PRINCIPLES OF CANCER PREVENTION

İSMAİL ÇELİK, MD, MS
PROFESSOR OF MEDICAL ONCOLOGY
MASTER OF SCIENCE IN CANCER EPIDEMIOLOGY
**Terminology**

- **Incidence**: New cases per a period of time (e.g. per year) / population under risk
- **Prevalence**: Total number of cases at a specific point of time / population under risk
- **Pool model**:
  - **Incidence**: Filling rate of the pool
  - **Prevalence**: Total amount of water in the pool
- **Prevalence** = Old cases + new cases - recovered cases - deaths
- **Prevalence** = Incidence × duration of disease
**Terminology**

- **Incidence**: Diseases which recover rapidly like diarrhea and measles or diseases with high mortality like cancer.
- **Prevalence**: Shows disease burden, important in chronic diseases.
- Prevalence is much higher than incidence for HT and DM.
- Prevalence is close to incidence in lung cancer (median survival ~ 1 year).
Epidemiology

- 12 million new cancer cases every year (incidence)
- 7.6 million deaths (mortality)
- 25-30 million patients living with cancer (prevalence)
- 2nd most common cause of death in developed countries
- 1/3 of men and 1/4 of women in developed countries will be diagnosed with cancer
Most common types of cancer in men

1. Prostate
2. Lung
3. Colorectal
4. Bladder
5. NHL

1. Lung
2. Gastric
3. Bladder
4. Colorectal
5. Larynx
Most common types of cancer in women

1. Breast
2. Lung
3. Colorectal
4. Endometrium
5. Ovary

1. Breast
2. Colorectal
3. Gastric
4. Ovary
5. Lung
Primary prevention

Aim: To prevent cancer development

- Tobacco control
- Prevent obesity and low physical activity
- Diet rich in fruits-vegetables, low red meat intake
- Protection from sunlight
- Limit alcohol intake
- Vaccines: Hepatitis B, HPV
- Chemoprevention
Secondary prevention (Early diagnosis)

Aim: To diagnose cancer before signs and symptoms appear

- Screening tests for asymptomatic individuals
  - Breast cancer: Mammography
  - Cervical cancer: Pap smear
  - Colon cancer: Colonoscopy
  - Prostate cancer: PSA (prostate specific antigen)
  - Malign melanoma: Skin examination
Tertiary prevention

**Aim: Improve survival and quality of life**

- Control of side-effects
- Psycho-social support
- Less invasive procedures with low morbidity
Natural course of cancer development

<table>
<thead>
<tr>
<th>Primary Prevention</th>
<th>Secondary Prevention</th>
<th>Tertiary prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biologic starting point</td>
<td>Early diagnosis</td>
<td>Signs &amp; symptoms</td>
</tr>
<tr>
<td>Outcome</td>
<td>Treatment</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Healthy</th>
<th>No signs</th>
<th>Signs present</th>
</tr>
</thead>
</table>
Primary prevention (Prevent development)

- Smoking
- BRCA-1
- NSAID
Alcohol: 4-6%
Others: 10-15%
Tobacco: 25-30%
Obesity: 10-20%
Infections: 15-20%
Diet: 30-35%
CAUSES OF CANCER

1. Tobacco
2. Diet
3. Obesity
4. Physical activity
5. Alcohol
6. Infections
7. Sun light
TOBACCO

- Butane Lighter Fluid
- Cadmium Batteries
- Stearic Acid Candle Wax
- Hexamine Barbecue Lighter
- Toluene Industrial Solvent
- Nicotine Insecticide
- Ammonia Toilet Cleaner
- Acetic Acid Vinegar
- Methane Sewer Gas
- Arsenic Poison
- Carbon Monoxide
- Methanol Rocket Fuel
Female Smoking

"Smoking behaviour of women differs from that of men. More likely motivated to smoke, they find it harder to stop smoking. Women are more neurasthenic than men. There may be a case for launching a female-oriented cigarette with relatively high deliveries of nicotine."

