

I'd like to say great thanks for your support after the Tohoku earthquake.





# Breast Cancer Screening in Japan

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President of Kitakyushu Municipal Medical Center,  
Fukuoka, Japan

Mt Fuji

# Content

1. Current status of mammographic screening for breast cancer in Japan

2. Randomized controlled trial on effectiveness of mammographic screening combined with ultrasonography for breast cancer in women aged 40-49 years

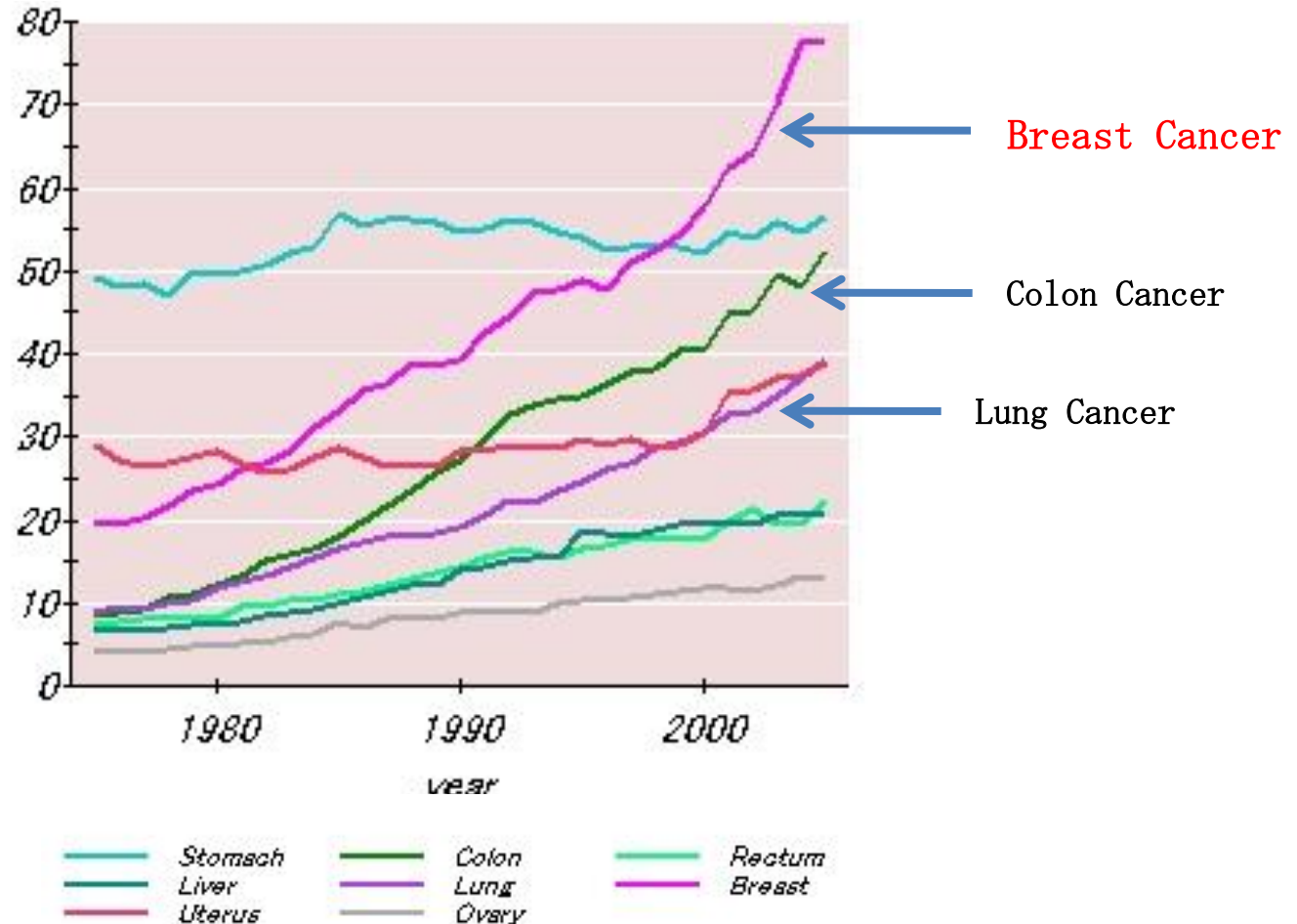
# Content

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# Trend in Crude Cancer Incidence Rate in Japan ( major sites ) [ female 1975-2005 ]

per 100000 population



Source: Center for Cancer Control and Information Services,  
National Cancer Center, Japan

