JOHN SNOW AWARD PRESENTATION
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- ALLEVIATING THE GLOBAL BURDEN OF CANCER : PERSPECTIVE on ADVANCES and FUTURE DIRECTIONS

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Outline of Presentation

- Global burden of cancer
- USA cancer statistics
- Tobacco carcinogenesis
- Obesity, energy expenditure and dietary guidelines
- Priorities in cancer control
- Tribute to John Snow

Global Cancer Statistics (2002)

- 10.9 million new cases (20 million in 2020)
  - Lung (1.35 million)
  - Breast (1.15 million)
  - Colorectal (1 million)
- 6.7 million deaths (10 million in 2020)
  - Lung (1.18 million)
  - Stomach (700,000)
  - Liver (598,000)
- Of approximately 55 million global deaths, 31% attributed to CVD, 12-13% to cancer

Source: Parkin et al. CA Cancer J Clin 2005;55:74-108.

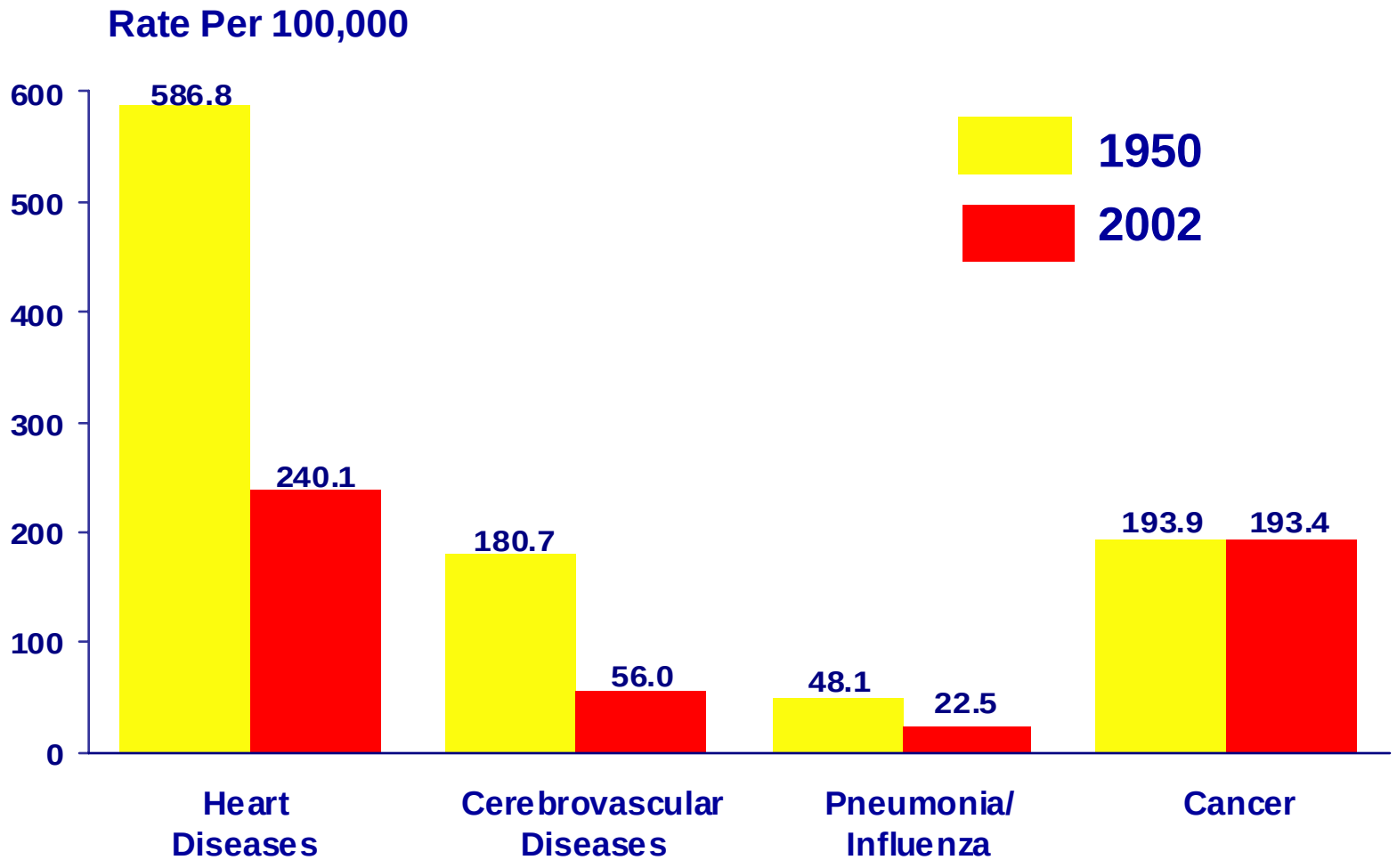
US Cancer Statistics (2005)