1976 research report, British American Tobacco

Smoking trends percentage of female smokers 1960-2000 selected countries

Japan: 1960: 1.4%, 1980: 2.5%, 2000: 4.2%
UK: 1960: 2.0%, 1980: 2.5%, 2000: 3.7%
USA: 1960: 2.0%, 1980: 2.5%, 2000: 3.7%
I. BASIC CONSTITUENTS
   1) Meat and meat products
   2) Fats, oils
   3) Cereals
   4) Sugar and salt
   5) Vegetable, fruits

II. WATER

III. ALCOHOL

IV. SUPPLEMENTS

V. FOOD PRODUCTION, PRESERVATION, PROCESSING, AND PREPARATION
WCRF/AICR Expert Report
Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective

- Expert Group (n ~ 5000)
  - Expert Panel
  - Investigators
  - Peer Reviewers
  - Observers
  - Executive Team
  - Secretariat

- 500,000 article
- 10 years
- 517 pages

http://www.dietandcancerreport.org/
In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td>Exposure</td>
</tr>
<tr>
<td>Cancer site</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Convincing</td>
<td>Red meat $^1$</td>
</tr>
<tr>
<td></td>
<td>Processed meat $^2$</td>
</tr>
<tr>
<td></td>
<td>Colorectum</td>
</tr>
<tr>
<td></td>
<td>Colorectum</td>
</tr>
<tr>
<td>Probable</td>
<td>Cantonese-style salted fish $^3$</td>
</tr>
<tr>
<td></td>
<td>Nasopharynx</td>
</tr>
</tbody>
</table>
FATS, OILS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Convincing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited —</td>
<td></td>
<td></td>
</tr>
<tr>
<td>suggestive</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CEREALS (GRAINS), STARCHY ROOTS AND TUBERS, PLANTAINS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure</td>
<td>Exposure</td>
</tr>
<tr>
<td>Convincing</td>
<td>Cancer site</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Probable</td>
<td>Foods containing</td>
<td>Aflatoxins¹</td>
</tr>
<tr>
<td></td>
<td>dietary fibre²</td>
<td>Liver</td>
</tr>
<tr>
<td></td>
<td>Colorectum</td>
<td></td>
</tr>
</tbody>
</table>
### SUGARS AND SALT, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Convincing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited—suggestive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
VEGETABLES, FRUITS, PULSES (LEGUMES), NUTS, SEEDS, HERBS, SPICES, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th></th>
<th>INCREASES RISK</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure</td>
<td>Cancer site</td>
<td>Exposure</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Convincing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-starchy vegetables</td>
<td></td>
<td></td>
<td>Mouth, pharynx, larynx</td>
<td></td>
</tr>
<tr>
<td>Allium vegetables</td>
<td></td>
<td></td>
<td>Stomach</td>
<td></td>
</tr>
<tr>
<td>Garlic</td>
<td></td>
<td></td>
<td>Stomach</td>
<td></td>
</tr>
<tr>
<td>Fruits</td>
<td></td>
<td></td>
<td>Colorectum</td>
<td></td>
</tr>
<tr>
<td>Foods containing folate</td>
<td></td>
<td></td>
<td>Mouth, pharynx, larynx</td>
<td>Lung</td>
</tr>
<tr>
<td>Foods containing</td>
<td></td>
<td></td>
<td>Oesophagus</td>
<td>Stomach</td>
</tr>
<tr>
<td>carotenoids</td>
<td></td>
<td></td>
<td>Lung</td>
<td>Stomach</td>
</tr>
<tr>
<td>Foods containing beta-carotene</td>
<td></td>
<td></td>
<td>Pancreas</td>
<td></td>
</tr>
</tbody>
</table>
## WATER, FRUIT JUICES, SOFT DRINKS, HOT DRINKS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th></th>
<th>INCREASES RISK</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure</td>
<td>Cancer site</td>
<td>Exposure</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Convincing</td>
<td></td>
<td></td>
<td>Arsenic in drinking water&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Lung</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td>Arsenic in drinking water&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Skin</td>
</tr>
</tbody>
</table>
Arsenic in drinking water and lung cancer: A systematic review

