

# CANCER EPIDEMIOLOGY & CANCER RISK FACTOR

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# What this lecture about ?

- Learning more about cancer epidemiology
- Investigating risk factors implicated cancer development
- Learning about prevention and early detection of cancer

True or False?

Smoking causes lung cancer

True or False?

Large percentage of cancers are preventable

True or False?

Preventing cancer is easier than treating cancer

True or False?

Screening tests are available for most cancers

# Epidemiology

The study of distribution and determinants of disease in human population ; why different population or group – different risks , different disease

Patterns of incidence and death rates of malignant disease : sex,age,race,geography

# Cancer Epidemiology Historical Perspective

Tight corsets and cancer

**1842**

**Rigoni-Stern, Italian physician, observed that married women in the city were getting cervical cancer, but nuns in nearby convents weren't. He also observed that nuns had higher rates of breast cancer, and suggested that the nuns' corsets were too tight.**

# Concept epidemiology

- 1. Disease is not randomly distributed
- 2. Disease causation is multifactorial

# Application epidemiology

- Planning
- Evaluation of cancer control
- Primary prevention
- Early detection

Scope of cancer epidemiology: broad

→ concern **causes of cancer** →

**identification of population where risk**

**reduced → “prevention”**



# **Sources of epidemiologic data in oncology**

- 1. Cancer registries**
- 2. Death certificates**

# General approach

- *What*
- *Who*
- *Where*
- *When*

## **Descriptive epidemiology**

## **Analytic epidemiology**

- *Why*
- *How*

# Methods of Cancer Epidemiology

- **Descriptive Studies**
  - Incidence, mortality, survival
  - Time Trends
  - Geographic Patterns
  - Patterns by Age, Gender, SES, Ethnicity
- **Analytic Studies**
  - Case-control
  - Cohort

