

**Requisite secondary prevention**

Woman, born in Hawaii and grown in Hiroshima  
 Married in China and returned Hiroshima after World War II  
 Healthy in general with five children (4 sons and one daughter)

Symptom of melena and constipation on December 21, 2003  
 Detected advanced rectal cancer with multiple lung metastasis on January 6, 2004

Never experienced cancer screening !!

Terminal care in hospice from April, 2005 and passed away on November 19th  
 "I am ready to die at any time"  
 「何時お迎えが来ても大丈夫だよ」

**Cost effectiveness of treatment by early detection of breast cancer (Aichi Cancer Center Hospital, 2005)**

Stage (Cases)	Average age (Years)	Period in hospital (Total)	Surgery	Radiation	Chemo- & hormonal-therapy	Total cost (Ratio)	5-year survival rates
Non-invasive (10)	47 (36-59)	12 days (-)	536	--	--	649 (1.0)	> 98%
Invasive without lymph node metastasis (9)	50 (43-59)	11 days (5 years)	653	270	2,312	2,687 (4.1)	> 92%
Invasive with lymph nodes metastasis (8)	50 (39-58)	12 days (5 years)	770	260	2,433	3,375 (5.2)	> 80%

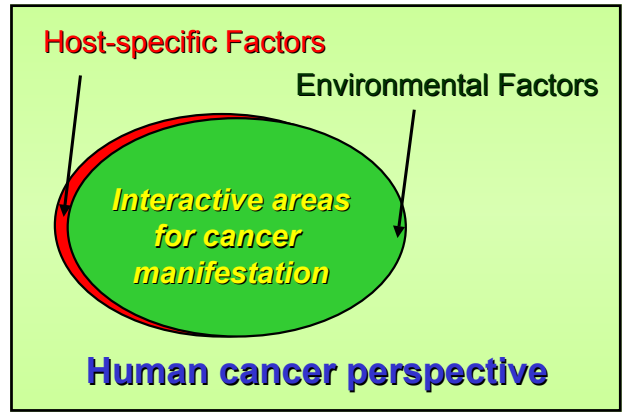
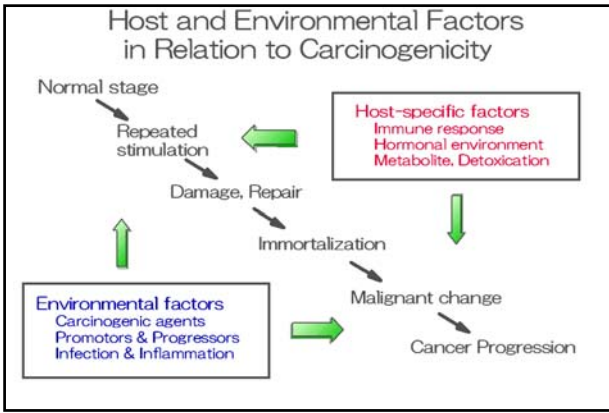
**We can save medical costs and many lives of women by early detection of breast cancer !!**

The 11<sup>th</sup> Japanese-German Symposium  
**Frontiers of Cancer Research**  
**Cancer Pattern and Its Prevention Strategy in Japan and Asia**

Kazuo Tajima  
 Aichi Cancer Center Research Institute

1. Cancer burden in Japan/Asia
2. Risk and protective factors
3. Prevention strategies

- The Third 10-Year Cancer Control Strategy Program "Reduction of Cancer Death and Incidence"**
- 1) Molecular mechanism of carcinogenicity
  - 2) Molecule-based study of clinical features of cancer
  - 3) Development of innovative cancer prevention
  - 4) Development of new diagnosis technology
  - 5) Development of new therapies
  - 6) Quality of life of cancer patients
  - 7) Establishment of cancer information net work



## Concept of Prevention Strategies

**Primary prevention**  
Incidence risk reduction of targeted cancer by eliminating carcinogenic agents and supplementing protective factors

**Secondary prevention**  
Mortality risk reduction of targeted cancer by curative treatment after periodical screening of early stage of targeted cancer