Ismail Celik\textsuperscript{a}, Lisa Gallicchio\textsuperscript{b,c}, Kristina Boyd\textsuperscript{c}, Tram K. Lam\textsuperscript{c}, Genevieve Matanoski\textsuperscript{c}, Xuguang Tao\textsuperscript{c,g}, Meredith Shiels\textsuperscript{c}, Edward Hammond\textsuperscript{c}, Liwei Chen\textsuperscript{d}, Karen A. Robinson\textsuperscript{e}, Laura E. Caulfield\textsuperscript{d}, James G. Herman\textsuperscript{f}, Eliseo Guallar\textsuperscript{c}, Anthony J. Alberg\textsuperscript{c,h,*}

\textsuperscript{a} Department of Medical Oncology, Hacettepe University Institute of Oncology, Ankara, Turkey
\textsuperscript{b} The Prevention and Research Center, Mercy Medical Center, USA
\textsuperscript{c} Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health, USA
\textsuperscript{d} Department of International Health, Center for Human Nutrition, Johns Hopkins University Bloomberg School of Public Health, USA
\textsuperscript{e} Department of General Internal Medicine, Johns Hopkins University School of Medicine, USA
\textsuperscript{f} Department of Oncology, Johns Hopkins University School of Medicine, USA
\textsuperscript{g} Department of Occupational and Environmental Medicine, Johns Hopkins University School of Medicine, USA
\textsuperscript{h} Cancer Prevention and Control Program, Hollings Cancer Center, and Department of Biostatistics, Biostatistics and Epidemiology, The Medical University of South Carolina, USA
Arsenic in drinking water and lung cancer has been described in areas with deep artesian wells contaminated with high levels of arsenic. The association was first observed in southwestern Taiwan, and later described in USA, Belgium, and particular regions of South America.
ALCOHOLIC DRINKS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Conving</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DIETARY CONSTITUENTS AND SUPPLEMENTS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exposure</td>
<td>Cancer site</td>
</tr>
<tr>
<td>Convincing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Beta-carotene supplements may increase the risk of lung cancer.
**DIETARY CONSTITUENTS, SUPPLEMENTS**

### DIETARY CONSTITUENTS AND SUPPLEMENTS, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure</strong></td>
<td>Cancer site</td>
<td></td>
</tr>
<tr>
<td><strong>Beta-carotene supplements</strong>[^1]</td>
<td>Lung</td>
<td></td>
</tr>
</tbody>
</table>

---

### VEGETABLES[^1], FRUITS[^1], PULSES (LEGUMES), NUTS, SEEDS, HERBS, SPICES, AND THE RISK OF CANCER

In the judgement of the Panel, the factors listed below modify the risk of cancer. Judgements are graded according to the strength of the evidence.

<table>
<thead>
<tr>
<th></th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure</strong></td>
<td>Cancer site</td>
<td></td>
</tr>
<tr>
<td><strong>Foods containing beta-carotene[^2]</strong></td>
<td>Oesophagus</td>
<td></td>
</tr>
</tbody>
</table>

[^1]: Refers to specific types of vegetables, fruits, pulses, nuts, seeds, herbs, and spices that may influence cancer risk.
[^2]: Refers to foods high in beta-carotene content, which may affect cancer risk.

[^1]: A dash or placeholder for various types of vegetables, fruits, pulses, nuts, seeds, herbs, and spices.
[^2]: A dash or placeholder for foods containing beta-carotene.
Paracelsus = “Sola dosis facit venenum”
Only dose makes the poison!