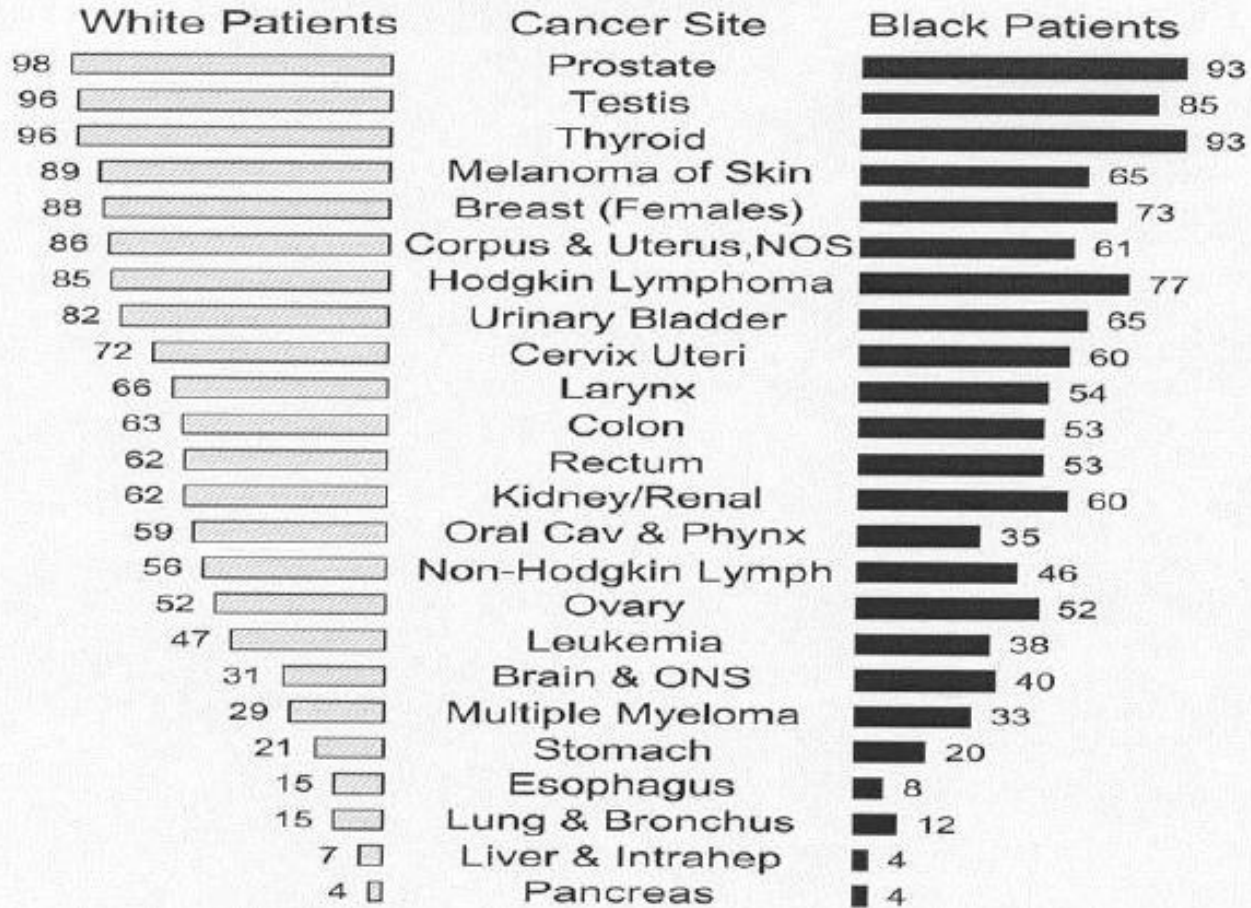
# Epidemiology ratios

- **Incidence** – number of new cases arising in a given period in a specified population\*
- **Prevalence** - number of persons in a defined population who have been diagnosed with that type of cancer, and who are still alive at a given point in time\*
- **Mortality** - number of deaths occurring in a given period in a specified population\*
- **Lethality** – mortality/incidence ratio

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\*per 100,000 persons

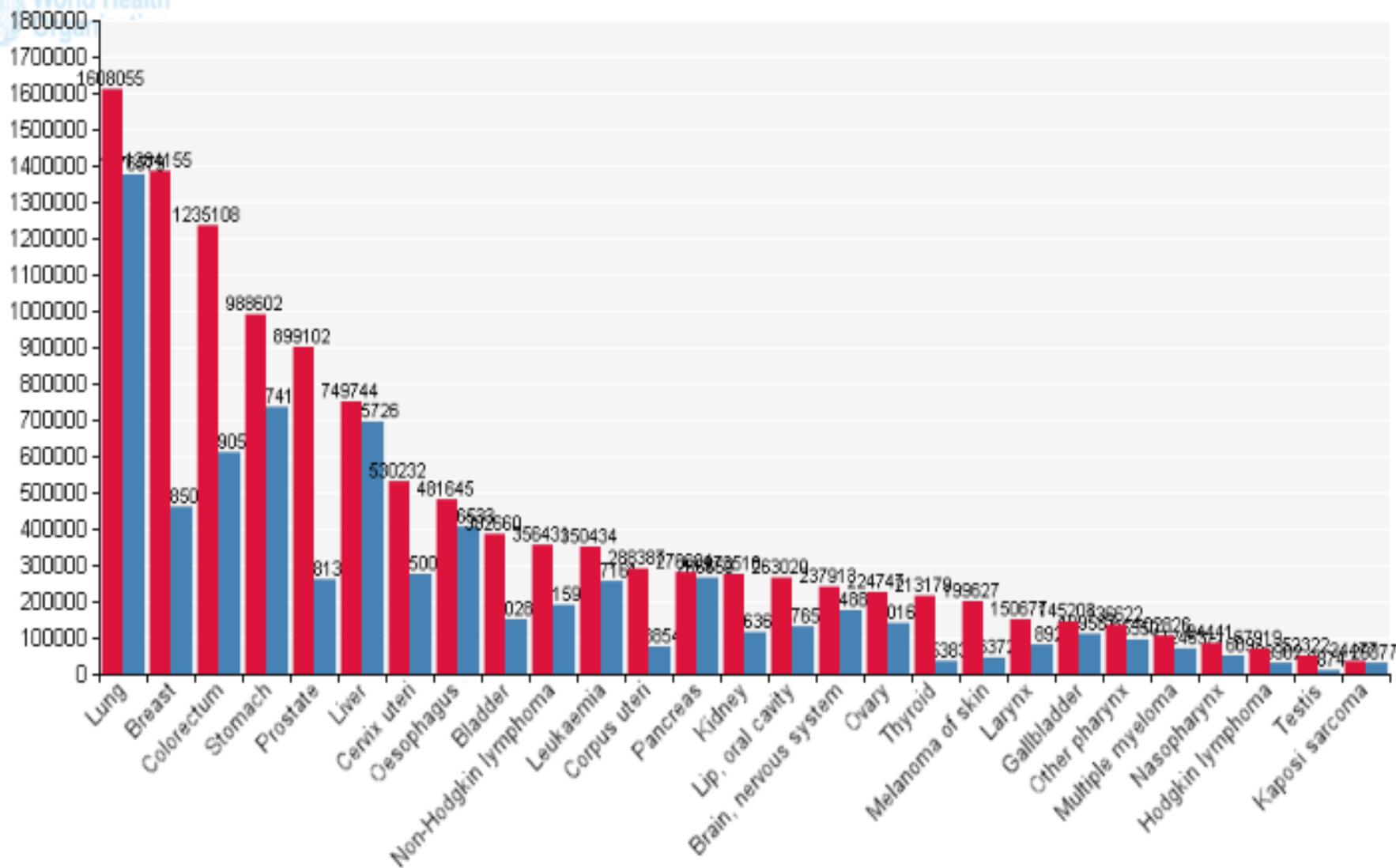
5-Year Relative Survival Rates  
SEER Program, 1992-1998  
Males and Females



Source: SEER 9 areas.