### Incidence Rate of Main Sites of Cancer in Asia\* (IARC in 2001)

Country	Esoph	Stomach	Intestine	Liver	Lung	Pro/Br	Hemato	Uterus
Japan	10 / 1	67 / 27	48 / 26	26 / 8	37 / 11	10 / 31	13 / 8	19
Korea	10 / 1	70 / 26	15 / 10	49 / 12	48 / 12	4 / 13	7 / 4	17
China	15 / 6	31 / 15	6 / 5	21 / 8	24 / 10	2 / 13	8 / 6	2
Mongolia	20 / 27	47 / 29	5 / 4	117 / 67	39 / 15	5 / 7	--	13
Singapore								
Chinese	7 / 1	26 / 12	45 / 32	22 / 5	57 / 20	14 / 47	14 / 9	24
Malay	3 / 2	8 / 6	8 / 15	7 / 2	9 / 5	8 / 37	10 / 6	14
Indian	1 / 1	6 / 4	20 / 16	16 / 3	30 / 11	12 / 40	17 / 11	35
Thailand	4 / 1	5 / 8	11 / 8	37 / 16	27 / 11	4 / 16	8 / 5	24
Vietnam	4 / 1	24 / 8	11 / 8	23 / 6	29 / 7	2 / 17	10 / 6	20
Pakistan	6 / 7	5 / 3	6 / 5	5 / 3	20 / 3	8 / 57	9 / 9	<1
India	7 / 6	7 / 4	5 / 5	--	9 / 2	5 / 23	8 / 6	28
Jordan	--	7 / 5	16 / 14	--	19 / 3	12 / 40	16 / 14	--
Oman	3 / 3	14 / 7	4 / <1	9 / 4	12 / 2	11 / 13	17 / 11	7
Iran	39 / 25	17 / 6	4 / 3	4 / 2	8 / 2	2 / 12	8 / 5	9

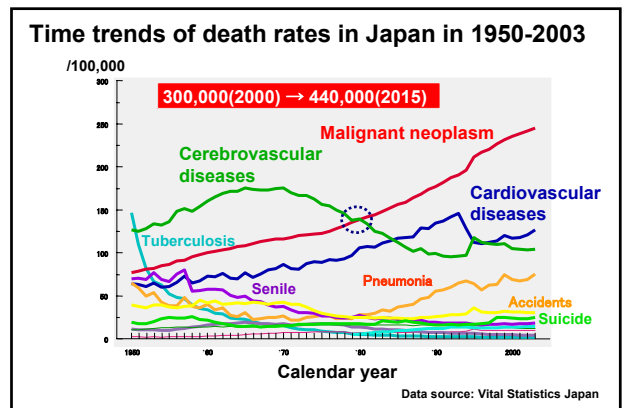
\*Male/Female per 100,000 (Adjusted by World Population)

## Estimated Risk Attribution of Main Cancers in Japan and Asia

**Infectious agents: 30-40%**  
Stomach Bladder & Bile duct (in part)  
Liver Cervix Naso-pharynx

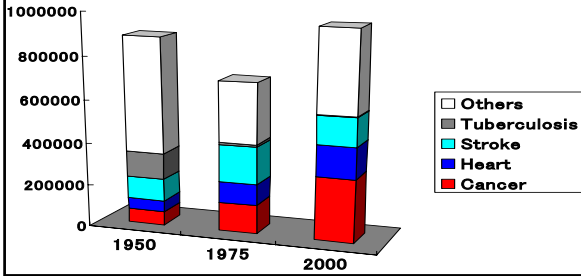
**Habitual smoking and drinking: 25-35%**  
Upper G-I tract Respiratory tract

**Dietary habit and physical inactivity: 20-30%**  
Colon & Rectum Bile ducts  
Breast Endometrium Prostate



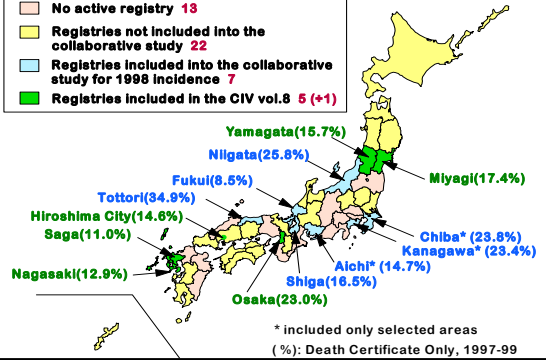
### Chronological change of top 3 causes of deaths in 1950, 1975 and 2000 in Japan

(Data source: Vital Statistics Japan, Ministry of Health, Labor and Welfare)



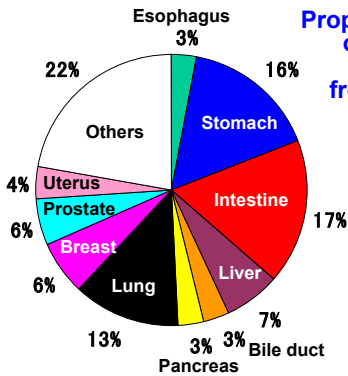
### Population-based Cancer Registries in Japan