- 1,372,910 new cases
  - Lifetime probability of developing cancer is 46% in males and 38% in females
  - 570,280 deaths with ~10 million cancer survivors diagnosed in previous 5 years
  - 16% of new cases are diagnosed in patients with a prior independent primary cancer (SEER, 2002)

In US, Cancer Surpasses Heart Disease as Leading Cause of Death Under age 85: 1999-2002

- Population < 85 years comprises 98% of population at risk and accounts for 72% of all deaths
- In 2002, < age 85 years there were 478,082 cancer deaths and 446,727 heart disease deaths
- Older than age 85, heart disease accounted for 3 times greater number of deaths in 2002 compared to cancer

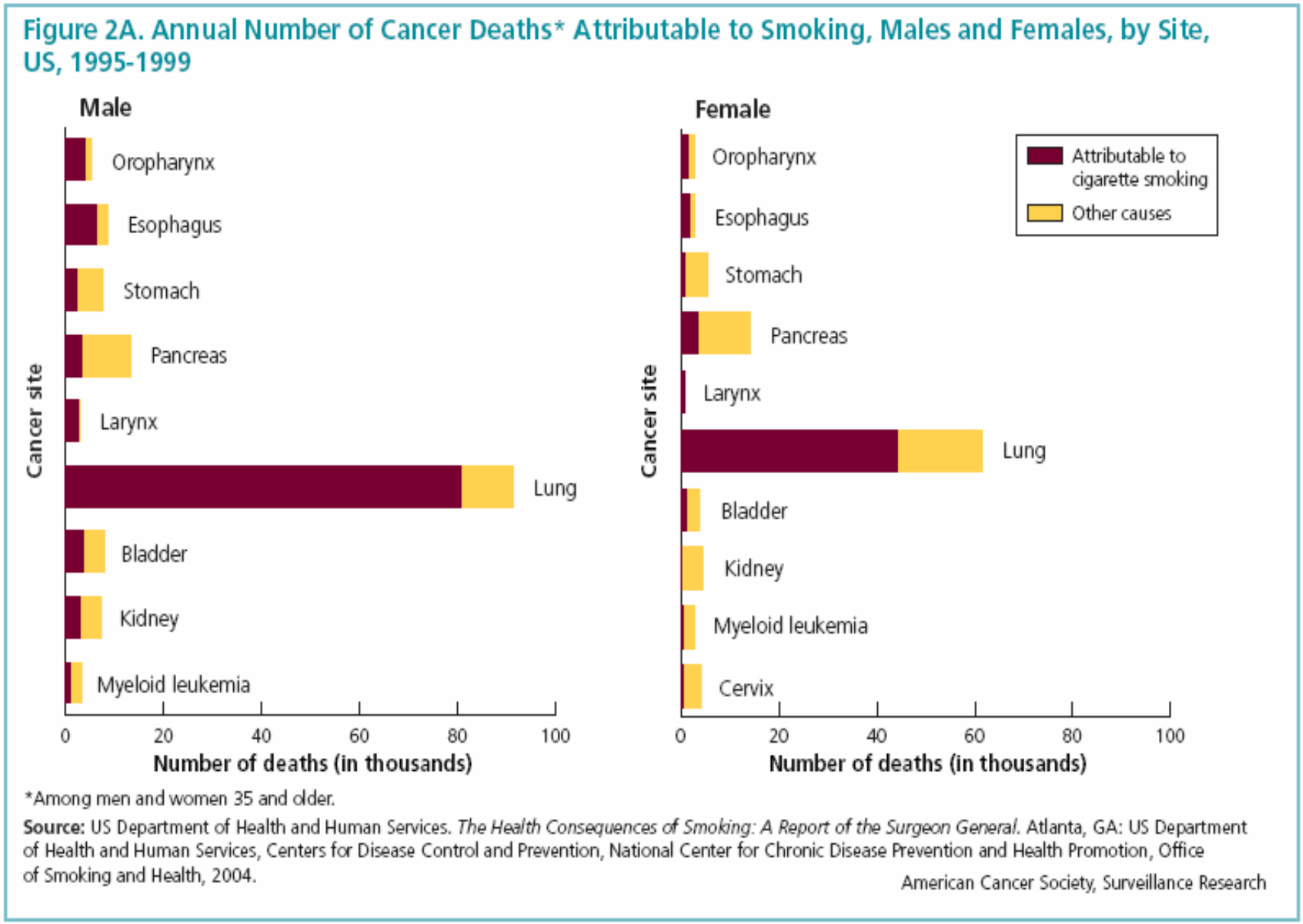
Change in the US Death Rates* by Cause, 1950 & 2002