World Health



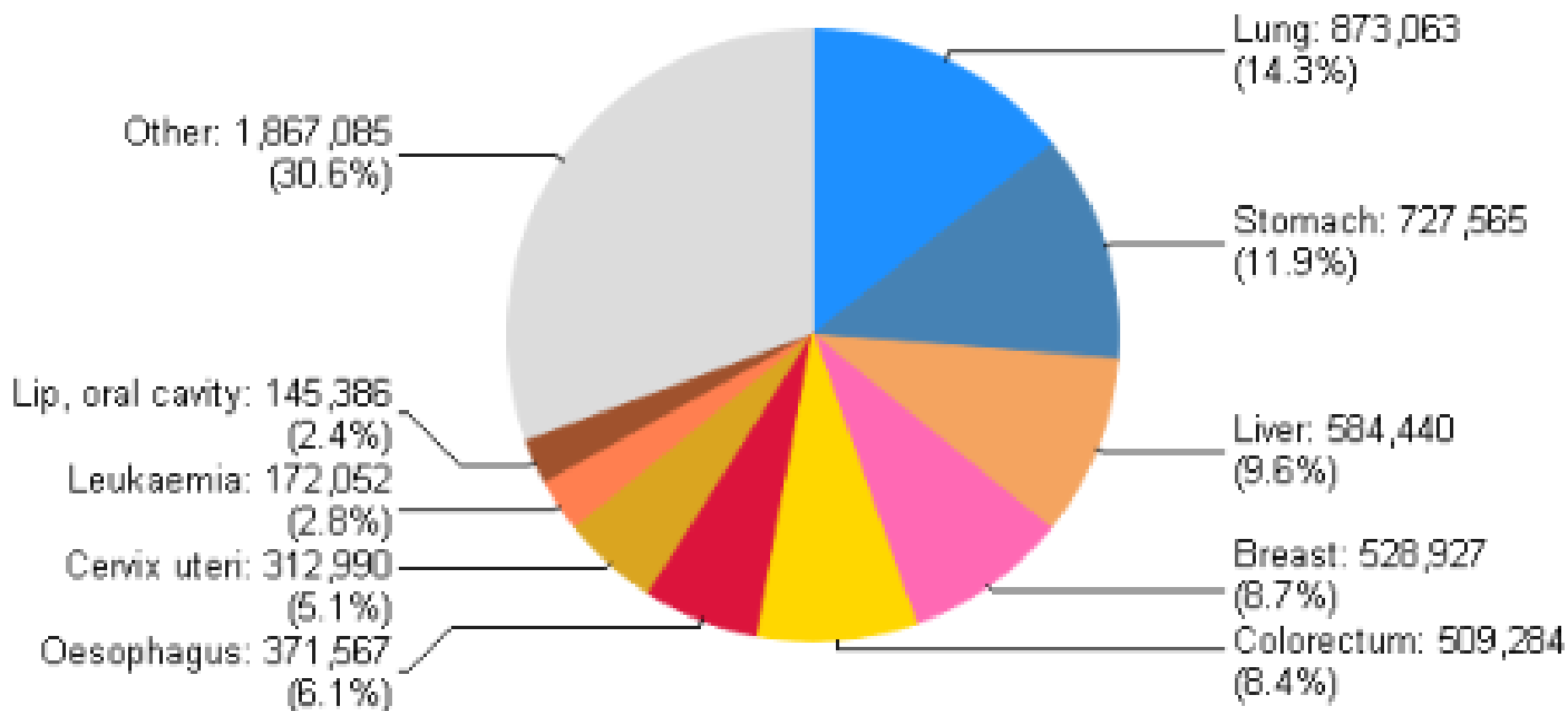
■ Incidence  
■ Mortality

### Asia: Both sexes



Estimated number of cancer cases, all ages (total: 6092,359)