- No active registry 13
- Registries not included into the collaborative study 22
- Registries included into the collaborative study for 1998 incidence 7
- Registries included in the CIV vol.8 5 (+1)

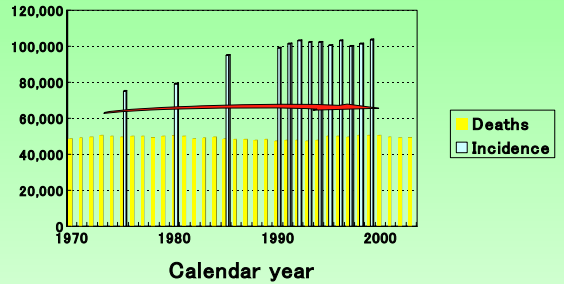


### Proportional distribution of top 10 cancers in Japan from 2005 estimates

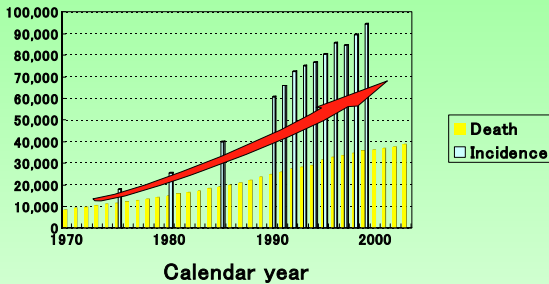
Data source: Ohno Y et al, in Gann Monogr. Cancer Res. edited by Tajima K et al, 2004



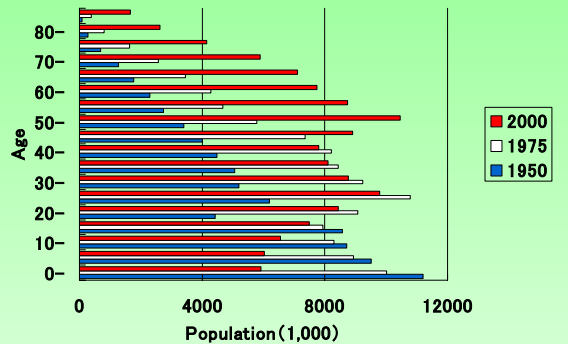
### Time trends in incidence and death of stomach cancer in Japan

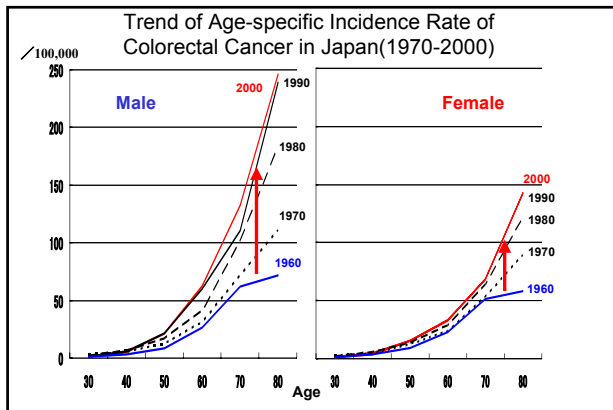
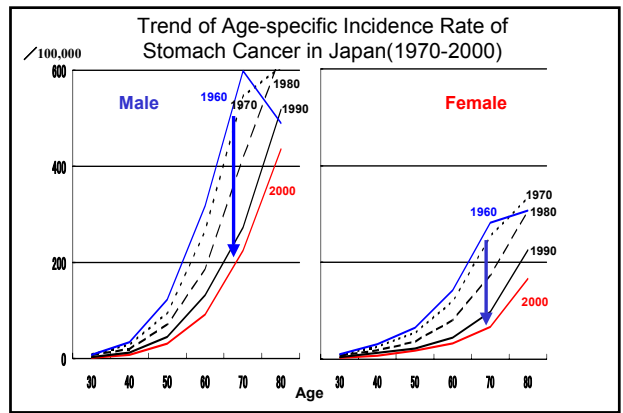
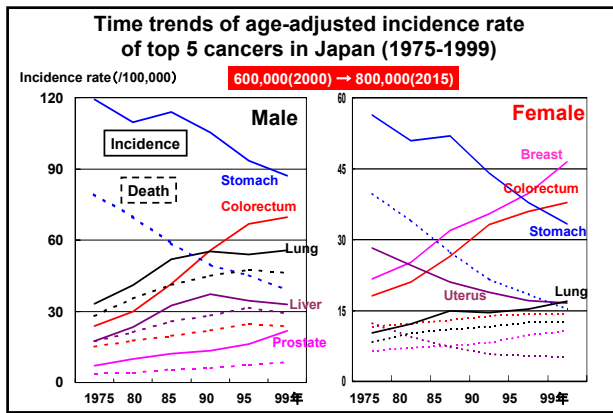


