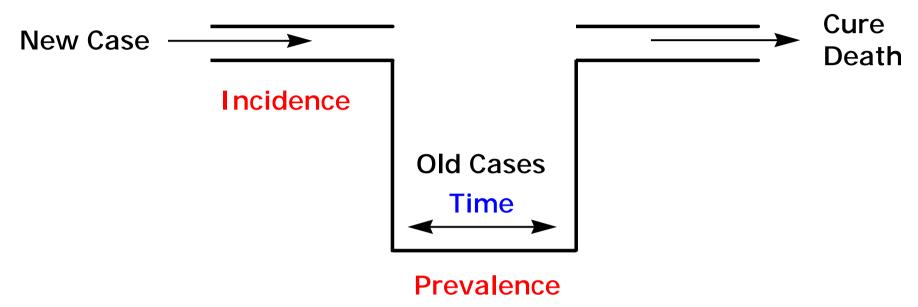
## PRINCIPLES OF CANCER PREVENTION

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

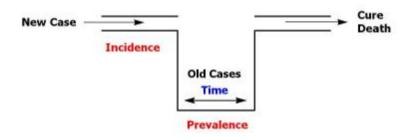
# **Terminology**



- •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 x duration of disease

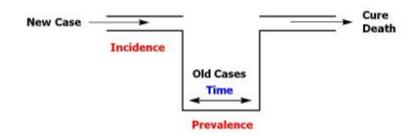
# **Terminology**

- n 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**

- n 12 million new cancer cases every year (incidence)
- n 7,6 million deaths (mortality)
- n 25-30 million patients living with cancer (prevalence)
- n 2nd most common cause of death in developed countries
- n 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 3. Bladder
- 4. Bladder
- 5. NHL

- 1. Lung
- 2. Gastric
- 4. Colorectal
  - 5. Larynx







## Most common types of cancer in women

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

- 1. Breast
- 2. Colorectal

  - 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
- Naccines: Hepatitis B, HPV
- n Chemoprevention

# Secondary prevention (Early diagnosis)

# Aim: To diagnose cancer before signs and symptoms appear

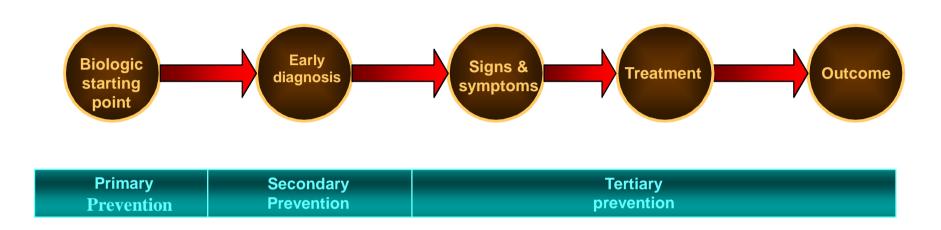
- Screening tests for asymptomatic individuals
  - Breast cancer: Mammography
  - n Cervical cancer: Pap smear
  - Colon cancer: Colonoscopy
  - Prostate cancer: PSA (prostate specific antigen)
  - Malign melanoma: Skin examination

# **Tertiary prevention**

### Aim: Improve survival and quality of life

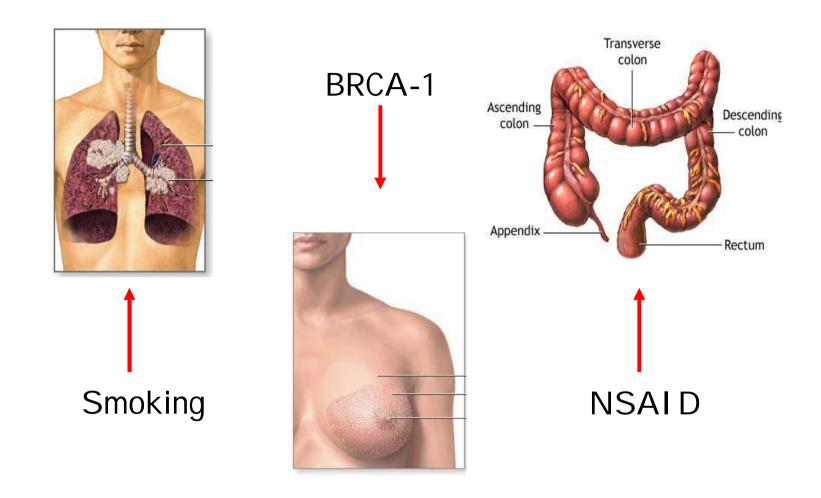
- Control of side-effects
- n Psycho-social support
- Less invasive procedures with low morbidity