* Age-adjusted to 2000 US standard population.
Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
2002 Mortality Data: US Mortality Public Use Data Tape, 2002, NCHS, Centers for Disease Control and Prevention, 2004 Source: www.cancer.org

Cancer Burden of Tobacco

- 20% of global cancer mortality
- 30% of USA cancer mortality
- Population attributable risk of lung cancer in USA men (88%), women (72%)
- 3000 lung cancer deaths each year in USA estimated for environmental tobacco smoke
- About 146.000 lung cancer deaths prevented or postponed in USA men, between 1991-2003,as a result of reductions in cigarette smoking
- Note: 440,000 deaths, all causes , estimated annually



Source: www.cancer.org (ACS Cancer Prevention and Early Detection Facts and Figures 2005)

Interaction of Genes and Tobacco

- Metabolic polymorphisms that control activation or detoxification of carcinogenic metabolites
- Capacity and fidelity of DNA repair mechanisms
- Polymorphisms affecting inflammatory cytokines…chronic inflammation as a co-carcinogenic pathway
- Intractable addictive behavior …dopamine and serotonin neurochemical pathways

Exploration of Candidate Genes Potentially Impacting the Risk of Lung Cancer

Type of Gene	Examples
Phase I Polymorphisms	CYP1A1, 1A2, 2D6
Phase II Polymorphisms	GSTM1, GSTT1, NAT1, NAT2
DNA Repair Genes	Nucleotide excision, mismatch repair
Immune Function	Interleukins, TNF, HLA I &II
Cell-cycle Control	TP53, HRAS
Nicotine Addiction Receptor and Transporter Genes	Dopamine D1 D2 and D4 receptors, CYP2A6, serotonin, and dopamine transporter genes