### Time trends in incidence and death of colorectal cancer in Japan



### Time Trends in Age Distribution in Japan



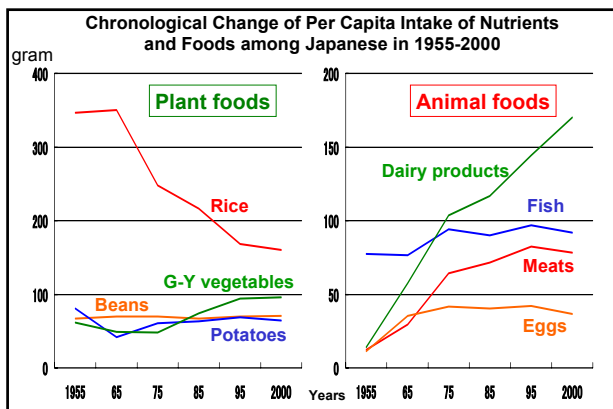


### Estimates of Cancer Incidence in Japan (1985-2015)

	Male			Female		
	1985	2000	2015 (Ratio)*	1985	2000	2015 (Ratio)*
All	353.5	404.8	407.4 (1.15)	224.8	252.8	273.4 (1.22)
Stomach	113.7	85.5	66.1 (0.58)	51.9	33.8	26.9 (0.52)
Intestine (Colon) (Rectum)	41.6	67.4	70.4 (1.69)	26.5	39.7	44.8 (1.69)
Liver	23.0	42.3	43.3 (1.88)	16.4	27.8	32.2 (1.96)
Lung	18.6	25.1	27.1 (1.46)	10.1	11.9	12.6 (1.25)
Prostate	32.2	33.5	28.0 (0.87)	8.9	10.7	10.1 (1.13)
Uterus	51.8	60.3	65.9 (1.28)	14.9	17.9	19.3 (1.30)
Breast	12.2	26.9	45.2 (3.70)	--	--	--
				27.3	31.2	54.1 (1.98)
				31.9	46.9	53.4 (1.67)

\* Ratio of increment of incidence rates (2015/1985)