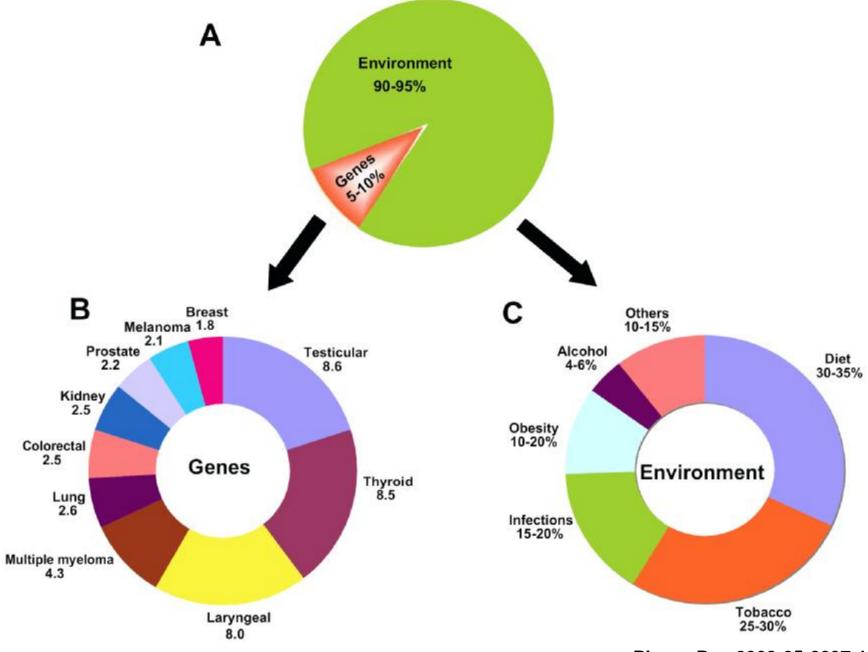
# Natural course of cancer development



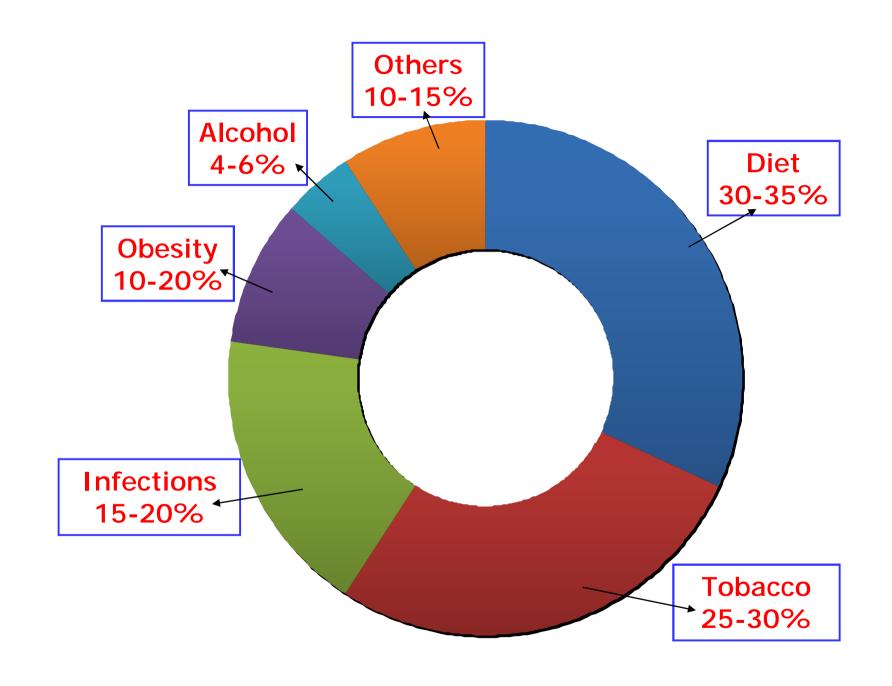
Healthy	No signs	Signs present
	_	

# Primary prevention (Prevent development)





Pharm Res 2008;25:2097-116.