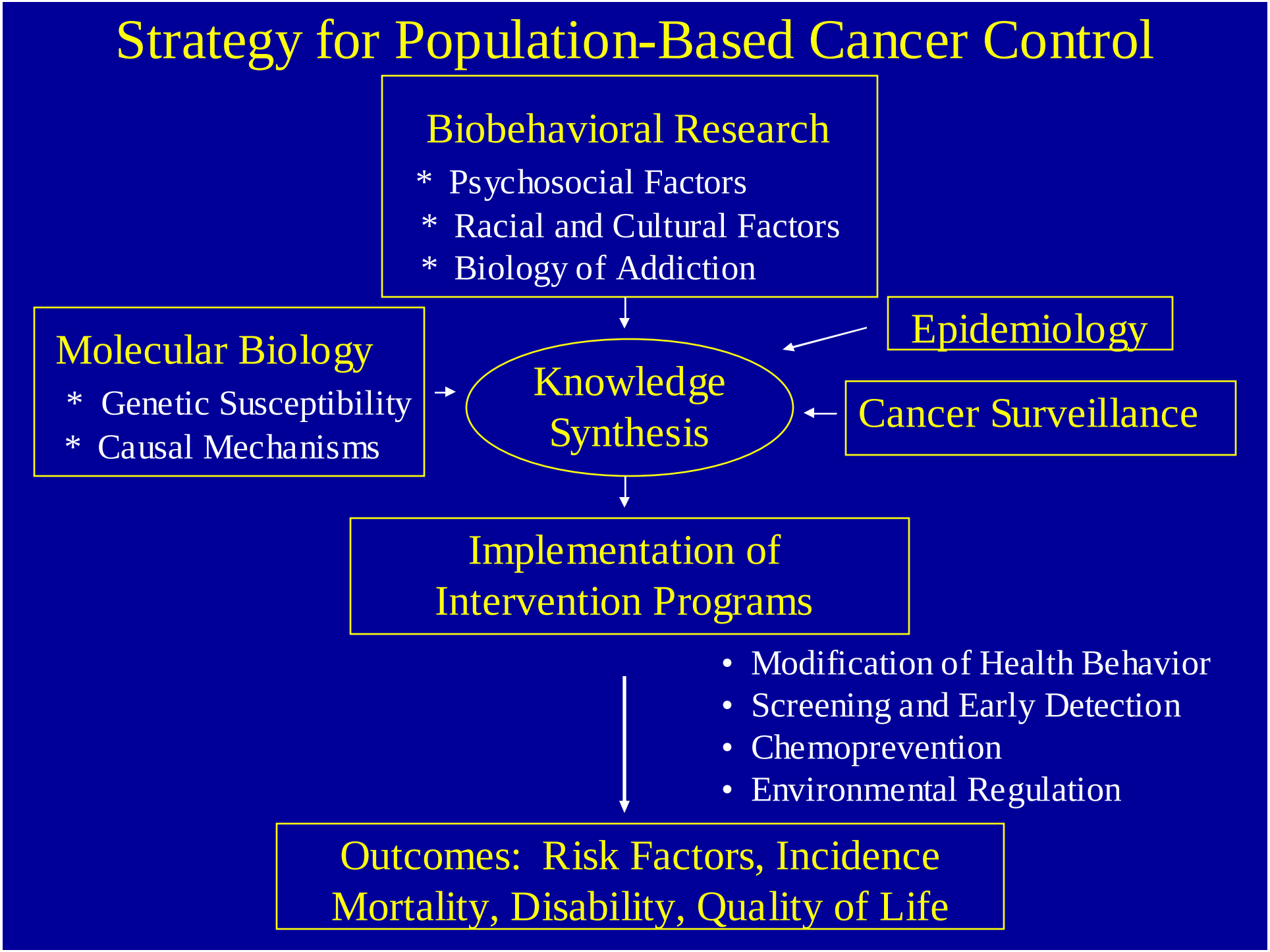
Interventions that Prevent Use of, or Promote Cessation of ,Tobacco Smoking*