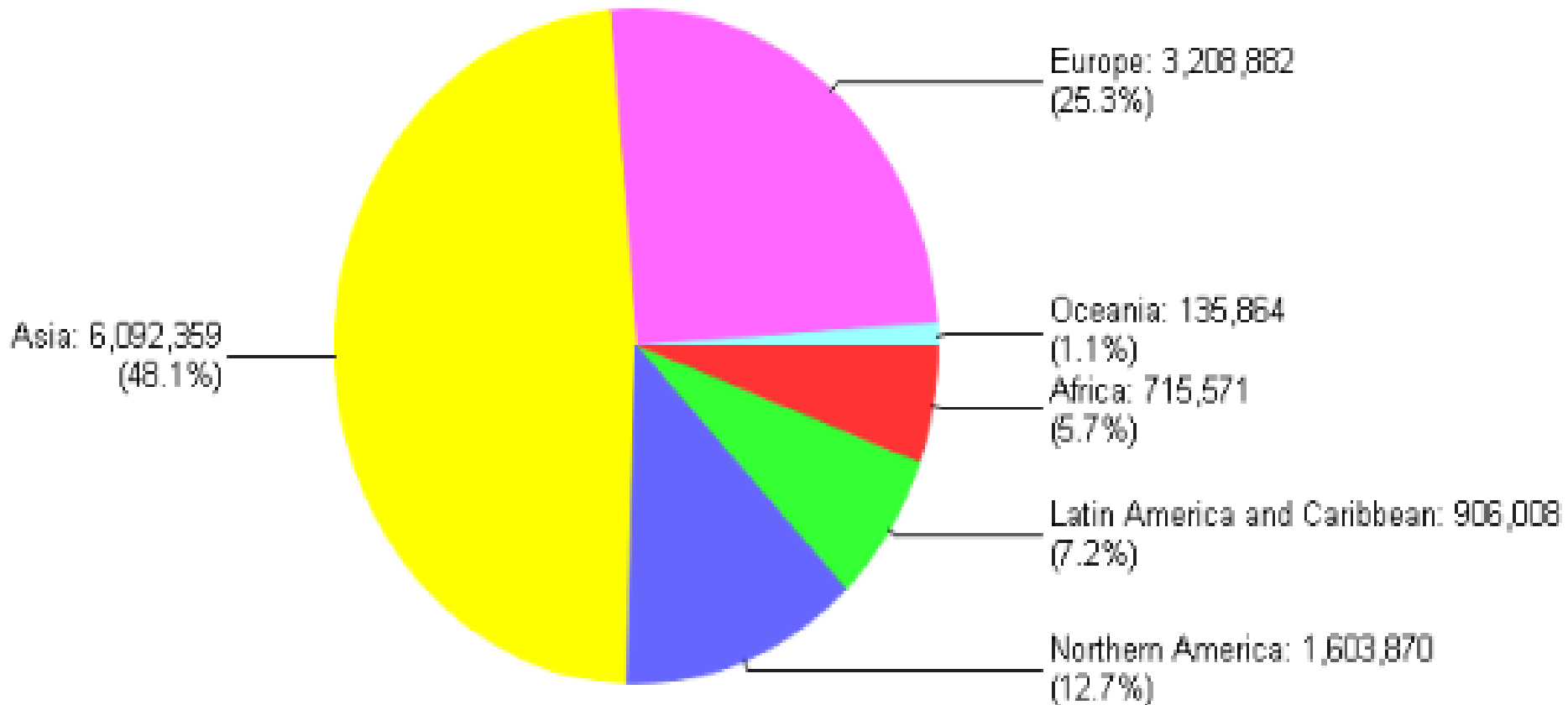
Organization





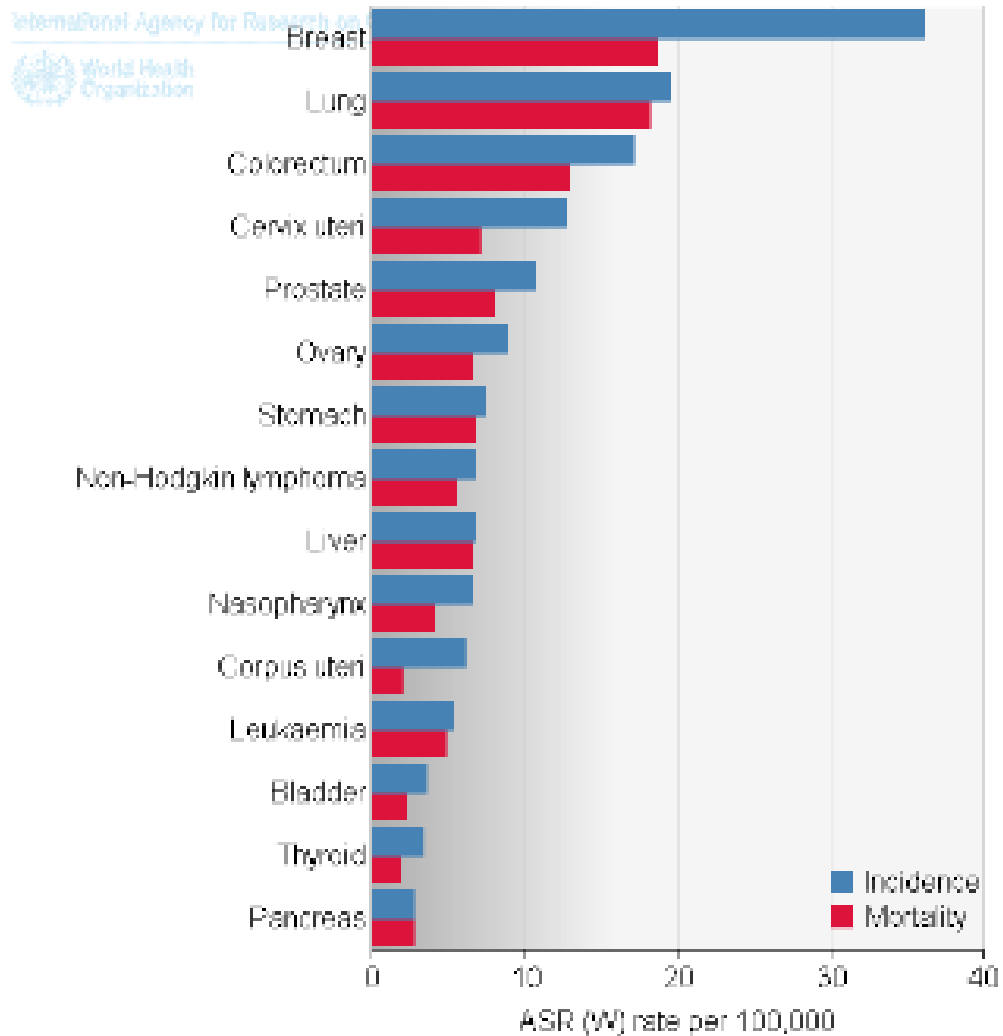
All cancers excl. non-melanoma skin cancer: both sexes  
Estimated number of cancer cases, all ages