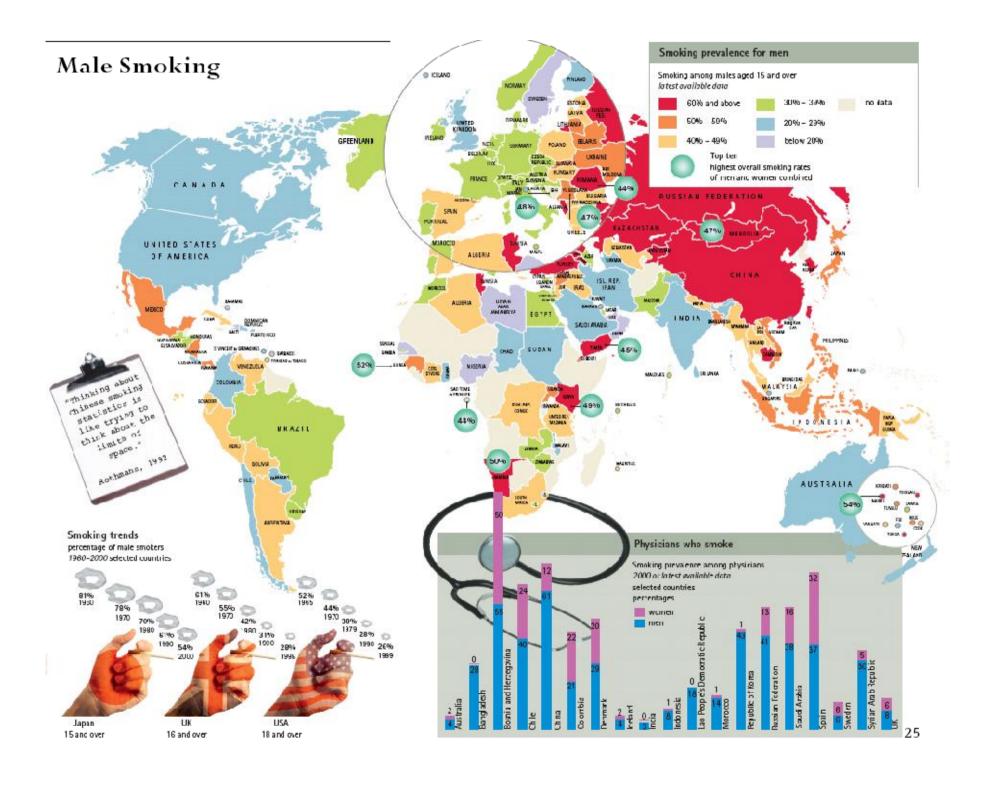


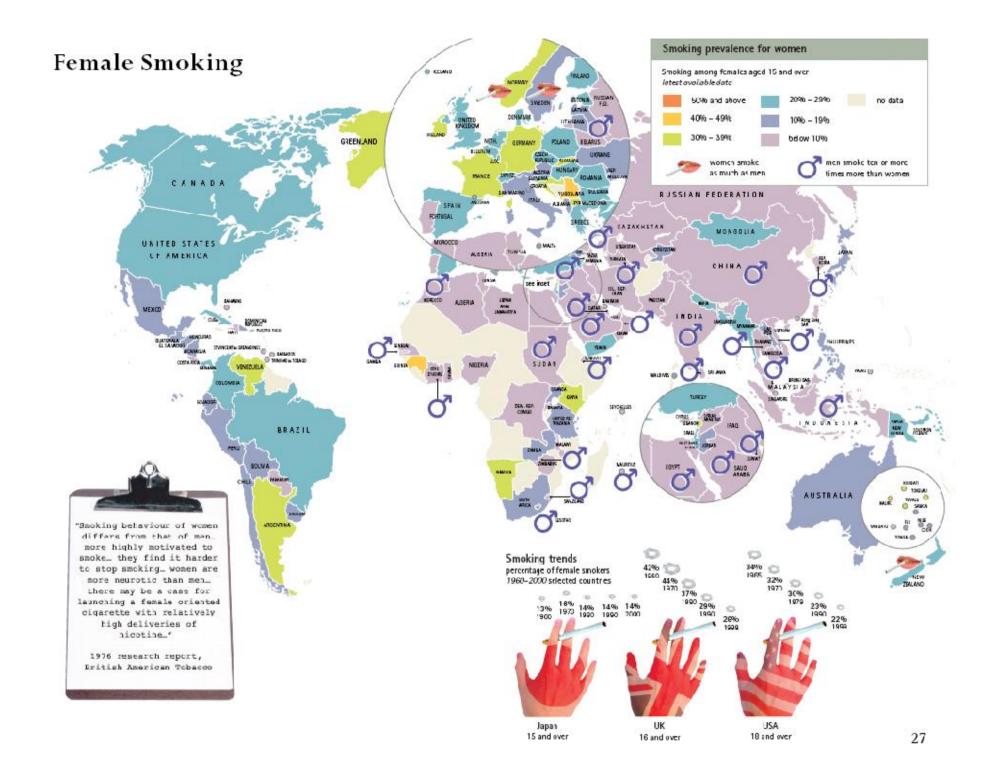
# **CAUSES OF CANCER**

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

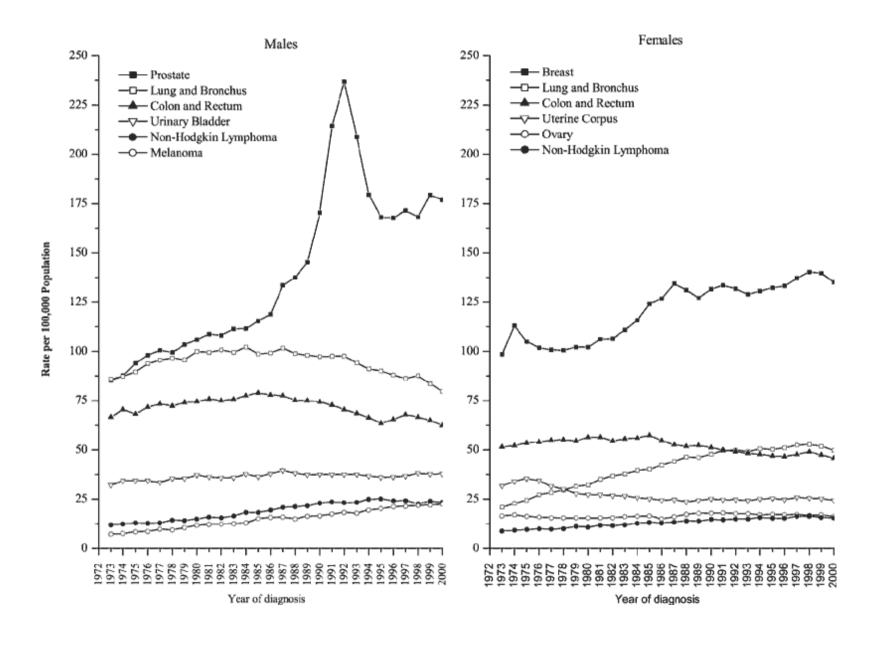
### **TOBACCO**



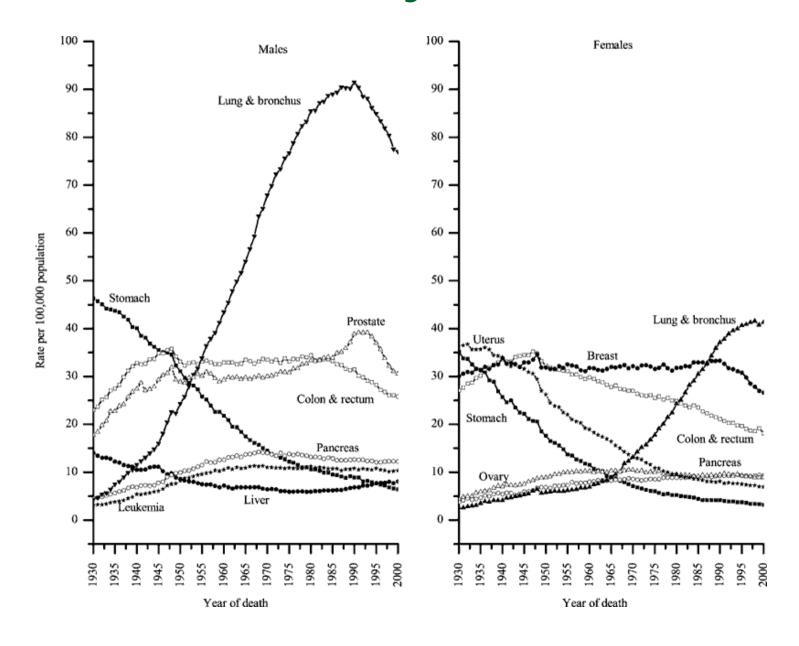




#### **USA-Cancer Incidence**



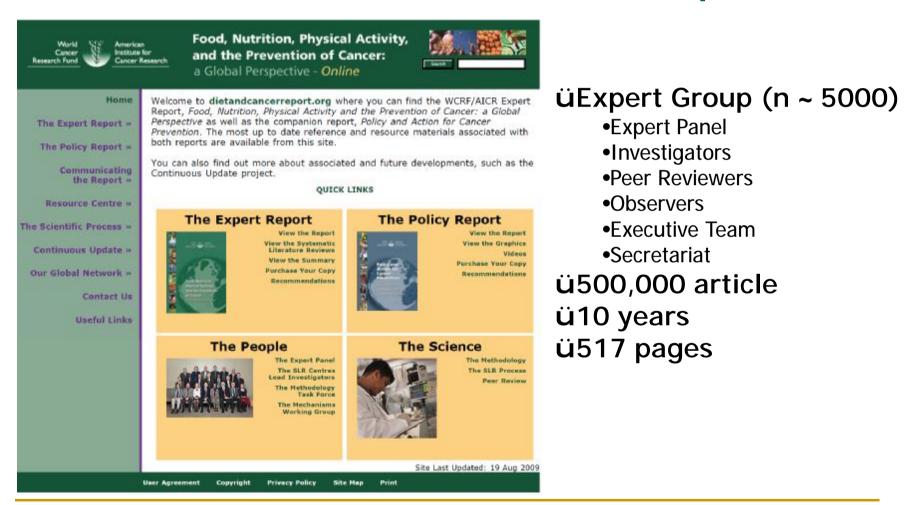
## **USA-Cancer Mortality**



#### **NUTRITION**

- 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



#### **MEAT AND MEAT PRODUCTS**

#### MEAT, POULTRY, FISH, EGGS, AND THE RISK OF CANCER

	DECREASES RISK		INCREA	SES RISK
	Exposure	Cancer site	Exposure	Cancer site
Convincing			Red meat <sup>1</sup> Processed meat <sup>2</sup>	Colorectum Colorectum
Probable			Cantonese-style salted fish <sup>3</sup>	Nasopharynx

# FATS, OILS

#### FATS, OILS, AND THE RISK OF CANCER

	DECREASES RISK		INCREASES RISK	
	Exposure	Cancer site	Exposure	Cancer site
Convincing				
Probable				
Limited — suggestive			Total fat	Lung Breast (postmenopause)
10.00			Foods containing animal fats1	Colorectum
			Butter	Lung

