer Registry from 1998-2001

Mousavi et al. Asian Pacific J Cancer Prev 2008
Naieni et al. Asian Pacific J Cancer Prev 2007

The breast that has never lactated is more liable to become cancerous (JE Lane-Claypon, 1926)

Cause of death = infections
Life expectancy <45 yrs
Per capita GNI < US\$200
Traditional medicine



1911



Janet Elizabeth Lane-Claypon



Cause of death = cancer
Life expectancy = 78 yrs
Per capita GNI = US\$20,000
Universal health insurance



2009

Female Breast Cancer (ICD C50) in selected countries of Asia