Organization





## Estimated age-standardised incidence and mortality rates: both sexes



## Leading cancer types in Indonesia

- 1. Cervix cancer
- 2. Breast cancer
- 3. Colorectal cancer
- 4. Lung cancer
- 5. Nasopharyng cancer

( POI=Perhimpunan Onkologi Indonesia)

# Result of Cancer Treatment Analysis

## Defining Response to Cancer Treatment

Term	Definition
Cure	Permanent absence of symptoms or signs of a disease, although patients who appear to be cured may still have viable tumor cells that eventually cause relapse
Complete remission (complete response)	Disappearance of clinical evidence of disease
Partial response	> 50% reduction in size of tumor mass or masses, sometimes leading to significant palliation and prolongation of life, but with inevitable regrowth of the tumor
Stable disease	Neither improvement nor worsening
Disease-free survival (disease-free interval)	Interval between disappearance of the tumor and relapse
Duration of response	Time from response to time of overt progression
Survival time	Time from diagnosis to death

# Disease Free Survival / Interval

- The time that a person with a disease lives without known recurrence; DFS is major clinical parameter used to evaluate the efficacy of a particular therapy, which is usually measured in 'units' of 1 or 5 yrs

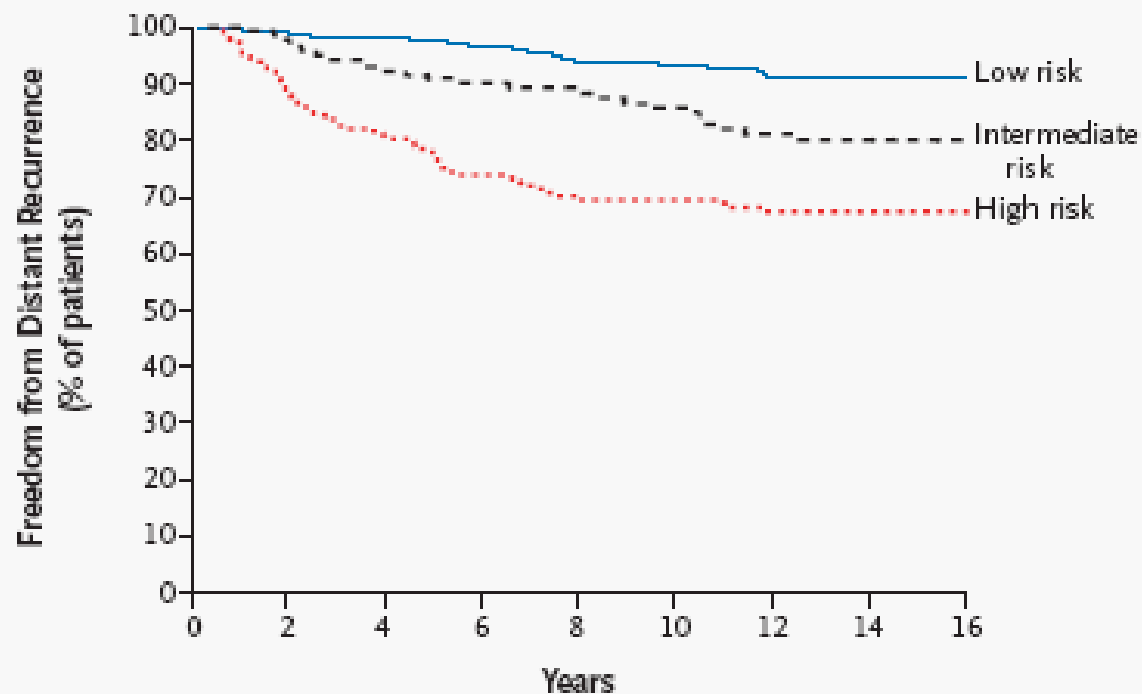
# Survival Analysis

- To describe the survival times of members of a group
  - Survival function
  - Hazard function
  - Kaplan-Meier curves
- To compare the survival times of two or more groups
  - Log-rank test