Dietary folate intake and colorectal cancer: cohort studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giovannucci 1998 Women</td>
<td>0.94 (0.76-1.15)</td>
</tr>
<tr>
<td>Su 2001 Women</td>
<td>0.89 (0.72-1.19)</td>
</tr>
<tr>
<td>Su 2001 Men</td>
<td>0.89 (0.82-1.00)</td>
</tr>
<tr>
<td>Norlings 2002 Men</td>
<td>0.91 (0.84-0.99)</td>
</tr>
<tr>
<td>Norlings 2002 Women</td>
<td>0.90 (0.83-0.98)</td>
</tr>
<tr>
<td>Larson 2002 Women</td>
<td>0.87 (0.69-1.08)</td>
</tr>
<tr>
<td>Summary estimate</td>
<td>0.94 (0.79-1.13)</td>
</tr>
</tbody>
</table>

Relative risk, per 100 μg/day

Too much folate: a risk factor for cancer and cardiovascular disease?
Julia Bauer, Joel B. Mason and Sang-Wook Choi

Purpose of review
The intent of this evidence-based review is to analyze the role of folate in chronic diseases, focusing on cancer and cardiovascular disease.

Recent findings
Low-folate status has been shown to be a risk factor for cancer and cardiovascular disease. Although epidemiological data suggest an inverse association between folate status and disease risk, intervention studies give equivocal results, suggesting the response to folate intake does not follow a linear continuum. Moreover, recent folate intervention trials raise concern about possible adverse effects of folate supplementation and suggest that too much folate in inappropriate settings may be potentially harmful in individuals at higher risk for cardiovascular disease and cancer.

Summary
Although folate intake at sufficient levels appears to be an effective cancer chemopreventive strategy, high-dose supplementation of folate has generally not been effective in reducing recurrence of cardiovascular events or colorectal adenomas in clinical intervention trials. Although controversial, high folate status achieved through folate fortification or supplementation may increase the risk of certain chronic diseases among certain individuals, possibly by interfering with the homeostasis of one-carbon metabolism. Further research is urgently needed to accurately define the relationship between supraphysiological intake of folate and chronic diseases.
Production, Preservation, Processing, and Preparation

1. **Production:** Pesticides, Bioengineered foods, Organic foods

2. **Preservation:** Drying, Fermenting, Canning, Pasteurisation, Chemical preservation (benzoates, nitrites and sulphites)

3. **Processing:** Additives (colours, flavours, solvents), Packaging materials

4. **Preparation:** Steaming-boiling, Baking-roasting, Microwaving, Frying-grilling-barbecuing (charbroiling)
Pesticides

- Pesticides and herbicides are only toxic when used improperly in industrial, agricultural, or other occupational settings.
- At present there is no evidence that residues of pesticides and herbicides at the low doses found in foods increase the risk of cancer, but fruits and vegetables should be washed thoroughly before eating.
Bioengineered foods and Organic foods

- There is no evidence at this time that the substances found in bioengineered foods are harmful or that they would either increase or decrease cancer risk because of the added genes.

- At this time, no research exists to demonstrate whether such organic foods are more effective in reducing cancer risk than those produced by other farming methods.
Nitrosamines

- **Nitrate** occurs naturally in plants.
- Nitrate in diets is converted by the body into **nitrite** but also used commercially to preserve processed meats.
- Nitrite can react with the degradation products of amino acids to form N-nitroso compounds (**nitrosamines** or **nitrosamides**) known as human or animal carcinogens particularly in the stomach.
Food additives

Additives are usually present in very small quantities in food, and no convincing evidence has shown that any additive at these levels causes human cancers.
Polycyclic aromatic hydrocarbons (PAH)