### **CEREALS**

#### CEREALS (GRAINS), STARCHY ROOTS AND TUBERS, PLANTAINS, AND THE RISK OF CANCER

	DECREASES RISK		INCRI	EASES RISK
	Exposure	Cancer site	Exposure	Cancer site
Convincing			Aflatoxins <sup>1</sup>	Liver
Probable	Foods containing dietary fibre <sup>2</sup>	Colorectum		

# **SUGAR AND SALT**

#### SUGARS AND SALT, AND THE RISK OF CANCER

osure	Cancer site	Exposure	Cancer site
		Salt <sup>1</sup>	Stomach
		Salted and salty foods	Stomach
		Foods containing sugars <sup>2</sup>	Colorectum
			Salted and salty foods

# **VEGETABLES, FRUITS**

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

	DECREAS	SES RISK	INCREASES RISK	
	Exposure	Cancer site	Exposure	Cancer site
Convincing				
Probable	Non-starchy vegetables <sup>1</sup>	Mouth, pharynx, larynx Oesophagus Stomach		
	Allium vegetables <sup>1</sup>	Stomach		
	Garlic <sup>1</sup>	Colorectum		
	Fruits¹	Mouth, pharynx, larynx Oesophagus Lung Stomach		
	Foods containing folate <sup>2</sup>	Pancreas		
	Foods containing carotenoids <sup>2</sup>	Mouth, pharynx, larynx Lung		
	Foods containing beta-carotene <sup>2</sup>	Oesophagus		