# Reasons for Increased Rate of Breast Cancer in Japan

## 1. Westernization of diet

- \*dietary fat intake, obesity after menopause

## 2. Reproductive factors

- \*early menarche and late menopause

- \*a high- aged first delivery

- \*declining birth-rate

## 3. Participation in society/employment

- \*no marriage or breast-feeding of babies

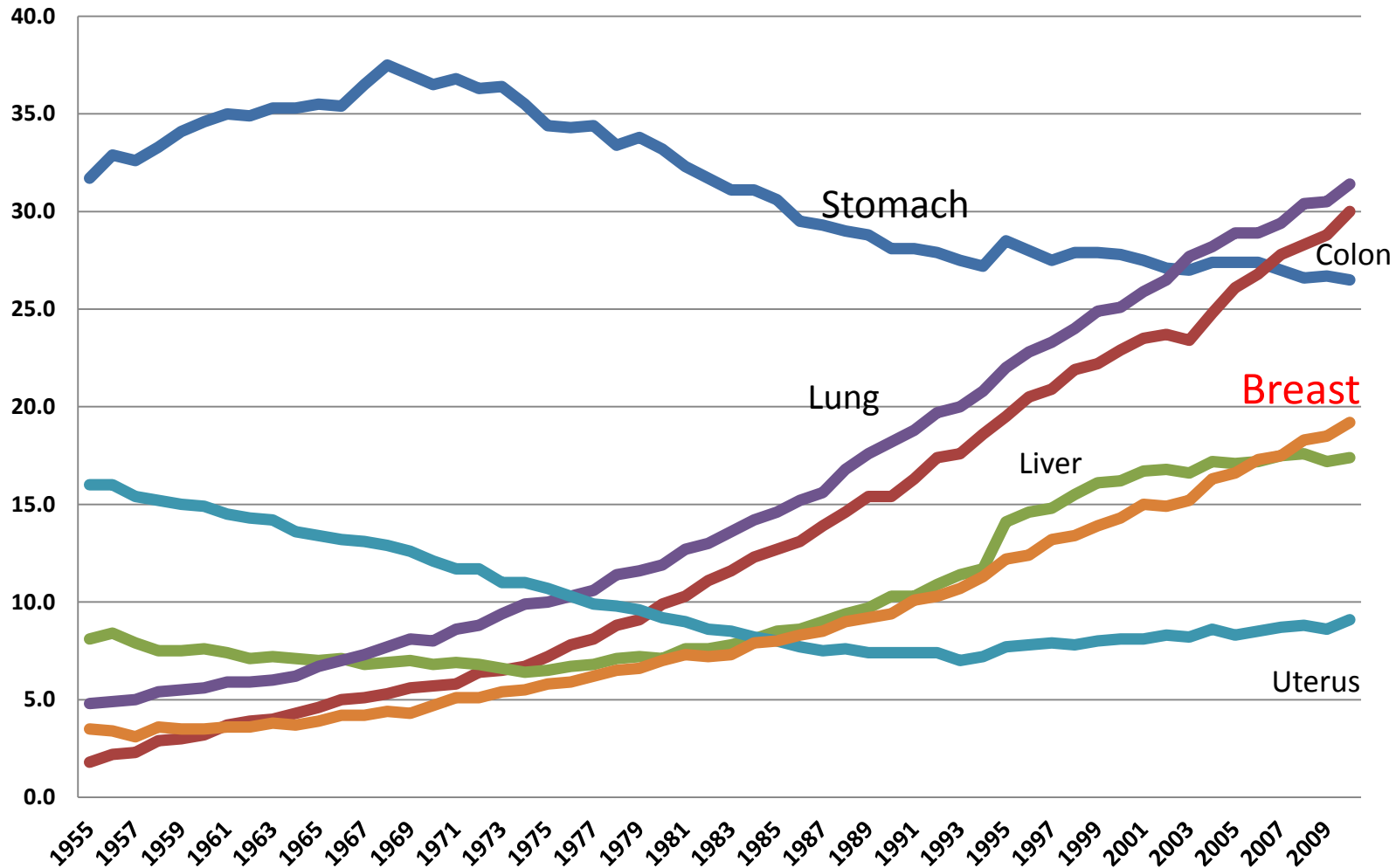
## 4. A change of lifestyle

- \*alcohol consumption and cigarette smoking

## 5. etc.

# Trend in Crude Cancer Mortality Rate in Japan (female, major sites)

per 100,000 population

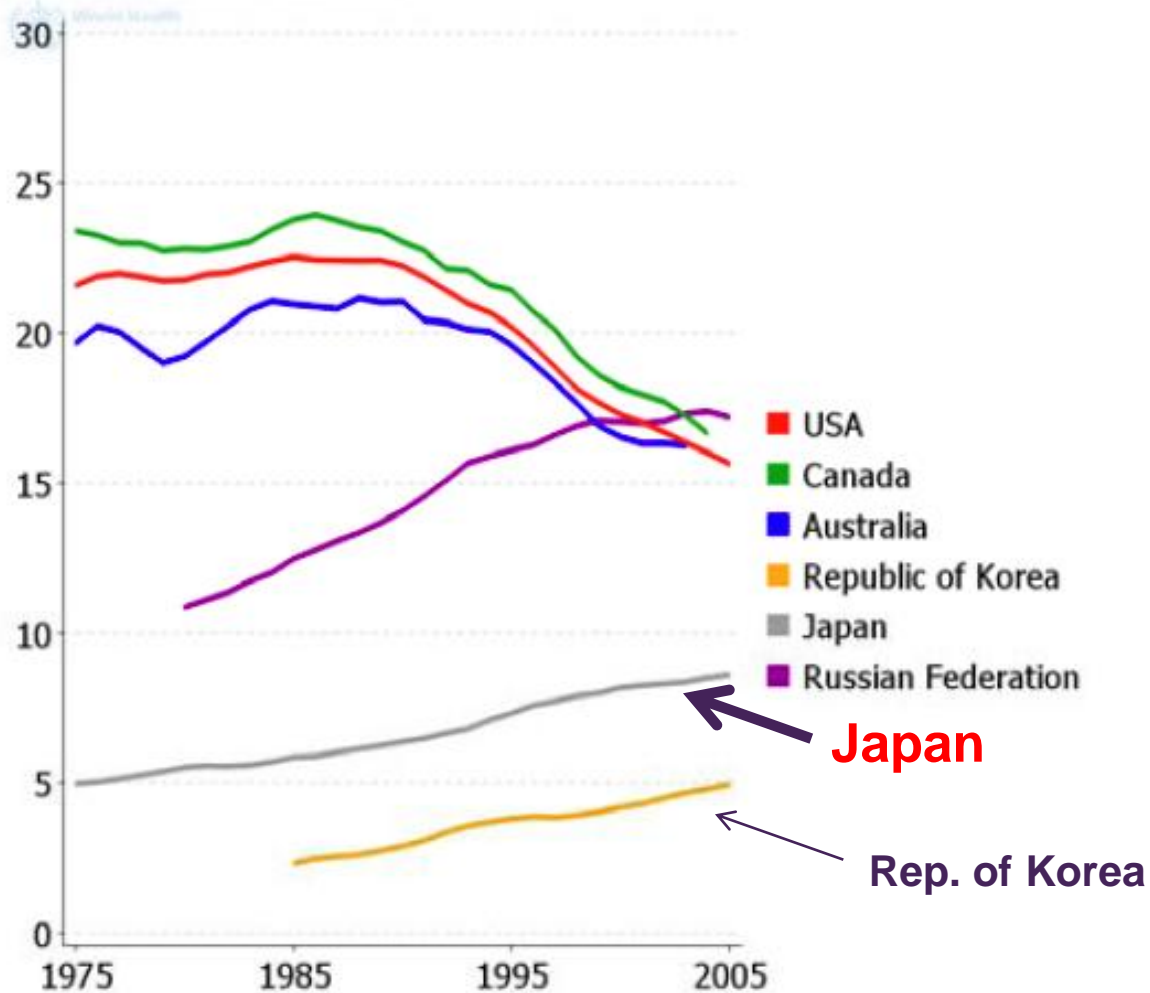


Source: Center for Cancer Control and Information Services,  
National Cancer Center, Japan

# Trends in Mortality of Breast Cancer

Age-standardized rate per 100,000

International Agency for Research on Cancer





# History of Breast Cancer Screening in Japan

- 
- 1987 • Clinical Breast Examination(CBE) alone started ( $\geq 30$  years old)
  - 1989 • Miyagi Mammography Screening Trial(MMG combined with CBE) started
  - 1998 • CBE alone not proven to be effective for early detection  
• Grant-in-Aid for Cancer Research on MMG screening recommended screening MMG
  - 2000 • MMG screening for women over 50 years of age
  - 2004 • Biennial MMG screening expanded to women aged 40 and over
  - 2007 • Japan strategic anti-cancer randomized trial(J-start) on effectiveness of ultrasound screening for women aged 40 ~ 49
  - 2009 • Basic plan to promote cancer control program  
• New project – a free coupon every five years for women between 40 and 60 years old

## IBSN (ICSN) Countries in 1995

Country	Age groups covered	Screening interval (Y)		Detection methods
		Age 40-49	Age 50+	
<b>IBSN program countries</b>				
•Australia	40-69	2	2	MG
•Canada	50-69	1	2	MG, CBE
•Finland	50-59	-	2	MG
•Hungary	50-64	-	1	MG, CBE
•Iceland	40-74	2	2	MG, CBE
•Israel	50-69	-	2	MG
•Italy	50-69	-	2	MG
•Japan	30-	1	1	CBE
•The Netherlands	50-69	-	2	MG
•Sweden	40-74	1.5	2	MG
•United Kingdom	50-64	-	3	MG
•United States	40-	1	1-2	MG, CBE
•Uruguay	45-	1	2	MG, CBE
<b>European Network pilot projects</b>				
•Belgium	50-69	-	2	MG
•Denmark	50-69	-	2	MG
•France	50-69	-	2-3	MG
•Germany	50-	-	2	MG
•Greece	40-64	2	2	MG, CBE
•Ireland	50-65	-	2	MG
•Luxembourg	50-65	-	2	MG, CBE
•Portugal	40-	-	2	MG
•Spain	45-64	-	2	MG

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# Results of Screening MMG in Japan

	Tokushima <sup>1)</sup>	Miyagi <sup>2)</sup>	Ibaragi <sup>3)</sup>	ACR(U.S.A.) <sup>4)</sup>
Number of Examineer	13.982	12.515	17.193	-
Recall Rate(%)	7.1	3.6	3.3	< 10
Detection of Breast Cancer (Number of patients)	43	36	41	-
Detection rate of Breast Cancer(%)	0.31	0.28 0.09% in CBE alone	0.24	0.2-1.0
Sensitivity(%)	93.5	97.2	95.3	>85
Positive Predictive value	4.3	8.2	7.3	5-10
% in situ	27.9	16.6	-	>30
% stagel	67.4	56.6	75.6	>50
% node-negative	79.1	-	-	>75

1)Morimoto et al:Anticancer Res 20.3689,2000

2)Ohuchi et al:Jpn J cancer Res 86.501,1995

3)Tsunoda:Personal communication

4)ACR BI-RADS:Analysis of Medical andit data:desirable goals

# History of Breast Cancer Screening in Japan

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## Methods of Breast Cancer Screening in Japan, 2004

Age	40-49y	50-59y	≥60y
Modality	MMG Two directions (MLO , CC) CBE / US	MMG One direction (MLO) CBE	MMG One direction (MLO)
Interval	Biennial	Biennial	Biennial