- PAHs are formed when meat and meat products are burnt incompletely.
- Grilling and barbecuing also result in fat dropping on hot fire which makes PAHs that stick to the surface of food.
| Foods containing dietary fibre | Allotaxes | Non-starchy vegetables¹ | Allium vegetables | Garlic | Fruits² | Foods containing folate | Foods containing lycopene | Fruits containing coloxam³ | Red meat | Processed meat | Cantonese-style salted fish | High in calcium⁴ | Energy-dense foods⁵ | Low energy-dense foods | Salt, salted and salty foods | Arsenic in drinking water | Mate | Sugary drinks | Alcoholic drinks⁶ | Beta-carotene⁷ | Physical activity | Sedentary living⁸ | Body fatness | Abdominal fatness | Adult weight gain | Adult attained height | Greater birth weight | Lactation | Breastfeeding

| Mouth, pharynx, larynx | Esophageal | Lung | Stomach | Pancreas | Gastric | Liver | Colon, rectum | Breast, prostate, breast, pancreatic, lung | Ovary | Endometrium | Prostate | Kidney | Skin | Weight gain, overweight and obesity

**KEY**
- Convincing decreased risk
- Probable decreased risk
- Probable increased risk
- Convincing increased risk

¹ Includes evidence on foods containing carotenoids for mouth, pharynx, larynx, esophagus, foods containing vitamin C for esophagus
² Includes evidence on foods containing carotenoids for mouth, pharynx, larynx and lung, foods containing beta-carotene for esophagus, foods containing vitamin C for esophagus
³ Includes evidence from supplements for prostate
⁴ Evidence is from trials and studies using supplements for colorectal
⁵ Includes 'fast foods'
⁶ Convincing harm for man and probable harm for women for colorectum
⁷ The evidence is derived from studies using supplements for lung
⁸ Includes evidence on television viewing
⁹ Judgement for physical activity applies to colon and rectum
ACS NUTRITION GUIDELINES FOR CANCER PREVENTION

1. Eat 5 or more servings of vegetables and fruits each day.
   - Include vegetables and fruits at every meal and for snacks.
   - Eat a variety of vegetables and fruits each day.
   - Limit French fries, snack chips, and other fried vegetable products.
   - Choose 100% juice if you drink vegetable or fruit juices.

2. Choose whole grains over processed (refined) grains and sugars.
   - Choose whole grain rice, bread, pasta, and cereals.
   - Limit intake of refined carbohydrates (starches), such as pastries, sweetened cereals, and other high-sugar foods.

3. Limit intake of processed meats and red meats.
   - Choose fish, poultry, or beans instead of beef, pork, and lamb.
   - When you eat meat, choose lean cuts and eat smaller portions.
   - Prepare meat by baking, broiling, or poaching, rather than by frying or charbroiling.

4. If you drink alcohol, limit your intake.
1. Maintain a healthy weight throughout life.
   - Balance calorie intake with physical activity.
   - Avoid excessive weight gain throughout life.
   - Achieve and maintain a healthy weight if currently overweight or obese.

2. Adopt a physically active lifestyle.
   - Engage in at least 30 minutes of moderate to vigorous physical activity, above usual activities, on 5 or more days of the week; 45 to 60 minutes of intentional physical activity are preferable.
Secondary prevention (Early diagnosis)

- Screening
- Early diagnosis
- Treatment
- Cure
# Screening vs. Diagnosis

<table>
<thead>
<tr>
<th>Screening</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applied to asymptomatic groups</td>
<td>Applied to symptomatic individuals</td>
</tr>
<tr>
<td>Lower cost per test</td>
<td>Higher cost; all necessary tests applied to identify disease</td>
</tr>
<tr>
<td>Lower yield per test</td>
<td>Higher probability of case detection</td>
</tr>
<tr>
<td>Lower adverse consequences of error</td>
<td>Failure to identify true positive scan delay treatment, worsen prognosis</td>
</tr>
</tbody>
</table>
Cancers Suitable for Screening

1. High prevalence
2. Long asymptomatic phase
3. Target precursor lesion
4. Effective treatment modalities for the precursor lesions
5. Effective screening tools
Screening

n **Population based screening**
  q Low risk subjects are included
  q Should be cheap, rational and reliable

n **High risk individual screening**
  q High risk individuals are included
  q Usually relatives of patients
  q Should be reliable and not too expensive
Why early diagnosis does not always improve survival?