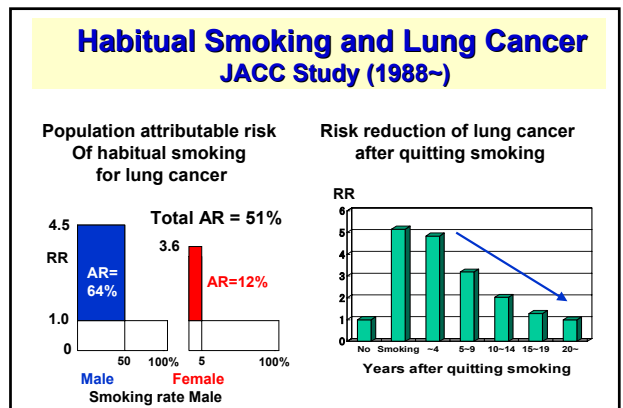
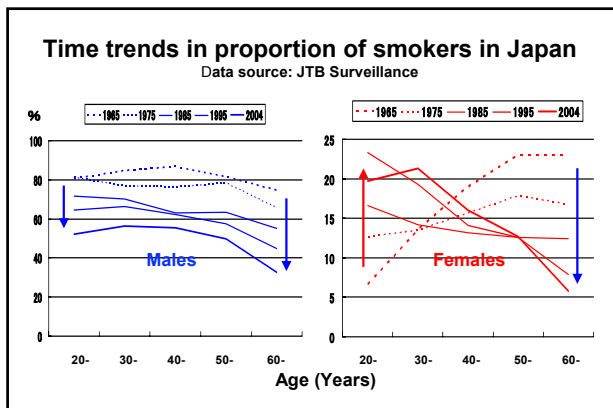
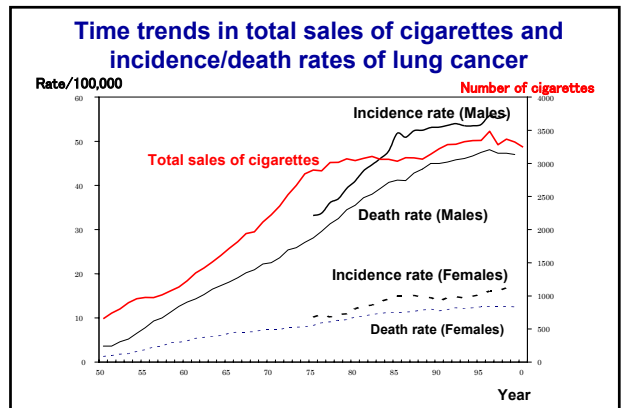
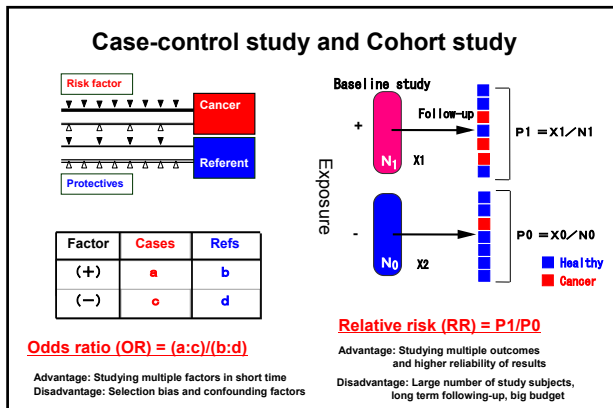
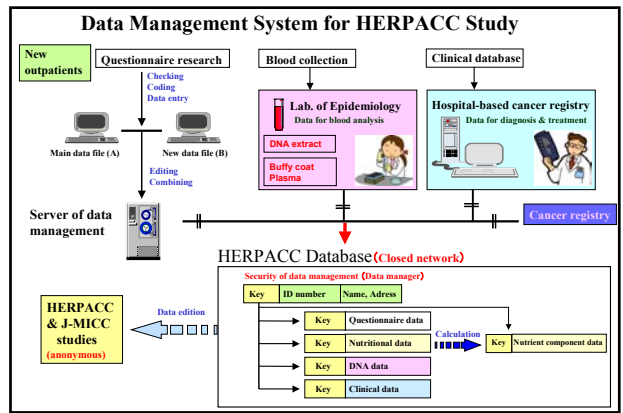
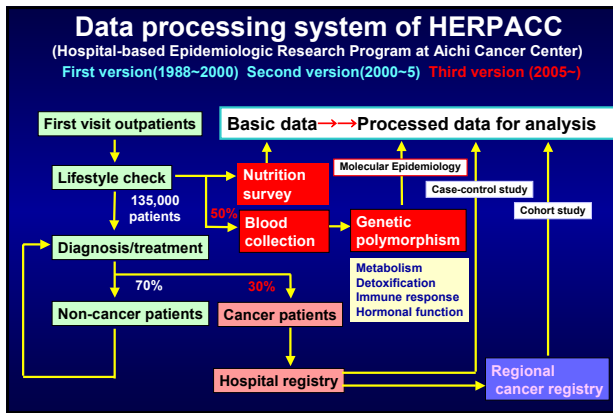
Data source: Ohno Y, 2004



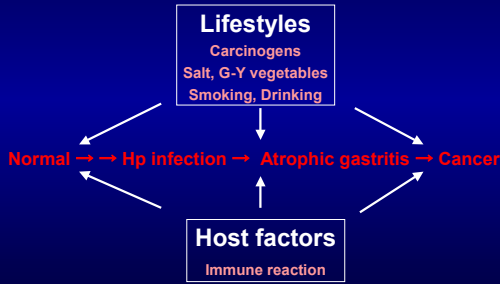
### Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC)

**Main purposes by step in progressing HERPACC**

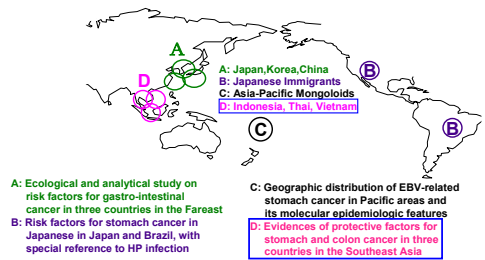
1. Clarifying lifestyle patterns of people in Aichi
2. Clarification of risk and protective factors for cancer
3. Testing interaction between gene and environment
4. Drawing up a guideline for cancer prevention
5. Establishment of a hospital-based cohort study
6. Defining diagnostic criteria of high risk people



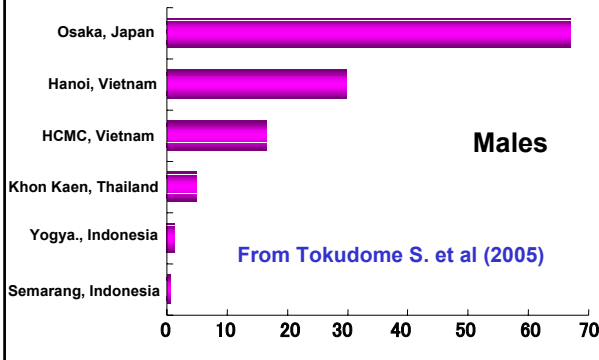
## Carcinogenic steps of gastric cancer (Host-specific and lifestyle factors)