MMG : Mammography      MLO : Medio-Lateral Oblique      CC : Cranio-Caudal

US : Ultrasonography

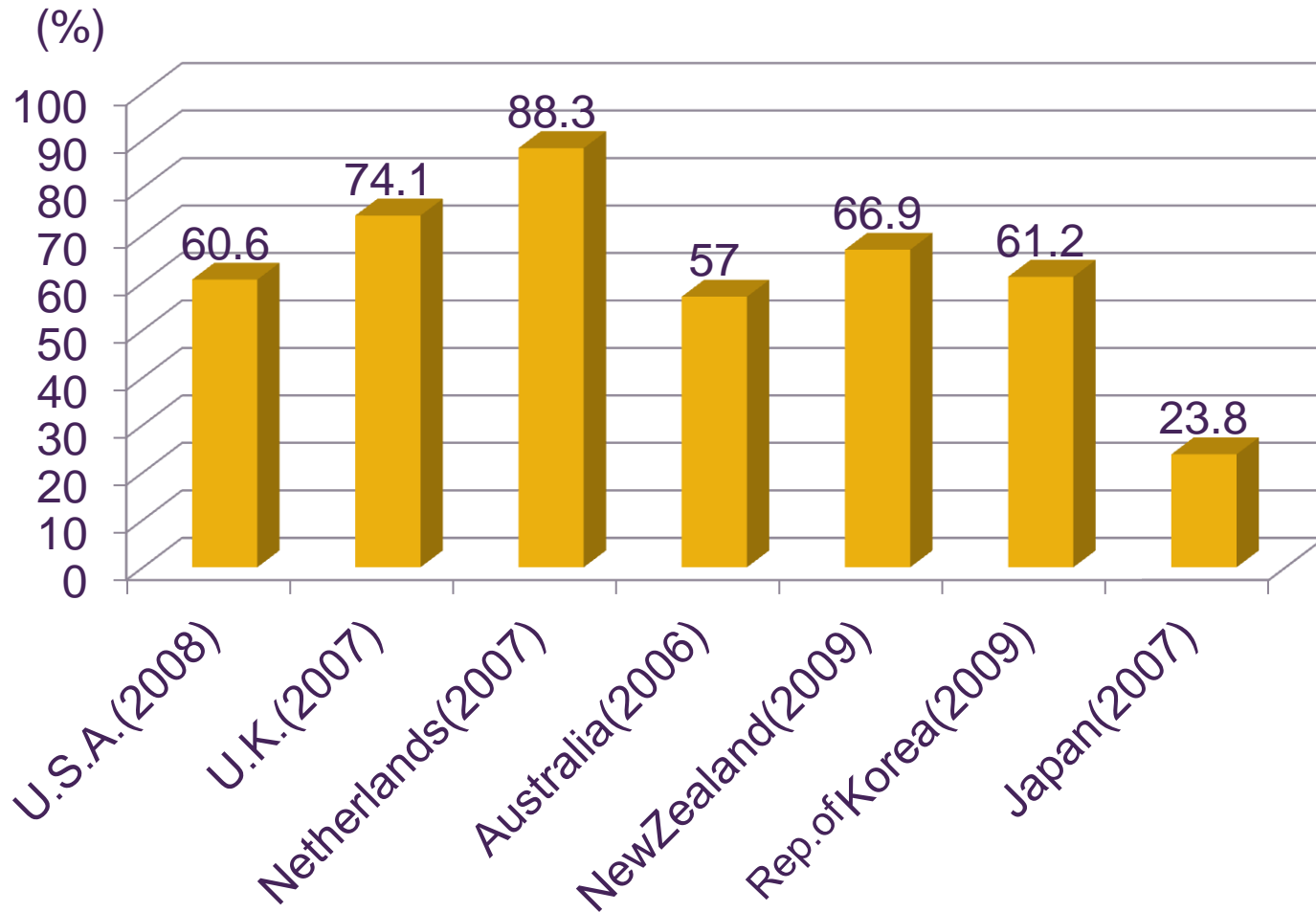
CBE : Clinical Breast Examination(Inspection and Palpation)

# Objectives of the Cancer Control Program

by the Ministry of Health, Labour and Welfare of Japan (2007-2014)

- 50% check up rate and early detection
- 20% reduction of cancer mortality
- etc.

## Check Up Rate (50 ~ 69y)



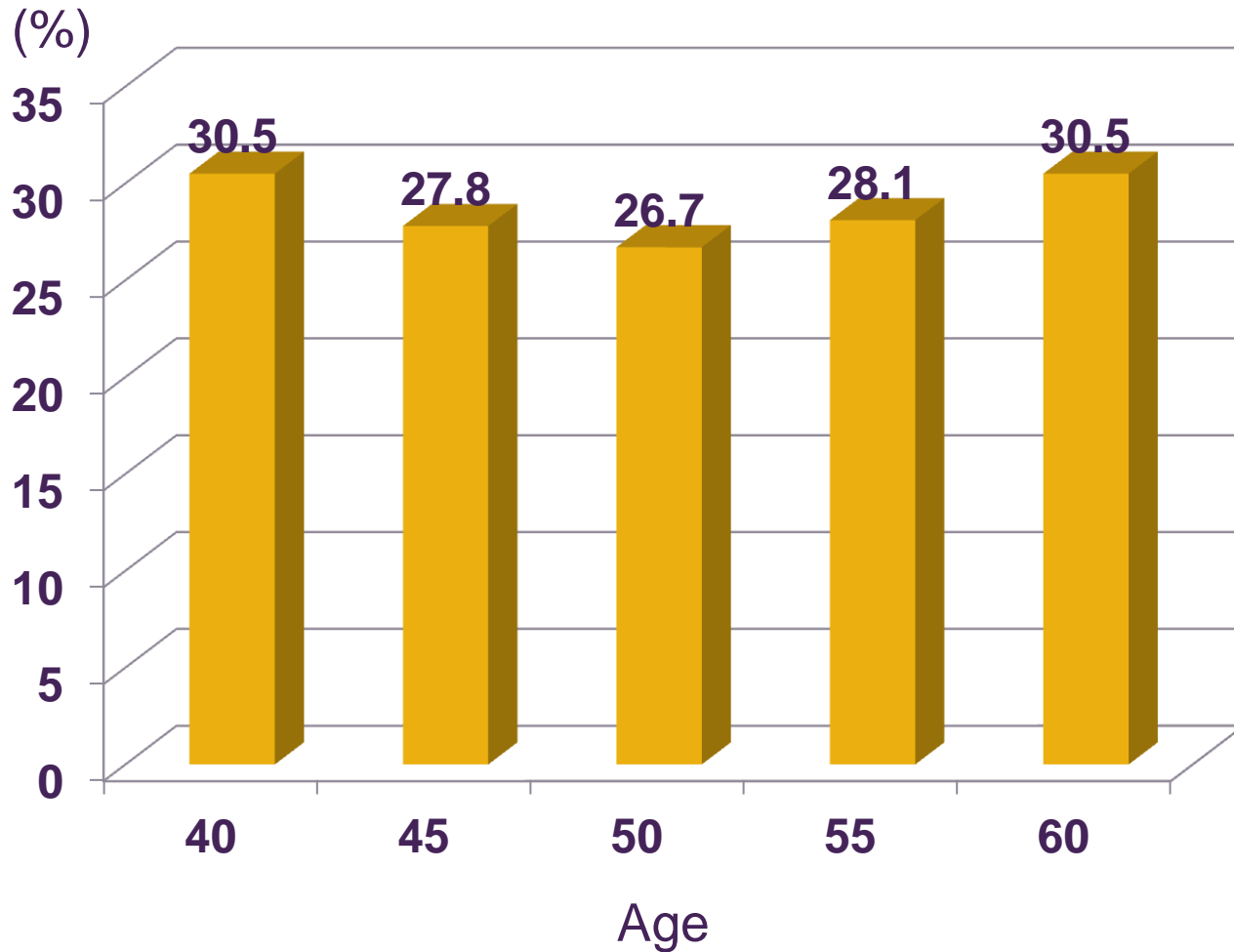


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Results of Female Cancer Screening  
Promotion Program in Japan, 2009

Rate of use of free coupons



# Reasons for Low Check Up Rate

- Little interest in breast cancer
- Having no problem about breast  
(misunderstanding of the purpose of screening)
- No time or opportunity for check up
- Inconvenient location of institute for check up
- Cost for mammographic screening
- etc.

# Proposal for the Achievement of a 50% Check Up Rate

- Further education and recommendation to the public of mammographic screening
  - \*through mass media
  - \*direct mail, or door to door visit by a public health nurse
- Lower the cost, or enable the use of public health insurance for mammographic screening
- Enable to have mammographic screening on holiday and at night
- Lower the treatment cost for breast cancer detected by mammographic screening
- etc.