- Screening tests can identify cancers with a slow course and low mortality but can miss rapidly progressive cancers (length bias).
- Even if the cancer is diagnosed early, you can not improve the disease if you do not have an effective treatment (lead-time bias).
- Slowly progressing cancers diagnosed in the elderly may not change patient survival. The patient may die from other causes (overdiagnosis bias).
Length Bias

Rapidly progressive disease
(6 cases)

Slowly progressive disease
(6 cases)

\[ o = \text{Beginning of disease} \]
\[ Dx = \text{Diagnosis at the symptomatic stage} \]
Lead-time Bias

Screening group

Diagnosis

Death

Survival

Time

Control group

Symptoms

Diagnosis

Death

Survival

Lead Time
Sample case: Lead-time bias

**Scenario 1:**
- The patient presents with hemoptysis on Feb 2009.
- Diagnosed with lung cancer and treatment starts on Feb 2009.
- The patient dies on Feb 2010.
- Survival = 12 months

**Scenario 2:**
- The patient is on a screening program.
- Lung CT on Oct 2008 reveals a mass and lymphadenopathies.
- The patient dies on Feb 2010.
- Survival = 16 months

**RESULT**
Screening prolongs survival. But the patient dies on Feb 2010 anyway. => ????
Lead-time Bias

- To test the efficacy of a screening test, you have to demonstrate the decrease in mortality, to overcome lead-time bias.
- Survival alone does not show that a screening test is useful.
Overdiagnosis Bias

- The disease specific survival of patients identified with a screening test seems prolonged. This is because patients with a clinically insignificant disease are also identified.

- Clinically insignificant disease does not progress or progresses so slowly that meantime the patient dies because of another reason.
Overdiagnosis Bias

![Diagram of overdiagnosis bias showing the timeline of screening group and control group. The screening group goes through diagnosis before natural death, while the control group shows symptoms before natural death.](image-url)
Possible risks of screening

- False negatives: False confidence
- False positives
- “Early diagnosis” / “Labelling”
- Screening test positive, subsequent tests negative
- Cost and risks of diagnostic procedures
- Cost and risks of treatment
Breast Cancer
Breast cancer

- **Prevention**
  - Careful use of hormone drugs
  - Prevent obesity
  - Limited alcohol use
  - Special follow up for high risk women

- **Early diagnosis**
  - Self breast exam
  - Clinical breast exam
  - Mammography
In mammography, each breast is compressed horizontally, then obliquely and an x-ray is taken of each position.
Breast self-examination (BSE)

Step 1: Begin by looking at your breasts in the mirror with your shoulders straight and your arms on your hips.

You should look for:
- size, shape, and color of the breasts
- any visible distortion or swelling

If you see any of the following changes, bring them to your doctor's attention:
- dimpling, puckering, or bulging of the skin
- a nipple that has changed position or an inverted nipple (pushed inward instead of sticking out)
- redness, soreness, rash, or swelling
Breast self-examination (BSE)

- **Step 2:** Now, raise your arms and look for the same changes.
- **Step 3:** While you're at the mirror, gently squeeze each nipple between your finger and thumb and check for nipple discharge (this could be a milky or yellow fluid or blood).
Breast self-examination (BSE)

Step 4: Next, feel your breasts while lying down, using your right hand to feel your left breast and then your left hand to feel your right breast.

Follow a pattern to be sure that you cover the whole breast. You can begin at the nipple, moving in larger and larger circles until you reach the outer edge of the breast.