## Ethnoepidemiologic Study on Cancer: Study Subjects and Areas



## Age-adjusted incidence of stomach cancer (/10<sup>5</sup>) in Asia

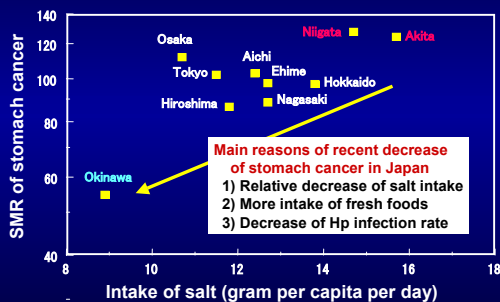


*H. pylori* infection rate, pepsinogen positive rate and excretion level of NaCl among people in Vietnam, Thailand, Indonesia and Japan

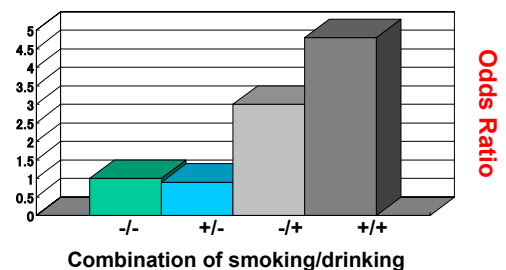
	<i>Hp</i> (+) <sup>a</sup> (%)		PG (+) (%)		NaCl (g/day)	
	M	F	M	F	M	F
Hanoi, Viet Nam	74	69	10	35	12.4	10.6
HCMC, Viet Nam	83	72	14	5	11.6	11.0
KK, Thailand	88	88	11	14	13.7	12.8
Semarang, Indonesia	0	0	0	0	11.1	10.4
Yogya., Indonesia	3	0	0	2	10.9	9.7
Japan	62	57	23	22	12.9	11.2

<sup>a</sup> *H. pylori* (+) was examined by serum IgG in Japan and UBT in other countries.  
From Tokudome, S. et al. Cancer Letter and Cancer Science (2005)

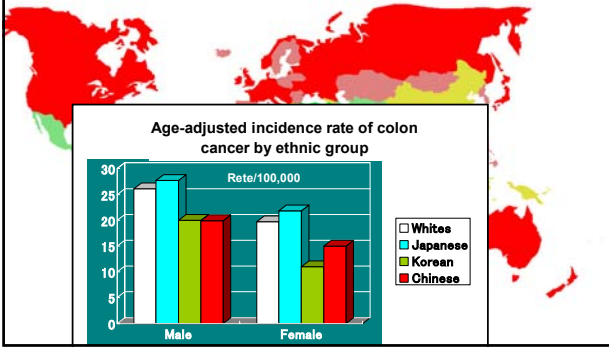
## Correlation between salt intake (1980-84) and SMR of stomach cancer (1990) in Japan



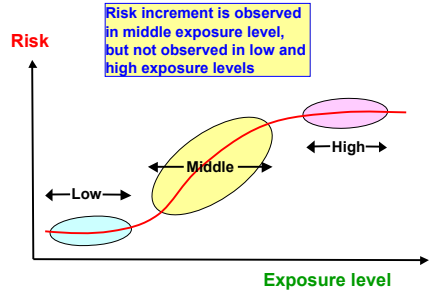
## Habitual Smoking and Drinking for Stomach Cancer Risk



**Age-adjusted Mortality Rate of Large Intestinal Cancer (Males)**  
 Source: Cancer Incidence in Five Continents Vol. 8 (1993-97)