ORIGINAL ARTICLE

# A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer

Soonmyung Paik, M.D., Steven Shak, M.D., Gong Tang, Ph.D.,  
Chungyeul Kim, M.D., Joffre Baker, Ph.D., Maureen Cronin, Ph.D.,  
Frederick L. Baehner, M.D., Michael G. Walker, Ph.D., Drew Watson, Ph.D.,  
Taesung Park, Ph.D., William Hiller, H.T., Edwin R. Fisher, M.D.,  
D. Lawrence Wickerham, M.D., John Bryant, Ph.D.,  
and Norman Wolmark, M.D.



**No. at Risk**

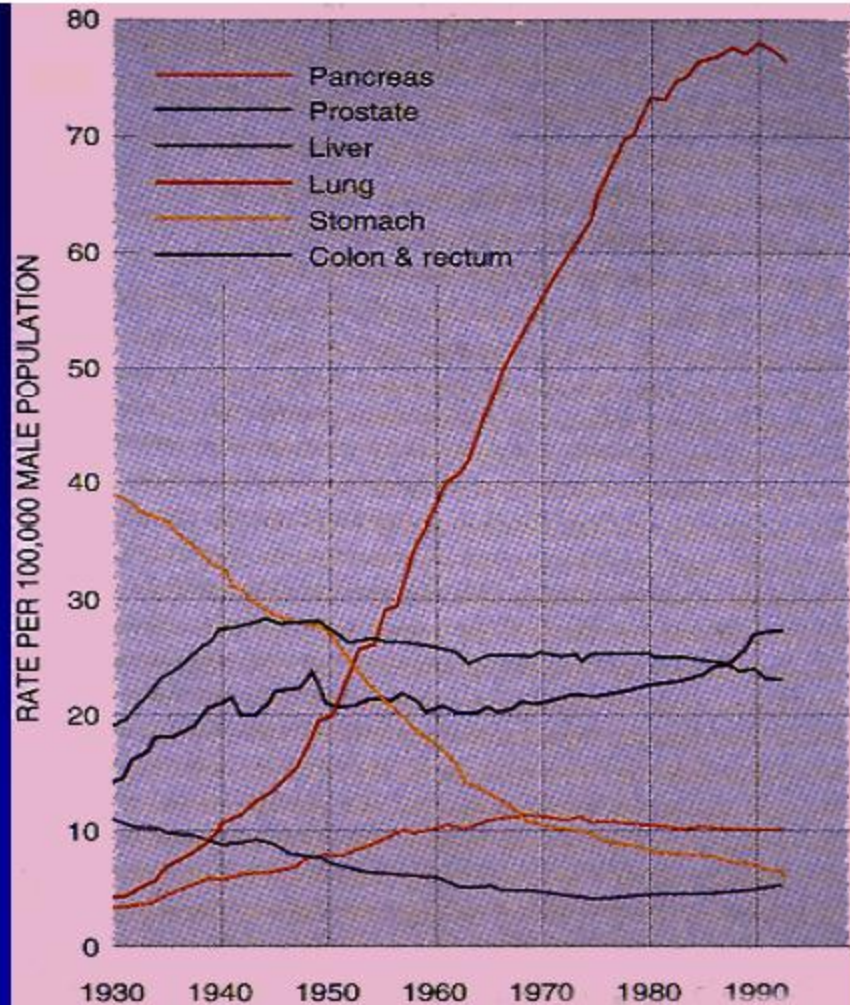
Low risk	338	328	313	298	276	258	231	170	38
Intermediate risk	149	139	128	116	104	96	80	66	16
High risk	181	154	137	119	105	91	83	63	13