Begin examining each area with a very soft touch, and then increase pressure so that you can feel the deeper tissue, down to your ribcage.
Breast self-examination (BSE)

Step 5: Finally, feel your breasts while you are standing or sitting. Many women find that the easiest way to examine themselves in the shower. Cover your entire breast, using the same hand movements described in Step 4.
Screening recommendations

- Age 20-40: Monthly self breast exam; clinical breast exam every 3 years
- Age 40-50: Monthly self breast exam; annual clinical breast exam, mammography every 1-2 years
- Age >50: Monthly self breast exam; annual clinical breast exam and mammography
Cervical Cancer
Cervical cancer

**Prevention**
- Safe sex, monogamy, condom
- Stop smoking
- Avoid long term OC use
- HPV vaccine

**Early diagnosis**
- Gynecologic exam
- Pap smear
Screening recommendations

- Start Pap test 3 years after first coitus
- Women with 3 consecutive negative tests after 30 years of age may have the test every 2-3 years
- HPV DNA test and liquid based tests are more sensitive
Malignant Melanoma
Melanoma signs

**ABCDE:**

1. Asymmetry (A)
2. Border (B) irregularity
3. Color (C) variation (heterogenous colorisation)
4. Diameter (D) change
5. Elevation (E) from skin

These signs may be present or absent at diagnosis, or they may also be present in other skin diseases.
Malignant melanoma
Malignant melanoma

**Prevention**
- Protection from sunlight (Avoid sunlight particularly at the midday, wear hats, sunscreens with UVB and >40 PF, etc.)
- Avoid solariums

**Early diagnosis**
- Self skin exam
- Clinical exam for suspicious lesions
Skin Self-Examination

- Examine your face, especially the nose, lips, mouth, and ears—front and back. Use one or both mirrors to get a clear view.

- Thoroughly inspect your scalp, using a blow-dryer and mirror to expose each section to view. Get a friend or family member to help, if you can.

- Check your hands carefully: palms and backs, between the fingers and under the fingernails. Continue up the wrists to examine both front and back of your forearms.

- Standing in front of the full-length mirror, begin at the elbows and scan all sides of your upper arms. Don't forget the underarms.
Skin Self-Examination

- Next focus on the neck, chest, and torso. Women should lift breasts to view the underside.

- With your back to the full-length mirror, use the hand mirror to inspect the back of your neck, shoulders, upper back, and any part of the back of your upper arms you could not view in step 4.

- Still using both mirrors, scan your lower back, buttocks, and backs of both legs.

- Sit down; prop each leg in turn on the other stool or chair. Check front and sides of both legs, thigh, ankles, tops of feet, between toes and under toenails. Examine soles of feet and heels.
Prostate Cancer
The most widely used technique for detection of prostate cancer is the digital rectal examination (DRE). DRE exhibits wide ranges in sensitivity (33% to 69%) and specificity (49% to 97%). The serum PSA assay allows for earlier detection of many prostate cancers. However, normal PSA values are found in approximately 1/3 of localized cancers (false negative), and PSA levels are often elevated in men with noncancerous conditions such as benign prostatic hyperplasia (false positive). Impact on mortality???
Screening recommendations

- DRE yearly starting at age 40
- PSA yearly starting at age 50
Colon Cancer
Colon cancer

**Prevention**
- Prevention of obesity
- Diet rich in fiber-vegetable, lower ingestion of red meat and fat
- Regular exercise
- NSAIDs?

**Early diagnosis**
- Fecal occult blood testing
- Rectosigmoidoscopy / colonoscopy
- Digital rectal exam
Individuals aged >50 should follow one of the following screening methods:
- Annual FOB testing and
- Flexible sigmoidoscopy every 5 years
  or
- Colonoscopy every 10 years
Lung Cancer
Lung cancer

- **Prevention**
  - Stop smoking and all other tobacco products

- **Early diagnosis**
  - Screening with chest X-ray, sputum cytology and CT have been unsuccessful
  - No reliable early diagnostic tool
Take home!
What you should do!

- Ingest fruits and vegetables
- Prefer whole grain cereals with fiber
- Low red meat and fat intake
- Safe sex, monogamy, condom
- Regular exercise
- Follow screening recommendations
What you should not do!

- Tobacco products
- Passive smoking
- Sunbathing/Solarium
- Obesity
- Alcohol
The best treatment for cancer is prevention!