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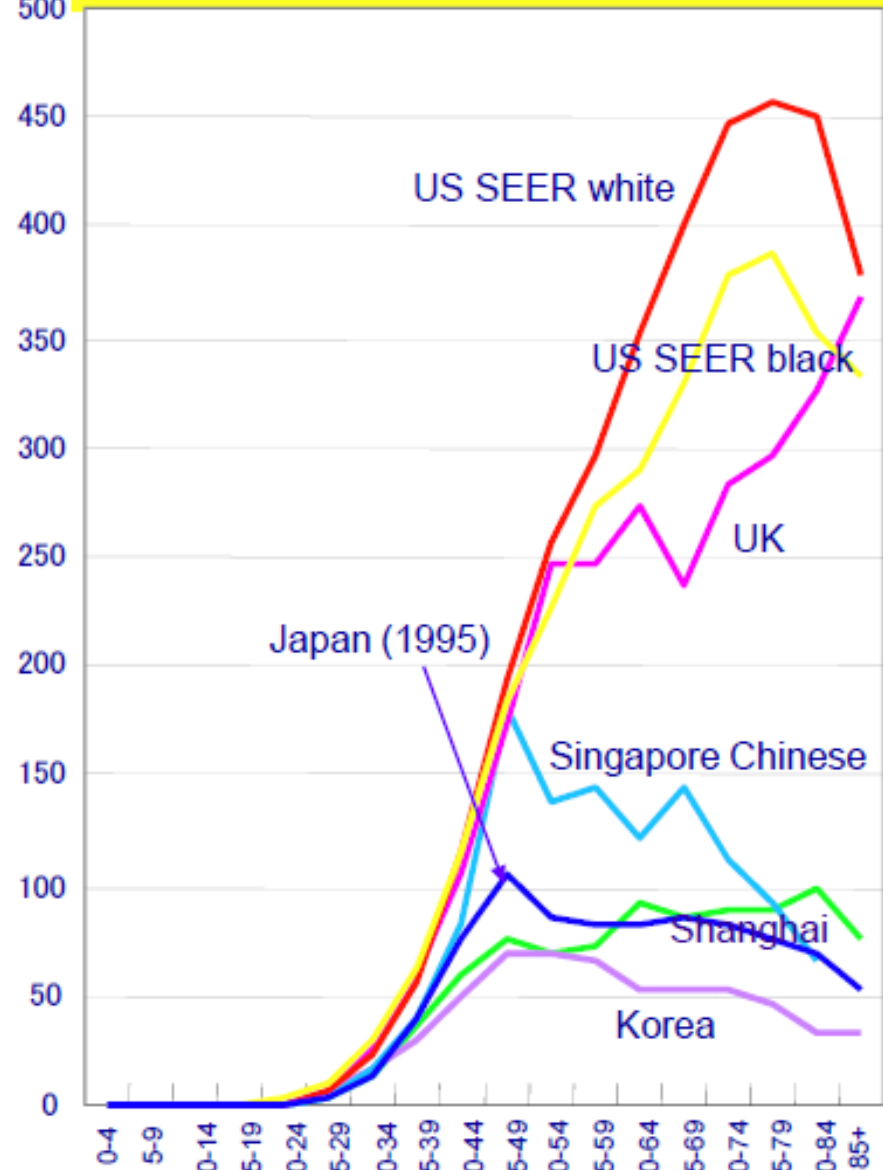
# Japan Strategic Anti-cancer Randomized Trial (J-start)



Kinkakuzi, Kyoto

# Is mammography effective enough for women aged 40-49?

Per 100,000 Breast cancer incidence according to age



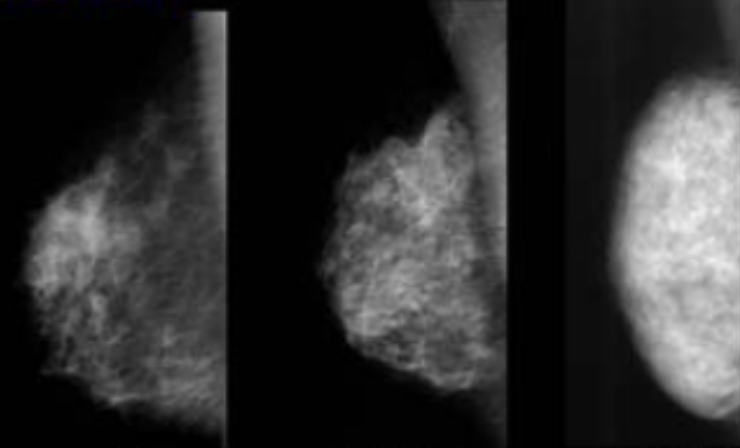
Breast density and sensitivity

Rate of mammograms based on breast density (High and heterogeneously dense)

- 40-49 69%
- 50-59 26%
- 60-69 12%

Sensitivity of mammography screening based on Miyagi cancer registry

- 40-49 71%
- 50-59 85%
- 60-69 87%



Scattered

Heterogeneously dense

Dense

## Sensitivity

### Age-specific interval breast cancers in Japan: estimation of the proper sensitivity of screening using a population-based cancer registry

Akihiko Suzuki<sup>1</sup>, Shinichi Kuriyama<sup>2</sup>, Masaaki Kawai<sup>1</sup>, Masakazu Amari<sup>1</sup>, Motohiro Takeda<sup>1</sup>, Takanori Ishida<sup>1</sup>, Koji Ohnuki<sup>3</sup>, Yoshikazu Nishino<sup>4</sup>, Ichiro Tsuji<sup>2</sup>, Daisuke Shibuya<sup>5</sup> and Noriaki Ohuchi<sup>1,B</sup>

Table 2. Sensitivity, specificity and positive predictive value according to the two screening groups and three age groups

Methods and age groups	MMG with CBE			CBE alone		
	40-49	50-59	60-69	40-49	50-59	60-69
Detected cancer	45	115	129	131	68	82
Reported interval cancers	2	9	10	21	11	15
Provisional sensitivity	95.7%	92.0%	92.8%	86.2%	86.1%	84.5%
Specificity	88.6%	90.7%	93.1%	92.0%	95.2%	96.5%
PPV	1.9	2.5	4.1	1.6	2.1	3.4
Interval cancers from population-based cancer registry	16	10	9	58	36	43
Total interval cancers	18	19	19	79	47	58
Proper sensitivity	71.4%	85.8%	87.2%	62.4%	59.1%	59.9%



CBE: clinical breast examination, MMG: mammography, PPV: positive predictive value.



# Background of Japan Strategic Anti-cancer Randomized Trial(J-start)

- Mammographic screening does not achieve sufficient accuracy in breasts with high density.
- Ultrasonography has the potential to detect early breast cancer not found by mammography.
- Several single institutional studies have already started using supplemental ultrasonography in Japan.
- But, worldwide, randomized clinical trials have not been completed to assess the efficacy of ultrasonographic screening to reduce breast cancer mortality.

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# 3<sup>rd</sup> term Comprehensive Control Research for Cancer

## RCT on effectiveness of ultrasound for breast cancer screening



Japan Strategic Anti-cancer Randomized Trial

- 2007~2011
- Budget: \$10Million

### Background

1. Breast cancer mortality is increasing in Japan
2. Highest incidence in 40s , with higher breast density
3. Ultrasound(US) is clinically available , but not for screening use
4. No evidence of mortality reduction by US screening



1

Standardization of US technique and interpretation in screening

2

RCT on effectiveness of US

Women aged 40-49 (100,000)

Randomized (RCT)



US + Mammography

VS

Mammography

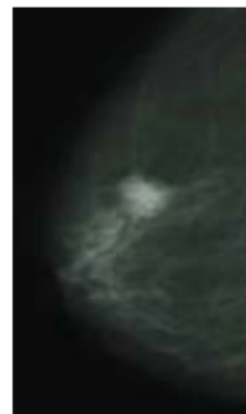


Primary Endpoint : Sensitivity, Specificity, Detection rate

Secondary Endpoint : Incidence rate of Advanced BC

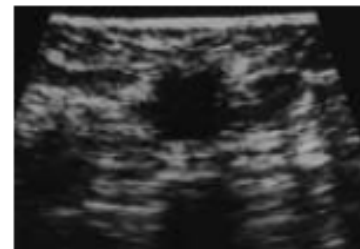


Final outcome: Mortality reduction



### Mammography

- Only EBM established in western countries
- QC/QA



### Ultrasound

- No evidence of reduced mortality
- QC/QA , not established

# Eligibility Criteria

## Inclusion criteria

- 1) Women aged 40-49 years when registered
- 2) Women who signed the informed consent to participate in this study

## Exclusion Criteria

- 1) Women with a history of breast cancer
- 2) Women with a history of malignant disease other than breast cancer within 5 years
- 3) Women in severe condition, who are not expected to live for 5 years

# Guideline for Ultrasound Screening and Training Program

Purpose: Standardization of ultrasound screening for breast cancer , including quality control

- Standardization of equipment and procedures
- Breast imaging lexicon for ultrasound
- Categorization , Reporting system , etc

Two day , 16 hour courses for doctors and technicians

- Doctor should master an intervention technique for CNB
- More than 1,500 doctors and 1,700 technicians finished

Ver 1.0 (Mar, 2007)  
Ver 2.0 (Aug, 2007)  
Ver 2.1 (Nov, 2007)  
Ver 3.0 (Jun, 2008)  
Ver 3.1 (Aug, 2008)  
Ver 3.2 (Jan, 2009)  
Ver 4.1 (Jul, 2009)  
Ver 5.0 (April, 2010)



Guideline



Breast Phantom



Hands-on training  
(intervention technique  
for doctors)