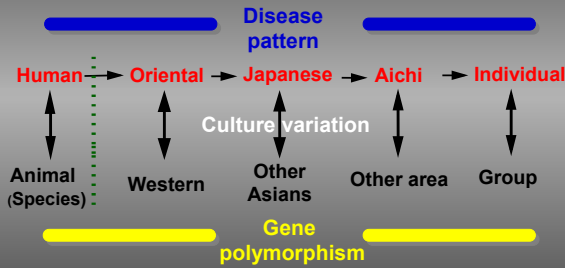


**Increment of cancer risk by exposure level of carcinogenic agents**



**Concept of Ethnoepidemiology**

Diversity & Universality of Diseases by Genetic & Cultural Background



Source: Gann Monogr Cancer Res No 44 "Ethnoepidemiology of Cancer", 1996

**The Second KOJACH Cooperative Study on G-I Tract and Breast Cancer**

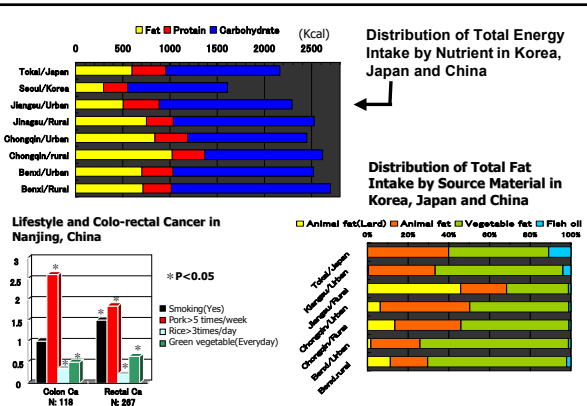


**Goal of Study**

- Searching of lifestyle factors
- Gene polymorphisms related to risk
- Gene-environment interaction for cancer
- Establishment of prevention measurement

**Methodology**

- Standardization of SQFFQ
- Case-referent study on risk factors
- Molecular epidemiologic study
- Evaluation of prevention trials



**Risk of Large Intestinal Cancer In Seoul, Korea**

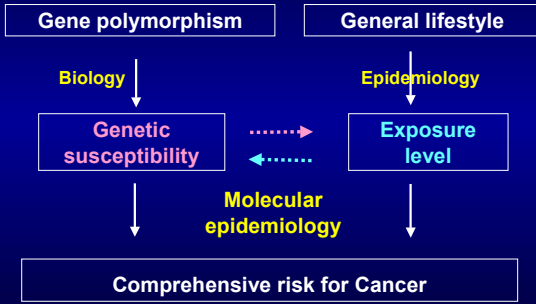
Risk Reduction by Nutrients Intake

Nutrient	Average Intake			
	Q1(Lower most)	Q2(Lower 25-%)	Q3(Upper)	Q4(Upper most)
Lactase	1.0	0.8	0.7	0.6*
Dietary fiber	1.0	1.1	0.6	0.6*
Calcium	1.0	0.8	0.9	0.8
Vegetable	1.0	0.8	1.3	0.8
Folic acid	1.0	0.9	0.8	0.5*
Meats	1.0	1.6	1.1	0.9

Odds ratio adjusted by age and sex  
 \* Statistically significant (P<0.05)

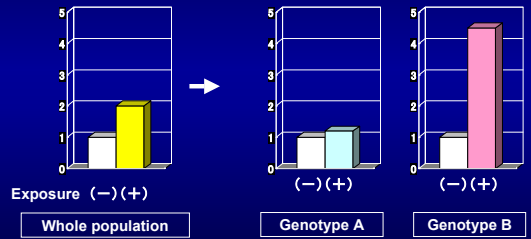
## Concepts of Molecular Epidemiology

Lifestyle, Genetic Susceptibility and Cancer Risk



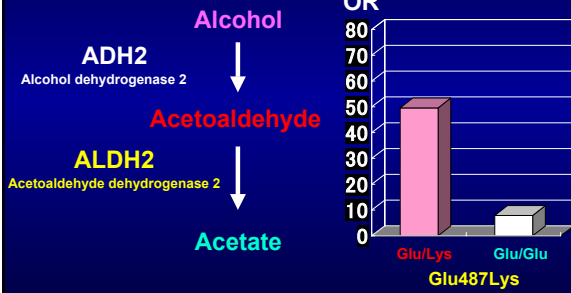
## Gene-environment Interaction

Different OR for environmental factors among different genotypes



## Risk of Esophageal Cancer by Habitual Drinking

(≥5 days/week, ≥45ml/day)



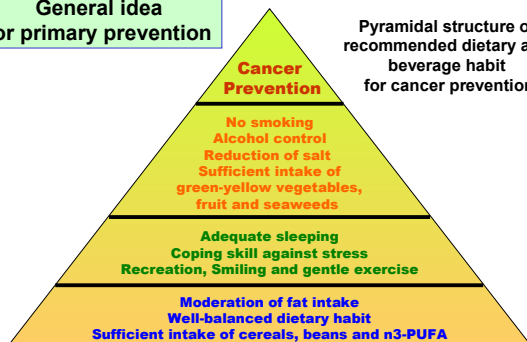
## Evidence-based related factors for cancer by site

