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

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

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

<table>
<thead>
<tr>
<th>Country</th>
<th>Stomach</th>
<th>Esoph</th>
<th>Intestine</th>
<th>Liver</th>
<th>Lung</th>
<th>Pro/Br</th>
<th>Hemato</th>
<th>Uterus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>16/10</td>
<td>2/10</td>
<td>10/10</td>
<td>15/10</td>
<td>22/15</td>
<td>4/15</td>
<td>4/15</td>
<td>1/15</td>
</tr>
<tr>
<td>Korea</td>
<td>15/10</td>
<td>17/15</td>
<td>14/15</td>
<td>13/10</td>
<td>22/15</td>
<td>3/15</td>
<td>2/15</td>
<td>0/15</td>
</tr>
<tr>
<td>China</td>
<td>10/10</td>
<td>5/10</td>
<td>5/10</td>
<td>10/10</td>
<td>5/10</td>
<td>3/10</td>
<td>3/10</td>
<td>0/10</td>
</tr>
<tr>
<td>Mongolia</td>
<td>30/25</td>
<td>18/15</td>
<td>12/15</td>
<td>12/10</td>
<td>20/15</td>
<td>2/15</td>
<td>2/15</td>
<td>0/15</td>
</tr>
</tbody>
</table>

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

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
(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 colorectal cancer in Japan

Time Trends in Age Distribution in Japan

* Included only selected areas
(%) Death Certificate Only, 1997-99
Time trends of age-adjusted incidence rate of top 5 cancers in Japan (1975-1999)

Trend of Age-specific Incidence Rate of Stomach Cancer in Japan(1970-2000)


Chronological Change of Per Capita Intake of Nutrients and Foods among Japanese in 1955-2000

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
### Data processing system of HERPACC
(Hospital-based Epidemiologic Research Program at Aichi Cancer Center)

- First visit outpatients
- Lifestyle check
- Diagnosis/treatment
- Non-cancer patients
- Hospital registry

**Second version (2000~5)**
- Blood collection
- Genetic polymorphism
- Metabolism
- Detoxification
- Immune response
- Hormonal function

**Third version (2005~)**
- Non-cancer patients
- Cancer patients
- Hospital registry
- Regional cancer registry

### Data Management System for HERPACC Study

- New data file (B)
- Editing
- Combining
- Server of data management

### Basic data → Processed data for analysis

**Hospital registry** → **Regional cancer registry**

### Case-control study and Cohort study

- **Risk factor**
  - Cancer
  - Referent

- **Protection**

- **Factor**
  - Cases
  - Refs

- **Odds ratio (OR) = (a/c)/(b/d)**

  - Advantage: Studying multiple factors in short time
  - Disadvantage: Selection bias and confounding factors

- **Relative risk (RR) = P1/P0**

  - Advantage: Studying multiple outcomes and higher reliability of results
  - Disadvantage: Large number of study subjects, long-term follow-up, big budget

### Time trends in total sales of cigarettes and incidence/death rates of lung cancer

- **Incidence rate (Males)**
- **Incidence rate (Females)**
- **Death rate (Males)**
- **Death rate (Females)**

### Population attributable risk
Of habitual smoking for lung cancer

- Total AR = 51%

### Risk reduction of lung cancer after quitting smoking

- Male Smoking rate Male
- Female Smoking rate Female
- Years after quitting smoking
Carcinogenic steps of gastric cancer
(Host-specific and lifestyle factors)

Host factors
Immune reaction

Lifestyles
Carcinogens
Salt, Q-Y vegetables
Smoking, Drinking

Normal → Hp infection → Atrophic gastritis → Cancer

Ethnoepidemiologic Study on Cancer:
Study Subjects and Areas

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

<table>
<thead>
<tr>
<th></th>
<th>Hp(+) (%)</th>
<th>PG(+) (%)</th>
<th>NaCl (g/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>Hanoi, Viet Nam</td>
<td>74</td>
<td>69</td>
<td>10</td>
</tr>
<tr>
<td>HCMC, Viet Nam</td>
<td>83</td>
<td>72</td>
<td>14</td>
</tr>
<tr>
<td>KK, Thailand</td>
<td>88</td>
<td>88</td>
<td>11</td>
</tr>
<tr>
<td>Semarang, Indonesia</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Yogy., Indonesia</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Japan</td>
<td>62</td>
<td>57</td>
<td>23</td>
</tr>
</tbody>
</table>

* H. pylori (+) was examined by serum IgG in Japan and UBT in other countries.


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

Main reasons of recent decrease of stomach cancer in Japan:
1) Relative decrease of salt intake
2) More intake of fresh foods
3) Decrease of Hp infection rate

Habitual Smoking and Drinking for Stomach Cancer Risk

Combination of smoking/drinking
Odds Ratio
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

Risk of Large Intestinal Cancer In Seoul, Korea
Risk Reduction by Nutrients Intake

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

Concept of Ethnoepidemiology
Diversity & Universality of Diseases by Genetic & Cultural Background

Distribution of Total Energy Intake by Nutrient in Korea, Japan and China

Lifestyle and Colorectal Cancer in Nanjing, China

Risk of Large Intestinal Cancer
Average Intake

Nutrient | 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 | 0.9 | 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 | 1.1 | 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 polymorphism
- General lifestyle
- Biology
- Genetic susceptibility
- Molecular epidemiology
- Exposure level

Comprehensive risk for Cancer

Gene-environment Interaction
Different OR for environmental factors among different genotypes

Risk of Esophageal Cancer by Habitual Drinking
(>5 days/week, >45 ml/day)

- Alcohol
  - ADH2: Alcohol dehydrogenase 2
  - ALDH2: Aldehyde dehydrogenase 2
- Acetaldehyde
- Acetate

Risk of Esophageal Cancer by Habitual Drinking

Evidence-based related factors for cancer by site

Prevention Strategy for Main Sites of Cancer
Incidence Rate, Mortality Rate and Its Ratio in Japan (1999)

- Male
  - Stomach: 66,307 (2.06)
  - Colon: 30,267 (2.71)
  - Rectum: 17,394 (2.52)
  - Prostate: 14,005
- Female
  - Stomach: --
  - Colon: --
  - Rectum: --
  - Prostate: --
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

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

Secondary Prevention Strategy
Evaluation Studies of Cancer Mass Screening
in Japan and International Consensus

<table>
<thead>
<tr>
<th>Cancer</th>
<th>RCT</th>
<th>Case-control study</th>
<th>Non-RCT cohort study</th>
<th>International consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>on-going</td>
<td>effective</td>
<td>effective</td>
<td>? in Western countries effective in Asia</td>
</tr>
<tr>
<td>Colon</td>
<td>(-)</td>
<td>effective</td>
<td>suggestive</td>
<td>effective</td>
</tr>
<tr>
<td>Cervix</td>
<td>(-)</td>
<td>suggestive</td>
<td>effective</td>
<td>effective</td>
</tr>
<tr>
<td>Lung</td>
<td>(-)</td>
<td>suggestive</td>
<td>(-)</td>
<td>not effective</td>
</tr>
<tr>
<td>Breast</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>effective</td>
</tr>
</tbody>
</table>

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

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.