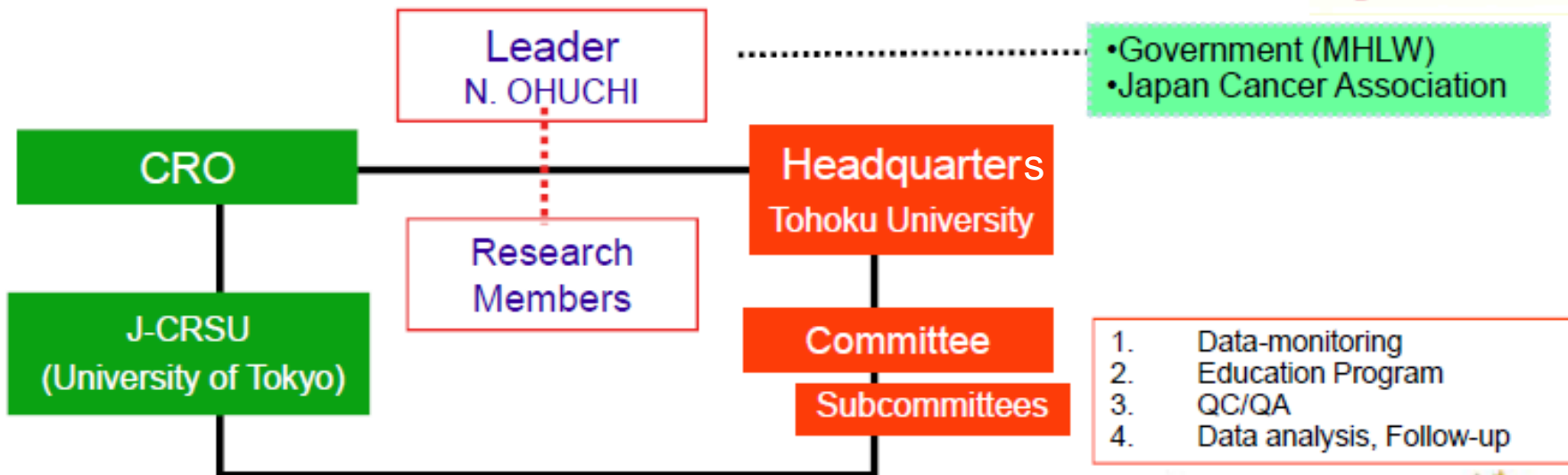


Group lecture



Qualifying test

# J-START Organization



•Government (MHLW)  
•Japan Cancer Association

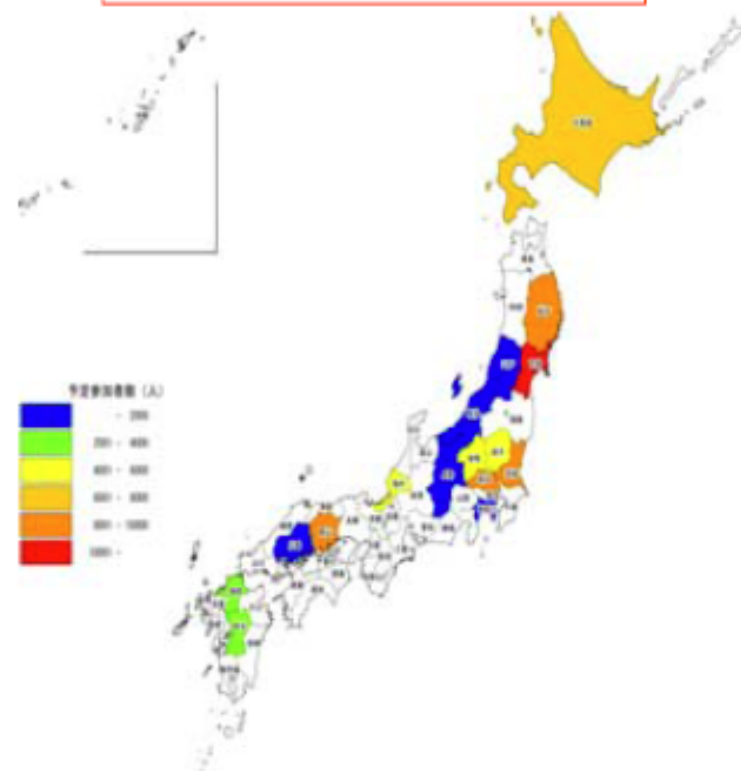
1. Data-monitoring
2. Education Program
3. QC/QA
4. Data analysis, Follow-up

Local Research Sites

Breast Cancer Screening Sites

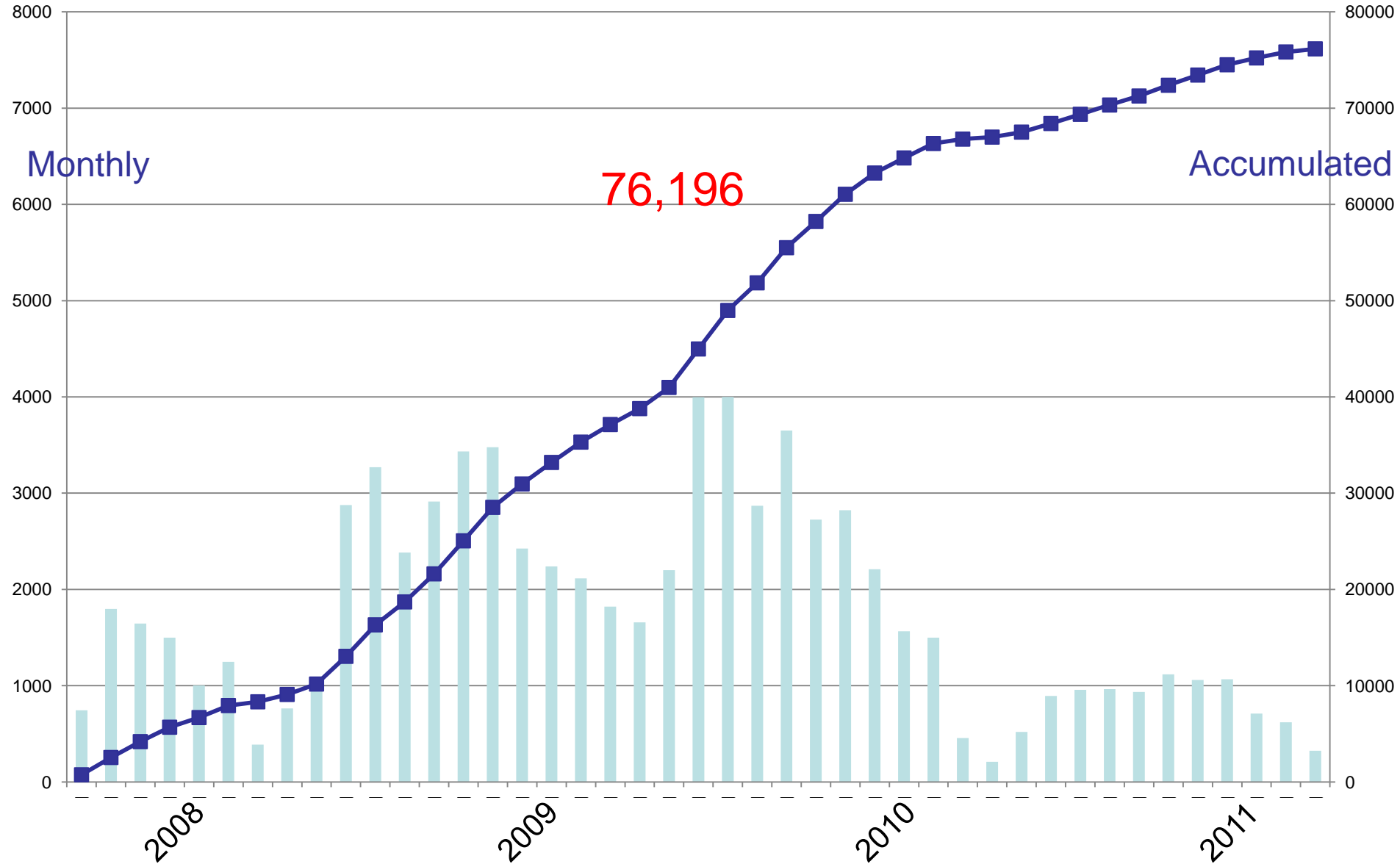


42 Research Sites in 23 Prefectures



**J-START**

# Participants Registered as of March 2011



# Follow- up Period

The participants are recalled to be screened 2 years after the first recruitment, or asked to answer questionnaires as follows :

- \*health status
- \*history of receiving other screening program
- \*incidence of breast cancer
- \*history of hospital consultation with any breast symptoms within 2 years
- \*etc.