**Figure 2. Likelihood of Distant Recurrence, According to Recurrence-Score Categories.**

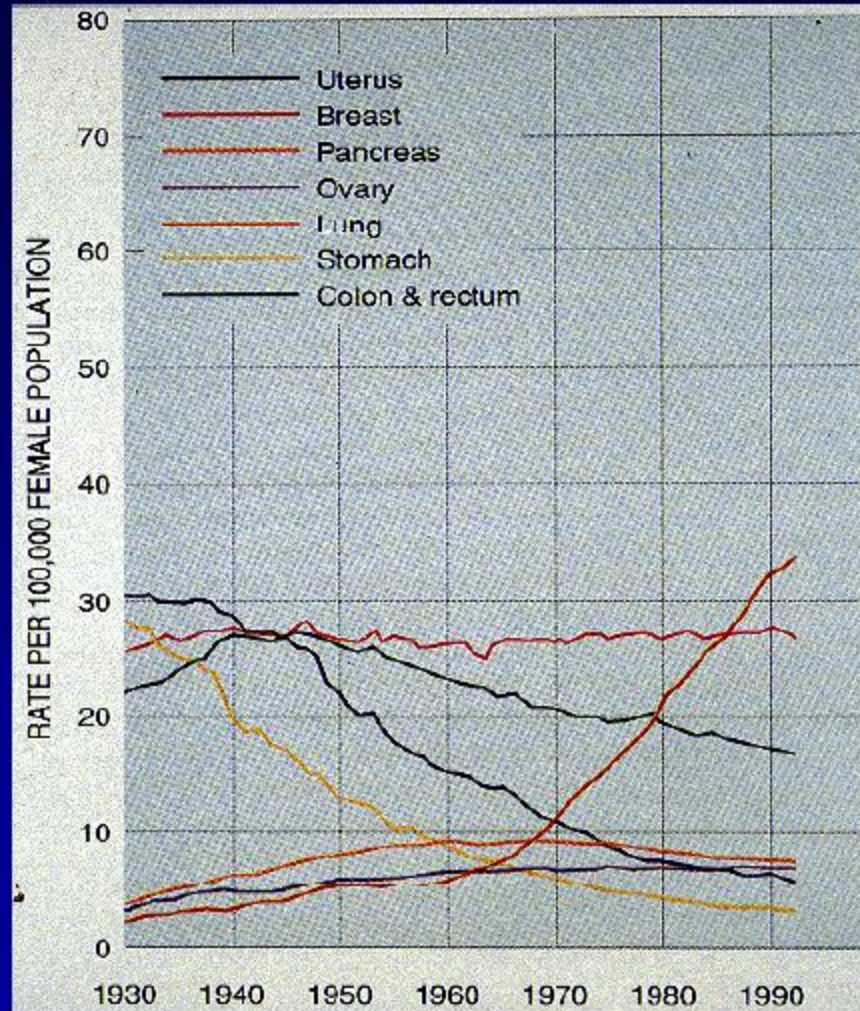
A low risk was defined as a recurrence score of less than 18, an intermediate risk as a score of 18 or higher but less than 31, and a high risk as a score of 31 or higher. There were 28 recurrences in the low-risk group, 25 in the intermediate-risk group, and 56 in the high-risk group. The difference among the groups is significant ( $P < 0.001$ ).



## Cancer mortality by tumor: males



## Cancer mortality by tumor: females



# Causes of increasing cancer mortality

- Ageing of populations
- Better diagnosis
- More reliable statistics
- Changes in life style and environmental factors

Etiology  
&  
Risk Factors

# Etiology

- Chemical carcinogens
- Environmental and industrial carcinogens
- Drug induced cancers
- Radiation carcinogenesis
- Viral and immunologic mechanisms

## Five Criteria for a Cause → Effect Relationship

Criteria	Risk Factor for Disease
1) Timing	◆ Exposure occurs before development of disease or during its progression
2) Strength	◆ Is dose-dependent ◆ Cessation of exposure can modify disease
3) Prevalence	◆ Occurs in multiple populations
4) Relationship to other risk factors	◆ Is independent ◆ Can also act synergistically
5) Plausibility	◆ Produces structural <sup>‡</sup> or functional changes which are events in mechanism of disease

<sup>‡</sup> anatomic or molecular

# **Cancer Epidemiology Historical Perspective**

- **Tobacco and Lung Cancer**
- **Asbestos and Lung Cancer**
- **Leather Industry and Nasal Cancer**
- **Dyes and Bladder Cancer**
- **Ionizing Radiation and Many Cancers**
- **DES and Vaginal Adenocarcinoma**
- **EBV and Burkitt's Lymphoma**
- **HPV and Cervical Cancer**

# RISK FACTORS

- HEREDITARY
- ENVIROMENTAL



# HEREDITARY

- MUTATION
  - BRCA 1 : breast cancer
  - BRCA 2 : ovarial cancer
  - HNPCC : colon cancer
  - etc

# Environmental Risk Factors

- **Tobacco**

- **Most important cause of cancer**

- Leading preventable cause of death

- Linked to cancer of the lung, lower urinary tract, upper aerodigestive tract, liver, kidney, pancreas, and cervix uteri

# Environmental Risk Factors

- **Ionizing radiation**

- Emission from x-rays, radioisotopes, and other radioactive sources
- Exposure causes cell death, gene mutation, and chromosome aberrations
- Accumulation of mutations → cancer
- Bystander effects - not directly radiated

# Environmental Risk Factors

- **Ultraviolet radiation**

- Causes basal cell carcinomas, squamous cell carcinomas, melanomas
- Principle source is sunlight (UVA, UVB)
- Specific gene mutations → inflammation (TNF alpha, free radicals) reduce immune surveillance

# Environmental Risk Factors

- Electromagnetic fields
  - Carcinogenic ?
    - Are they, or aren't they?
    - Living arround high voltage wire.
    - Cellular phone ?