## **WATER**

#### WATER, FRUIT JUICES, SOFT DRINKS, HOT DRINKS, AND THE RISK OF CANCER

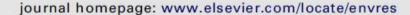
	DECREASES RISK		INCREASES RISK	
	Exposure	Cancer site	Exposure	Cancer site
Convincing			Arsenic in drinking water <sup>1</sup>	Lung
Probable			Arsenic in drinking water <sup>1</sup>	Skin

Environmental Research ( ( ) III- III



Contents lists available at ScienceDirect

#### Environmental Research





#### Arsenic in drinking water and lung cancer: A systematic review

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

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e Department of General Internal Medicine, Johns Hopkins University School of Medicine, USA

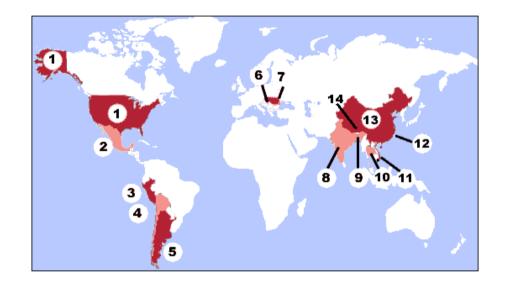
f Department of Oncology, Johns Hopkins University School of Medicine, USA

g Department of Occupational and Environmental Medicine, Johns Hopkins University School of Medicine, USA

h Cancer Prevention and Control Program, Hollings Cancer Center, and Department of Biostatistics, Bioinformatics and Epidemiology, The Medical University of South Carolina, USA

#### **WATER-Arsenic risk**

- n Arsenic in drinking water and lung cancer has been described in areas with deep artesian wells contaminated with high levels of arsenic.
- n The association was first observed in southwestern Taiwan, and later described in USA, Belgium, and particular regions of South America.



# **ALCOHOL**

#### ALCOHOLIC DRINKS, AND THE RISK OF CANCER

	DECREASES RISK		INCREASES RISK	
	Exposure	Cancer site	Exposure	Cancer site
Convincing			Alcoholic drinks	Mouth, pharynx and larynx Oesophagus Colorectum (men) <sup>1</sup> Breast (pre- and postmenopause)
Probable	1		Alcoholic drinks	Liver² Colorectum (women)¹

# DIETARY CONSTITUENTS, SUPPLEMENTS

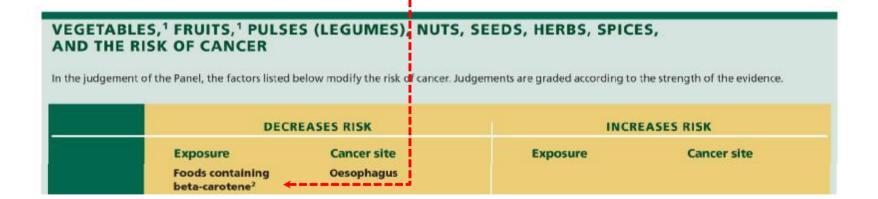
#### DIETARY CONSTITUENTS AND SUPPLEMENTS, AND THE RISK OF CANCER

	DECREASES RISK		INCREA	ASES RISK
	Exposure	Cancer site	Exposure	Cancer site
Convincing			Beta-carotene supplements <sup>1</sup>	Lung

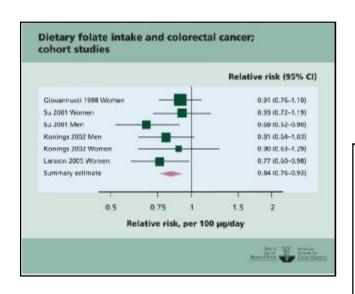
### DIETARY CONSTITUENTS, SUPPLEMENTS

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

	DECREASES RISK			INCREASES RISK	
	Exposure	Cancer site		Exposure	Cancer site
Convincing			·	Beta-carotene supplements <sup>1</sup>	Lung



# Paracelsus="Sola dosis facit venenum" Only dose makes the poison!



### Too much folate: a risk factor for cancer and cardiovascular disease?

Julia Sauer, Joel B. Mason and Sang-Woon Choi

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Current Opinion in Clinical Nutrition and Metabolic Care 2009, 12:30-36

#### 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 inopportune settings may be potentially harmful in individuals at higher risk for cardiovascular disease and cancer.

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: <u>Pesticides</u>, <u>Bioengineered foods</u>, <u>Organic foods</u>
- 2. Preservation: Drying, Fermenting, Canning, Pasteurisation, Chemical preservation (benzoates, <u>nitrites</u> and sulphites)
- Processing: <u>Additives</u> (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.
- n 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.