# Schedule



2006      2007      2008      2009      2010      2011      2012      2013

Strategic Anti-Cancer Program (5 years)

Another Grant (2 years, at least)



(A1, B1)  
10,000



(A1, B1)  
10,000

A2, B2  
30,000



A2, B2  
30,000

A3, B3  
30,000



A3, B3  
30,000

A4, B4  
20,000



A4, B4  
20,000

2<sup>nd</sup> SCR, 2 years on

Mortality Reduction?

Registered	10,000	40,000	70,000	90,000	70,000	90,000
2 <sup>nd</sup> SCR, 2y on			10,000	40,000		

- Primary Endpoint: Sensitivity, Specificity
  - Cancer detection rate , Recall rate, False negative rate
- Secondary Endpoint: Rate of advanced breast cancer
  - Pathological staging, Lymph node status
- QC/QA for Ultrasound screening
  - PPV based on Categorization

# Summary

1. Breast cancer is now the most common cancer among females in Japan.

- The number of both breast cancer incidence and mortality are continuously increasing.
- The check up rate of mammographic screening is very low , approximately 24%.
- We have to promote mammographic screening further for the achievement of a 50% check up rate.

2. There is an on-going RCT(J-start) with mammography combined with ultrasonography for women aged 40-49 years.

- It will take a long time until the effectiveness, especially against mortality, can be proven.

# Acknowledgment

Noriaki Ohuchi, M.D.

Director, Cancer Center

Tohoku University Hospital

Sendai, Miyagi Pref., Japan

# The Next Evolutionary Step Forward

今、踏み出す明日への一步

演題募集期間

2011年

10月25日(火)~12月13日(火) 正午

## 第20回 日本乳癌学会学術総会 The 20th Annual Meeting of The Japanese Breast Cancer Society

# IN KUMAMOTO

2012年6月28日(木)・29日(金)・30日(土)

会場 / 熊本市会館、ホテル日航熊本、熊本ホテルキャッスルほか

会長 / 西村令喜 (熊本市立熊本市市民病院 乳腺内分泌外科)

事務局

熊本市立熊本市市民病院 乳腺内分泌外科  
〒862-8505 熊本市湖東1-1-60  
TEL: 096-367-0712  
FAX: 096-367-0713

運営準備室

熊本市立熊本市市民病院内 株式会社メッド 〒862-8505 熊本市湖東1-1-60  
TEL: 096-367-0712 FAX: 096-367-0713  
株式会社メッド 福岡営業所 〒812-0013 福岡市博多区博多駅東2-5-28  
TEL: 092-432-2533 FAX: 092-432-2534

E-mail: 20jbc@med-gakkai.org URL: www.med-gakkai.org/20jbc/



A photograph of a volcanic crater. In the center, there is a bright green lake. To the right, a large plume of white smoke or steam rises from the crater. The surrounding cliffs are dark and rocky. The sky is blue with some light clouds.

Thank you for your attention!

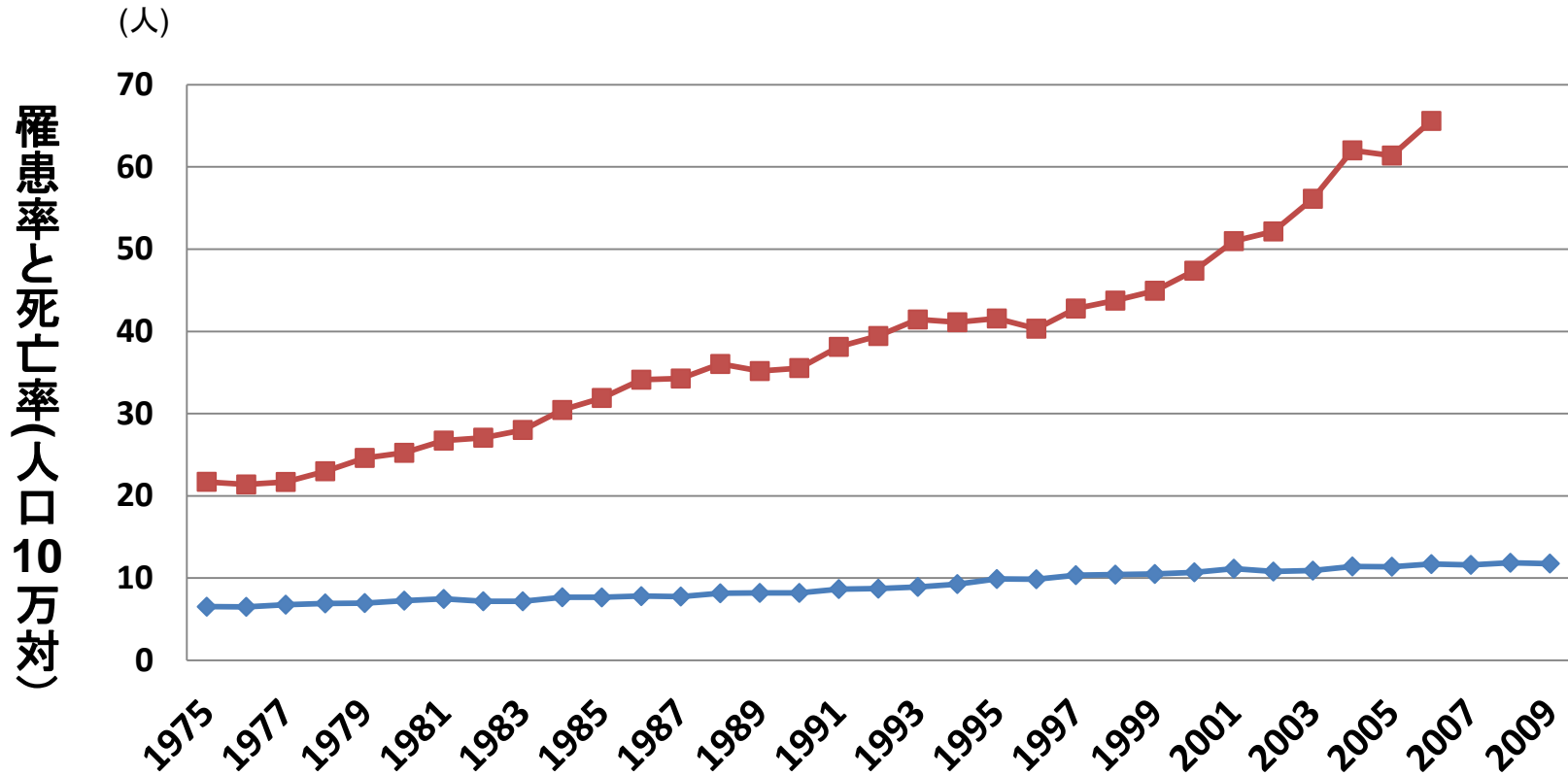
Mt. Aso in Kumamoto Pref.