Factor Site	Smoking	Drink ing	G-Y veget able	Fat	Exer size	Other risk factors	Other protective factors
Esophagus	⊙	⊙	⊙				
Stomach	○	○				Hp infection High salt	
Colon Rectum		○	○	○	○	Chronic inflammation	Fresh fish
Liver	○				○	Virus(HCV,HBV)	
Lung	⊙		○				Fresh fish
Prostate					○		
Breast		○	○		○	Obesity	
Uterus		○	○		○	Obesity	
Cervix	○		○			virus(HPV)	

⊙ Convicted ○ Probable

General idea for primary prevention

Pyramidal structure of recommended dietary and beverage habit for cancer prevention

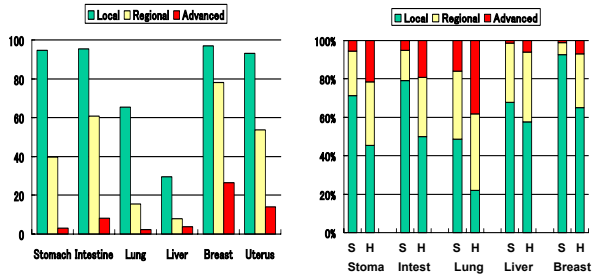


## Prevention Strategy for Main Sites of Cancer

	Male			Female		
	Incidence	Death	I/D ratio	Incidence	Death	I/D ratio
<b>Total</b>	275,280	167,076	1.65	203,879	108,337	1.88
<b>Recommendation of primary &amp; secondary prevention</b>						
Stomach	66,307	32,218	2.06	33,011	17,521	1.88
Colon	30,267	11,162	2.71	23,823	10,538	2.26
Rectum	17,394	7,302	2.52	11,208	4,411	2.54
Prostate	14,005	6,251	2.24	--	--	--
<b>Preference of primary prevention</b>						
Liver	24,868	22,937	1.08	10,499	9,422	1.11
Lung	41,523	35,700	1.16	16,267	13,294	1.22
<b>Feasibility of secondary prevention</b>						
Uterus	--	--	--	17,980	5,008	3.59
Breast	--	--	--	31,897	8,393	3.80

## 5-year survival rates of main cancers in Osaka, Japan by stage (left) and place detected (right)

Data source: Osaka Cancer Registry (1955-99)



## Recommended Methods for Screening

Cancer	Main methods of first screening	Age	Interval
Stomach	Roentgenographic screening by barium photofluorography	40~	1/year
Colon	Fecal occult blood test 2 days Immunological test	40~	2/year
Uterus	Cytology (Pap smear) test	30~	1/year
Lung	Roentgenographic screening and/or sputa cytology (smoker)	50~	1/year
Breast	Monthly self-examination and Mammography		30~
Prostate	PSA test	40~ 60~	1/2 years 1/year

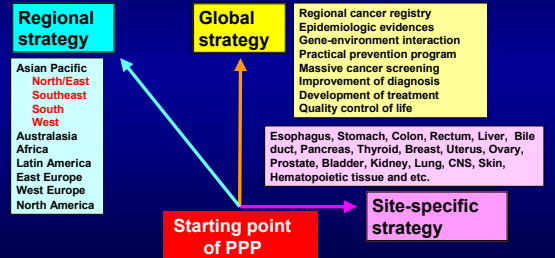
## Secondary Prevention Strategy

Evaluation Studies of Cancer Mass Screening in Japan and International Consensus

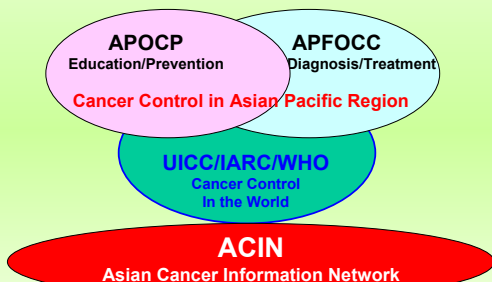
Cancer	RCT	Case-control study	Non-RCT cohort study	International consensus
Stomach	on-going	effective	effective	? in Western countries effective in Asia
Colon	(-)	effective	suggestive	effective
Cervix	(-)	effective	effective	effective
Lung	(-)	suggestive	(-)	not effective
Breast	(-)	(-)	(-)	effective

RCT: Randomized controlled trial, (-): not conducted

## Three Dimensional Strategic Directions in Practical Prevention Program (PPP) against Cancer



## Situation of the Organizations for Cancer Control in Asia



## Concluding Remarks

Strategies of cancer control may change over time with new developments in technology, but the principle idea remains based on general lifestyle improvement.

Establishing a practical prevention program for cancer prevention in Asian countries including Japan could be a model of cancer control program in developing countries in the world. Now establishment of Asian cancer information network is requisite for the practical cancer control program in Asia.