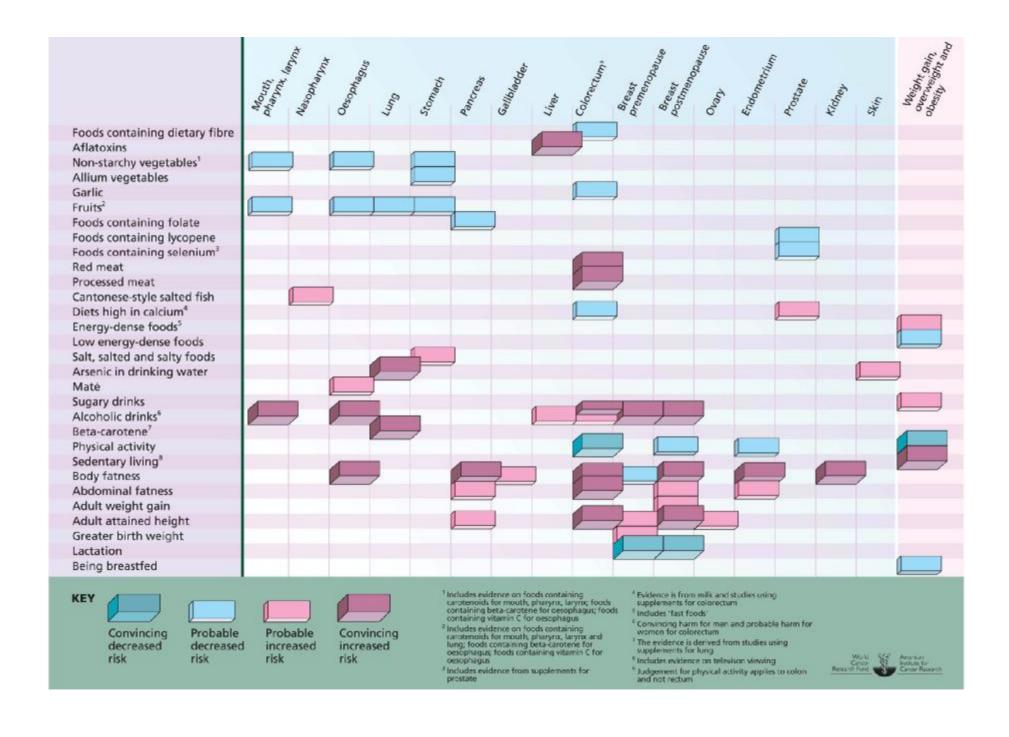
## **Food additives**

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)

- n PAHs are formed when meat and meat products are burnt incompletely.
- n Grilling and barbecuing also result in fat dropping on hot fire which makes PAHs that stick to the surface of food.





# ACS NUTRITION GUIDELINES FOR CANCER PREVENTION

- 1. Eat 5 or more servings of vegetables and fruits each day.
  - q Include vegetables and fruits at every meal and for snacks.
  - **q** Eat a variety of vegetables and fruits each day.
  - **q** 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.
  - **q** 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.
  - **q** 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.

# **OBESITY/PHYSICAL ACTIVITY**

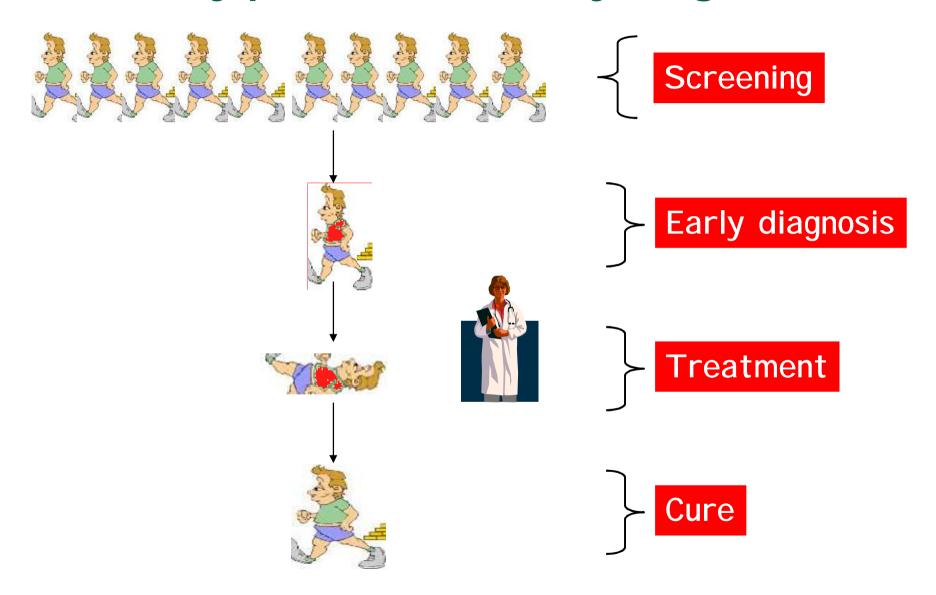
# 1. Maintain a healthy weight throughout life.

- **q** Balance calorie intake with physical activity.
- **q** 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 vs. Diagnosis

Screening	Diagnosis
Applied to asymptomatic groups	Applied to symptomatic individuals
Lower cost per test	Higher cost; all necessary tests applied to identify disease
Lower yield per test	Higher probability of case detection
Lower adverse consequences	Failure to identify true positive scan
of error	delay treatment, worsen prognosis

# **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

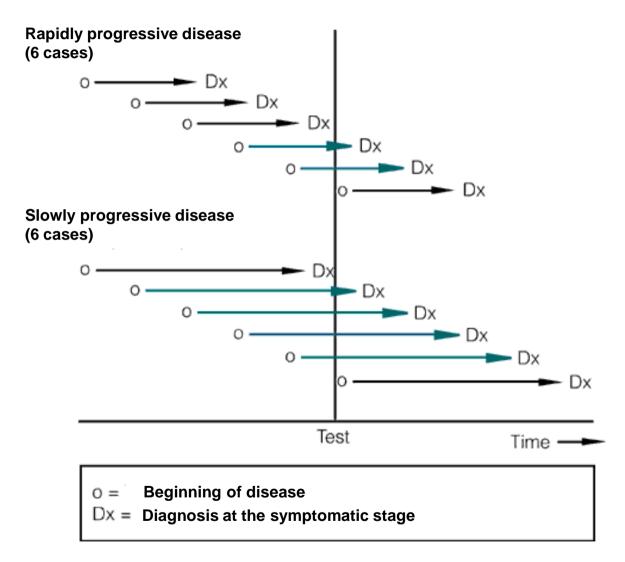
- Population based screeening
- Low risk subjects are included
- Should be cheap, rational and reliable