# Screening MMG for Aged 40-49 Years

## The results of an investigation in Japan

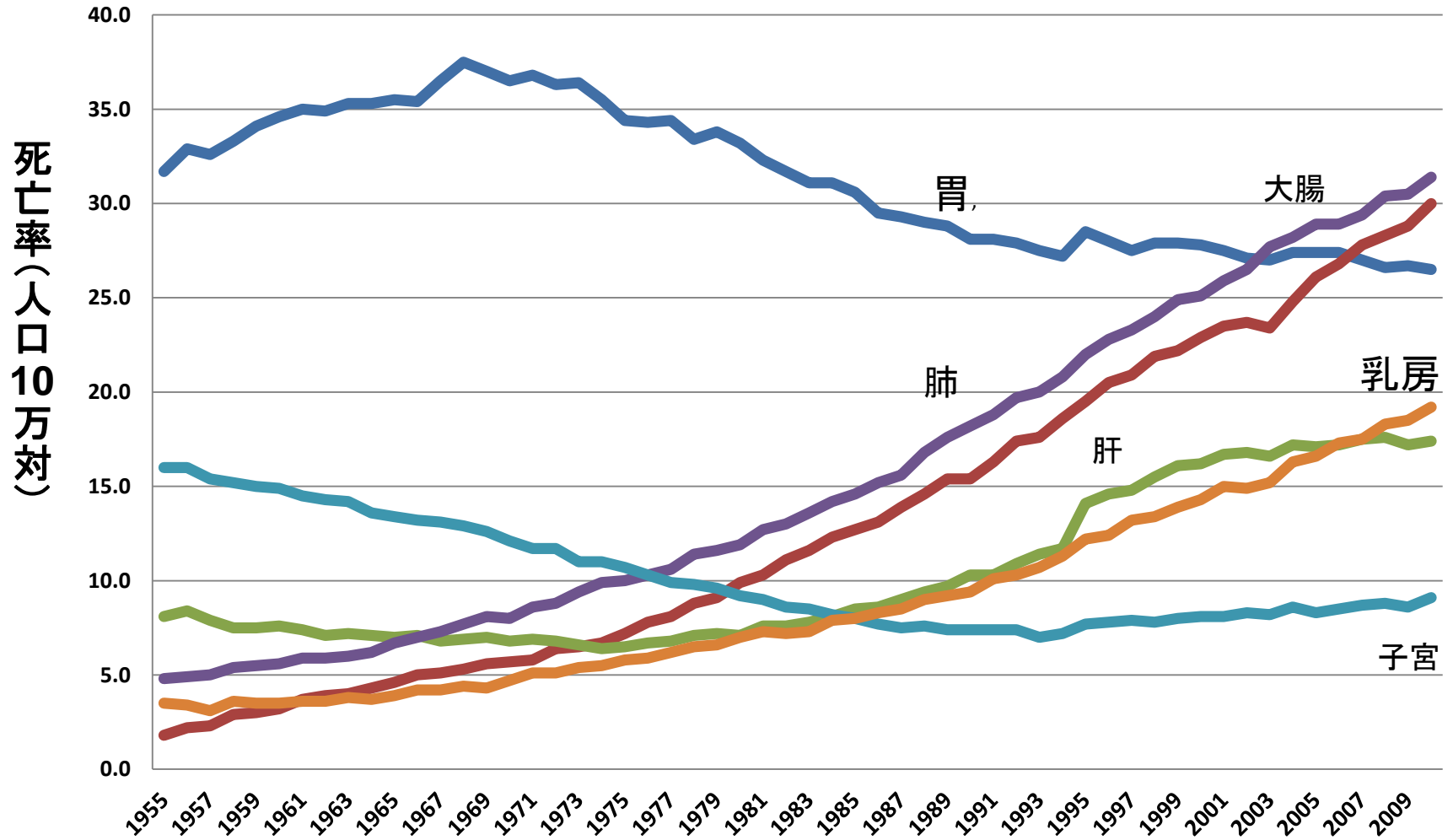
- False positives, recalls and biopsy rate were higher compared with other age groups in Japan, but lower than those of the U.S.A.
- The detection rate of breast cancer was a little higher than that of the U.S.A.
- There is little harm of the screening MMG for detection of breast cancer, but the benefit might be nearly equivalent or a little superior compared with that of the U.S.A.
- It is important to let the examinees know this information properly.

# 乳がんの罹患率と死亡率



地域がん登録全国集計によるがん罹患データ(1975年~2005年)、国立がんセンターがん対策情報センター人口動態統計(1975年~2005年)、厚生労働省

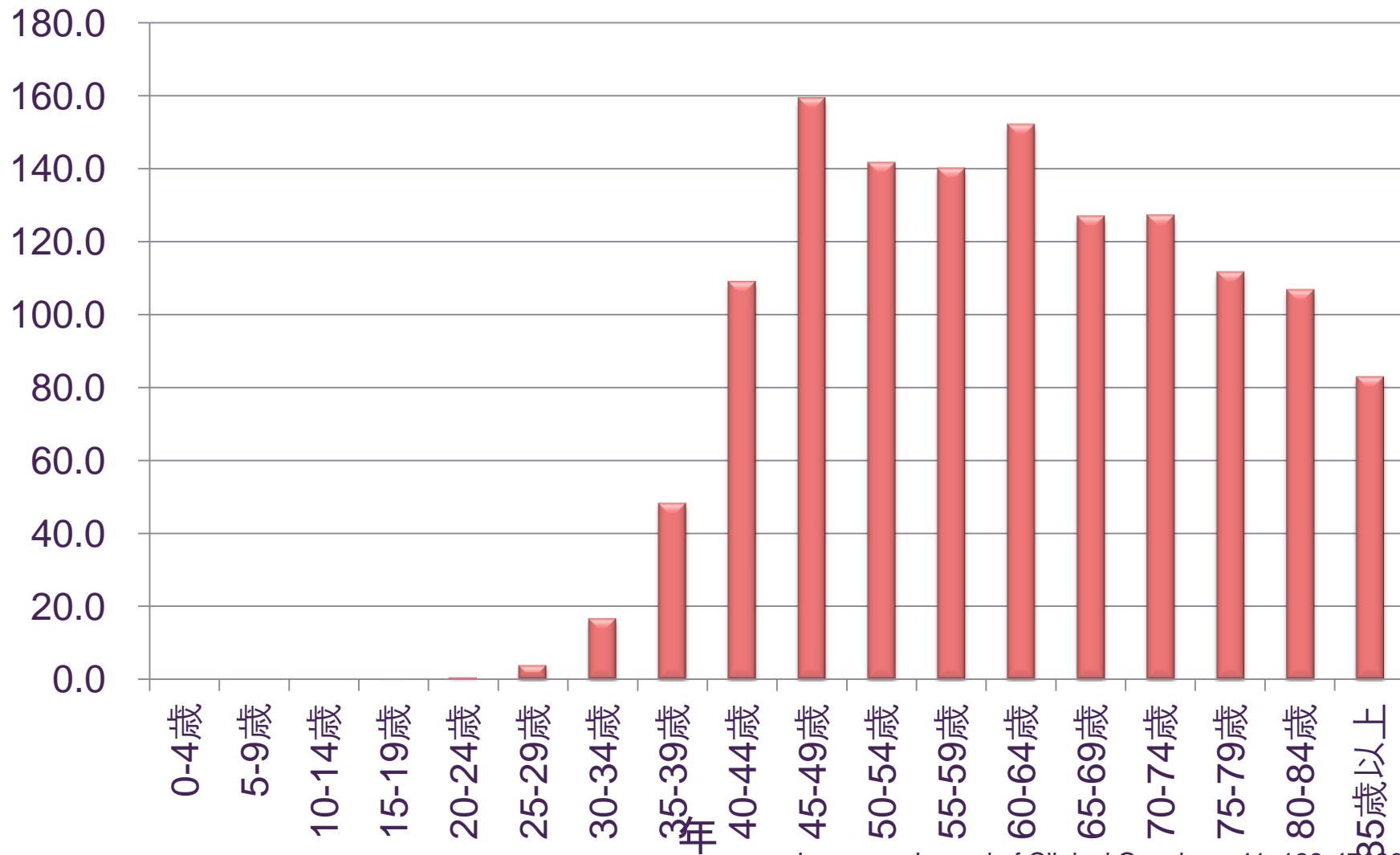
# 悪性新生物の主な部位別死亡率の年次推移（女性）





# 乳癌の年齢階級別推定罹患率(2005年)

全国年齢階級別推定罹患率(対人口10万人)



# がん対策推進基本計画

全ての患者・家族の安心

がんによる死亡者の減少  
(20%減)

全てのがん患者・家族の  
苦痛の軽減・療養生活の質の向上

重点的に取り組むべき事項

がんの  
早期発見

受診率  
50%

放射線療法・化学療法の推進、  
医療従事者の育成

すべての拠点病院で  
「放射線療法・外来化学療法」  
を実施

治療の初期段階からの  
緩和ケアの実施

すべてのがん診療に携わる医師に  
緩和ケアの基本的な研修を実施

がん医療  
に関する  
相談支援・  
情報提供

がんの  
予 防

未成年者  
の喫煙率  
0%

がん登録の推進

院内がん登録を行う医療機関数の増加

すべての  
2次医療圏に  
相談支援センター  
を設置し、研修を  
修了した相談員  
を配置

医療機関の整備等

原則、すべての2次医療圏に拠点病院を設置し、  
5大がんの地域連携クリティカルパスを整備

がん 研究

# US Preventive Services Task Force(USPSTF)の推奨変更(2009.11)

## 推奨グレードC

40歳代の女性に対しては、MMGを  
用いた定期的な乳がん検診を  
行うことを推奨しない

### その後修正

50歳未満の定期的なMMG検診を行うに当たって  
は  
対象者個人ごとの利益と不利益に関する価値判  
断を

## University of Missouri-Columbiaでの最新のデータ

- 40-49歳での検討で、47%はMMGで発見、有症状での発見が53%
- MMG発見乳がんは平均2cmで、有症状は3cm
- リンパ節転移も25%対56%
- 5年無再発生存も94%対71%

American Cancer Society は40歳からのMMG推奨

# 日本乳癌検診学会の見解

- 今回の改定はアメリカのデータに基づいた判断であり、日本に  
そのまま当てはめることはできない
- 不利益に関する日本のデータが不足しているため、早急に収集する必要がある
- 死亡減少効果については、比較に問題があり、過小評価の可能性があり、又観察年数調整をしていないので、検討を要する
- 日本における科学的根拠に基づく推奨度を改定するまでは、現行の推奨度を継続する