## Environmental Risk Factors

- **Diet**

- Xenobiotics

- Toxic, mutagenic, and carcinogenic chemicals in food

- Examples

- Compounds produced in the cooking of fat meat or protein – polycyclic aromatic hydrocarbons
      - Industrial contaminants (diesel exhaust, pesticides in food & water)
      - Some prescribed in medicine

## Environmental Risk Factors

- **Obesity\***

– Body mass index =  $\frac{\text{Weight kg}}{\text{Height (cm)}^2}$

Underweight	< 18.5	
Normal	18.5 – 24.9	
Overweight	25 – 29.9	
Obese	30 – 34.9	I
	35 – 39.9	II
Extreme Obesity	> 40	III

also waist circumference

men                    40 inches

women                35 inches

\* **colon,breast,pancreas,uterine**

# Environmental Risk Factors

- **Obesity**

- Adipose tissue is active endocrine and metabolic tissue
- In response to endocrine and metabolic signaling, adipose tissue releases free fatty acids
  - Leads to insulin resistance → chronic hyperinsulinemia
  - Correlates with **colon, breast, pancreatic and endometrial(uterine) cancer**



# Environmental Risk Factors

- **Exogenous hormones**
  - Hormone replacement therapy
- **Endogenous hormones**
  - Adipose tissue metabolizes androgen precursors to estrogens (breast, uterine cancer)
  - Adipose cells ↑ circulating insulin levels and IGF-1 → ↓ liver synthesis SHBG leading to ↑ estradiol
  - High insulin levels → ↑ ovarian, possibly adrenal synthesis of androgens.
  - Diabetes Miletus

# Environmental Risk Factors

- **Alcohol**

- Risk factor for oral cavity, pharynx, hypopharynx, larynx, esophagus and liver cancer (**breast** – maybe 2007)
- **Cigarettes/alcohol combination ↑ risk**

# Environmental Risk Factors

- **Hepatitis B/C → hepatocellular cancer**
- **Sexual reproductive behavior**
  - Carcinogenic **human papilloma virus**
    - HPV-16 (60%), HPV-18 (10%), HPV-31/35 (5% each) – cervical cancer
  - Persistence – prerequisite for cancer
    - Most resolve with time

## Role of infection

### Epstein-Barr virus (EBV)

Underdeveloped country → rate infection in infancy, high the age of onset HD

-EBV is present in 40 – 60% of cases

-chronic viral infection → activation of cellular oncogenes, loss of tumour suppressor genes and deregulation of several cytin

# Environmental Risk Factors

- **Physical activity**
  - Reduces cancer risk
    - ↓ insulin and IGF-1
    - ↓ obesity
    - ↓ inflammatory mediators and free radicals
    - ↑ gut motility

# Environmental Risk Factors

- **Occupational hazards**
  - Substantial number of occupational carcinogenic agents
    - Asbestos
    - Dyes, rubber, paint, explosives, rubber cement, heavy metals, air pollutants, etc.

# Environmental Risk Factors

- **Air pollution**

- Inhales 20,000 L/day – potential for appreciable doses of pollutants
- Industrial – arsenicals, benzene, chloroform, formaldehyde, sulfuric acid, mustard gas, vinyl chloride and acrylonitriles
- Radon – radioactive gas, uranium decay – rocks and soil → “trapped in houses”

# Risk factors associated with the development of breast cancer

- **family history and genetic factors**
  - **previous history of breast cancer in one breast**
  - **fibrocystic disease (atypical hyperplasia)**
  - **ionizing radiation**
- 
- **age at menarche and menopause**
  - **age at first delivery, number of children**
  - **nulliparity**
  - **oral contraceptives and hormone replacement therapy**



# Risk factors associated with the development of breast cancer

## **Life-style related factors**

- **diet**
- **alcohol**
- **physical activity**

# Cancer prevention

**Primary** – reduction of exposure to carcinogenic factors

**Secondary** – early detection and treatment of precancerous lesions

# Cancer detection

- Clinically apparent disease
  - noticed by a patient
- Asymptomatic disease
  - detected at routine physical examination
  - detected by mass screening programs

# Cancer's 7 warning signals

1. Change in bowel or bladder habits
2. A sore that does not heal
3. Unusual bleeding or discharge
4. Thickening or lump in breast or elsewhere
5. Indigestion or difficulty in swallowing
6. Obvious change in wart or mole
7. Nagging cough or hoarseness

**If you have a warning signal ,see your doctor**

# Screening programmes

- Include populations without symptoms of a particular disease
- Aim at **decreasing mortality** caused by a particular disease, by means of its earlier detection
- Including large populations: **mass screening**

## Effective cancer screening methods

- Cervix                      Cervical cytology
- Breast                      Mammography
- Colon-rectum              Faecal occult blood