- n High risk individual screening
- High risk individuals are included
- Usually relatives of patients
- Should be reliable and not too expensive

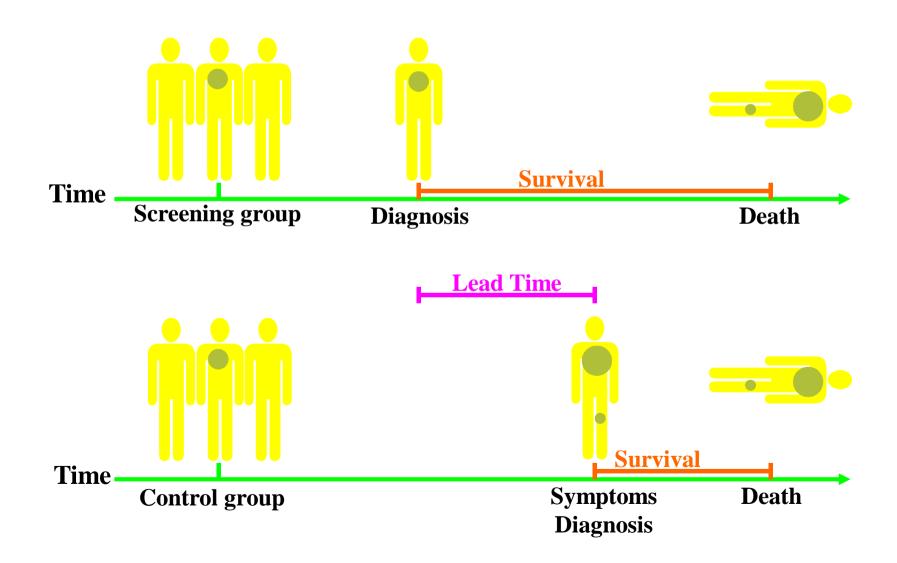
# Why early diagnosis does not always improve survival?

- Screening tests can identify cancers with a slow course and low mortality but can miss rapidly progressive cancers (length bias).
- n 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**



### **Lead-time Bias**



# Sample case: Lead-time bias

#### Scenario 1:

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

#### Scenario 2:

- n The patient is on a screening program.
- n Lung CT on Oct 2008 reveals a mass and lymphadenopathies.
- n Diagnosed with lung cancer and treatment starts on Oct 2008.
- n The patient dies on Feb 2010.
- Survival = 16 months

#### **RESULT**

Screening prolongs survival.

But the patient dies on Feb 2010 anyway. => ????

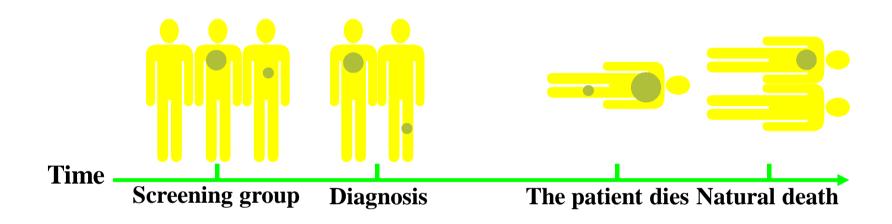
# **Lead-time Bias**

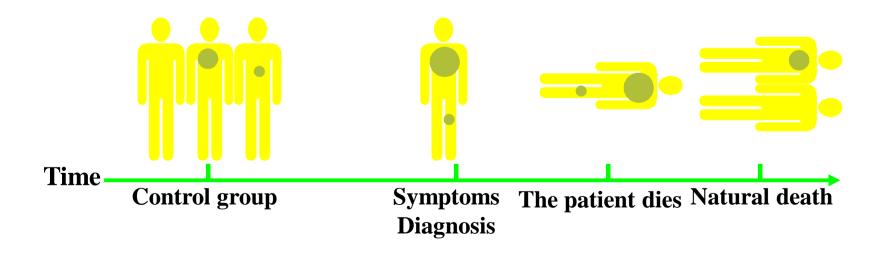
- n To test the efficacy of a screening test, you have to demonstrate the decrease in mortality, to overcome lead-time bias.
- Survival alone does not show that a screening test is useful.

# **Overdiagnosis Bias**

- The disease specific survival of patients identified with a screening test seems prolonged. This is because patients with a <u>clinically insignificant disease</u> are also identified.
- n <u>Clinically insignificant disease</u> does not progress or progresses so slowly that meantime the patient dies because of another reason.