# 40代の日本の乳癌検診(推測)

- 偽陽性率、精密画像検査、生検率は他の年代より高いが、米国よりも低かった
- 乳癌発見率は米国より若干高かった

米国と比べて不利益は少なく、効果は  
ほぼ同等か、それ以上であろう



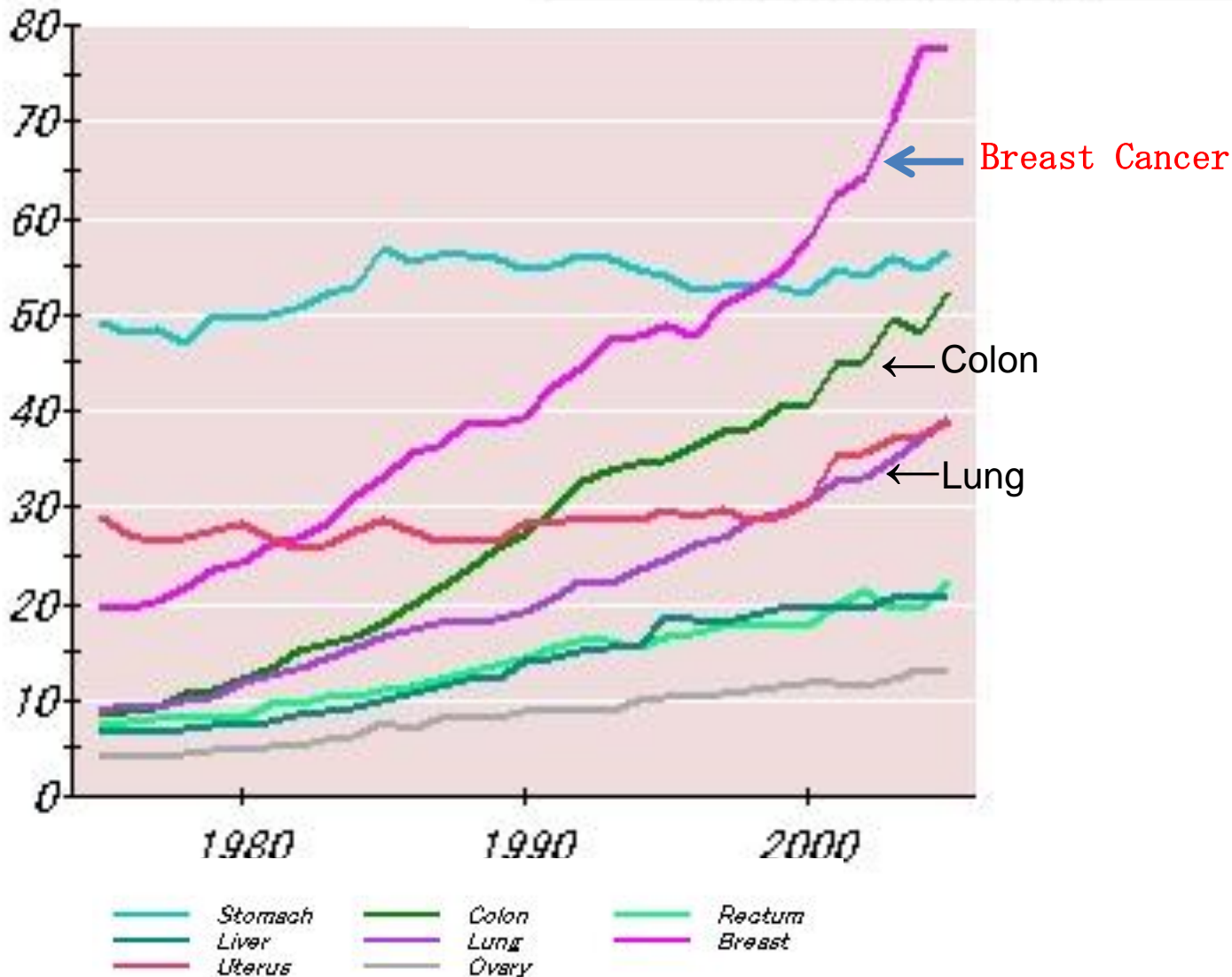
この情報を受診者に正しく伝えることが重要

# MMG検診50%達成のための小生の提案

- ・がん対策法などに国の検診責務を明確に盛り込む
- ・マスコミ(新聞、テレビなど)を通じて検診の目的・重要性のアピールを国レベルで定期的に行う。
- ・中学生、高校生などへの啓発活動—本人と関係者への啓発につながる
- ・全国共通の無料クーポン券の配布(特に罹患年齢の40、50歳代)
- ・保健師などによる戸別訪問、ダイレクトメール
- ・MMG検診に対する個人負担の更なる補助(ワンコイン500円) 或いは保険診療
- ・MMG検診で発見された乳がん患者に対する治療費の軽減、保険会社による優遇
- ・休日・夜間のMMG検診体制の確立
- ・検診方法の見直し

Trend in crude cancer incidence rate  
(major sites)  
[ female 1975-2005 ]

per 100000 population

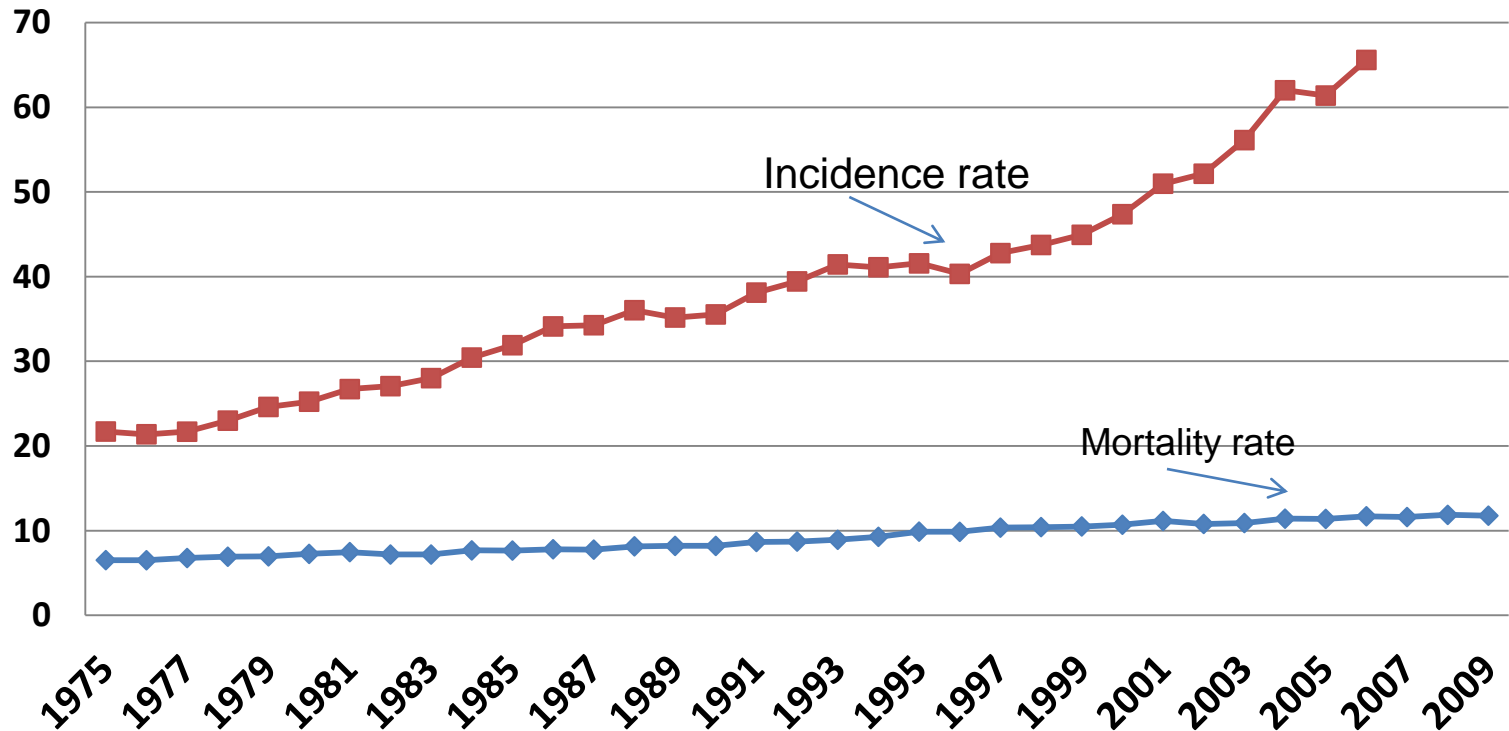


Source: Center for Cancer Control and Information Services,  
National Cancer Center, Japan



# Incidence and Mortality Rate in Japan

per 100,000 population



Source: Center for Cancer Control and Information Services, National Cancer Center, Japan