# **Overdiagnosis Bias**





# Possible risks of screening

- n False negatives: False confidence
- n 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**

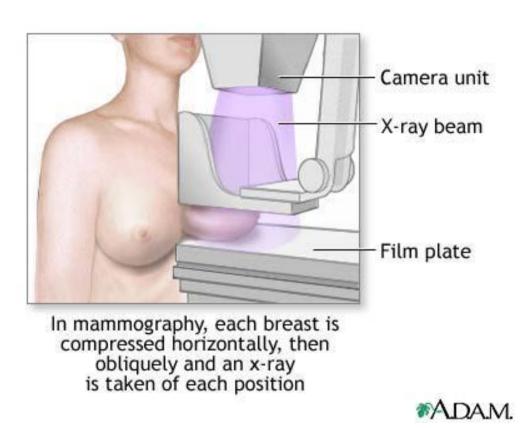
#### Prevention

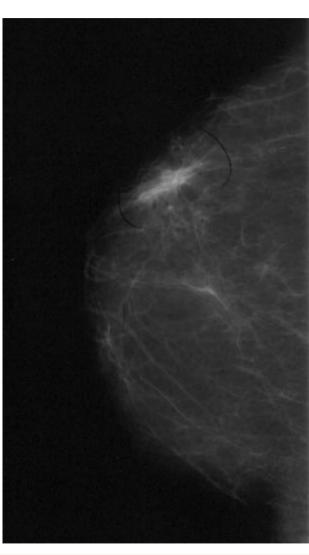
- Careful use of hormone drugs
- q Prevent obesity
- a Limited alcohol use
- Special follow up for high risk women

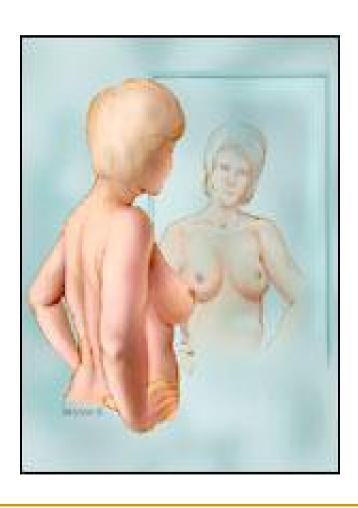
# n Early diagnosis

- Self breast exam
- Clinical breast exam
- **q** Mammography

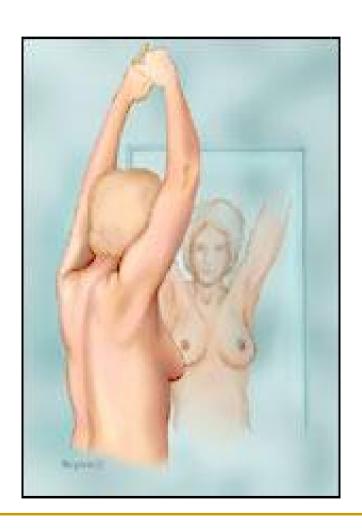
# Mammography







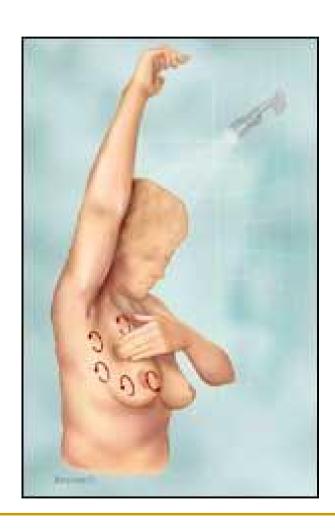
- Step 1: Begin by looking at your breasts in the mirror with your shoulders straight and your arms on your hips.
- n You should look for:
  - size, shape, and color of the breasts
  - any visible distortion or swelling
- If you see any of the following changes, bring them to your doctor's attention:
  - dimpling, puckering, or bulging of the skin
  - a nipple that has changed position or an inverted nipple (pushed inward instead of sticking out)
  - q redness, soreness, rash, or swelling



- Step 2: Now, raise your arms and look for the same changes.
- n 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).



- while lying down, using your right hand to feel your left breast and then your left hand to feel your right breast.
- n 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.



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
- n Age 40-50: Monthly self breast exam; annual clinical breast exam, mammography every 1-2 years
- n Age >50: Monthly self breast exam; annual clinical breast exam and mammography

# Cervical Cancer

# **Cervical cancer**

#### Prevention

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

### n Early diagnosis

- q Gynecologic exam
- q Pap smear

# **Screening recommendations**

- Start Pap test 3 years after first coitus
- Momen with 3 consequtive 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.)
- **q** Avoid solariums

# n Early diagnosis

- Self skin exam
- q Clinical exam for suspicious lesions

### **Skin Self-Examination**



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



n 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.

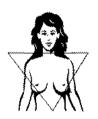


n Check your hands carefully: palms and backs, between the fingers and under the fingernails. Continue up the wrists to examine both front and back of your forearms.



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.

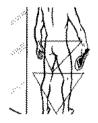
# **Skin Self-Examination**



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**

# **Screening Tools**

- n The most widely used technique for detection of prostate cancer is the digital rectal examination (DRE)
- n DRE exhibits wide ranges in sensitivity (33% to 69%) and specificity (49% to 97%)
- n 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)
- n Impact on mortality???

# **Screening recommendations**

- n 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 read meat and fat
- Regular exercise
- q NSAIDs?

## n Early diagnosis

- Fecal occult blood testing
- Rectosigmoidoscopy / colonoscopy
- Digital rectal exam

# Screening recommendations

- Individuals aged >50 should follow one of the following screening methods:
  - Annual FOB testing and
  - Flexible sigmoidoscopy every 5 yearsor
  - Colonoscopy every 10 years

# **Lung Cancer**

# Lung cancer

#### Prevention

Stop smoking and all other tobacco products

# n 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!

- n 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
- n Obesity
- n Alcohol

# The best treatment for cancer is prevention!