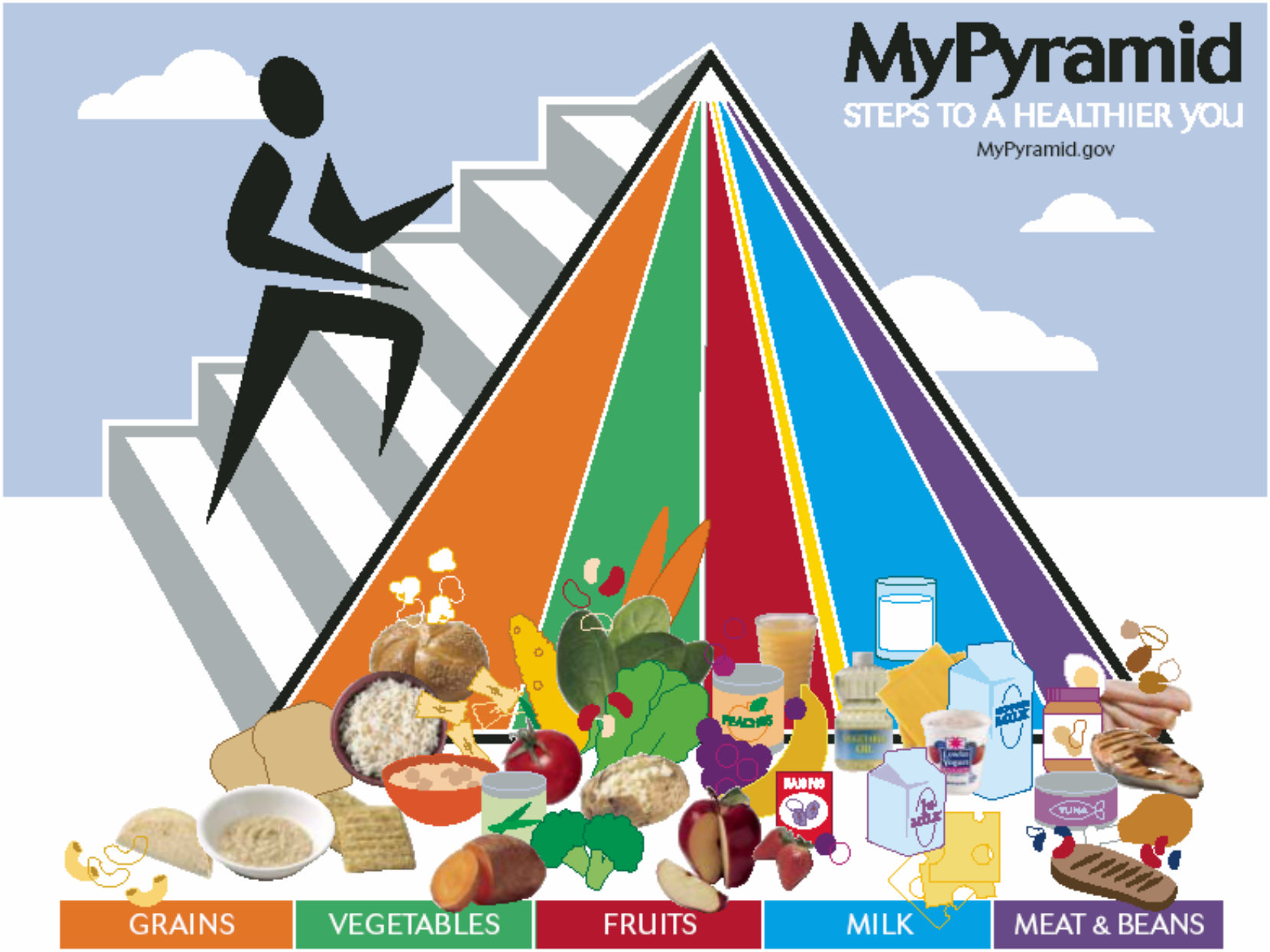
- Increasing unit costs of tobacco products ; for adults, a 10% increase in cigarette prices is projected to reduce demand by 3% to 5%. With younger smokers, the elasticity of tobacco demand in relationship to increasing costs is greater
- Regulating a smoke-free environment in public places and use of public transportation
- Adopt and implement effective health-warning labeling on the packaging of tobacco products. Prohibition of use of tobacco products by minors
- Increase availability of counseling by trained and dedicated professionals for smokers seeking behavioral interventions

Interventions that Prevent Use of ,and Promote Cessation of, Tobacco Smoking*(continued)

- Availability of pharmacologic therapies (e.g., nicotine replacement therapies as transdermal patches, inhalers, sprays and gums, and antidepressants) that are used in conjunction with psychotherapy
- Restrictions on tobacco industry advertising
- Congressional intervention to elevate Federal regulation of tobacco production, distribution and marketing; the appropriate agency will establish minimal national standards, while allowing states to be more restrictive.
- *Adopted from the WHO –sponsored Framework Convention for Tobacco Control (2005),and the IOM publication "Ending The Tobacco Problem: A Blueprint For The Nation" (2007)

Strategy for Population-Based Cancer Control





Diet, Nutrition and Human Cancer: Causal Mechanisms Affected by Deficiencies and Excesses

- Toxic chemicals contained in foods or produced in food preparation
- Endogenous formation of carcinogens derived partially from food sources
- Dietary deficiencies associated with impaired:

  a) neutralization of oxygen - free radicals

  b) methylation of DNA and DNA synthesis and repair

  c) integrity of cell-mediated immunity

Diet, Nutrition and Human Cancer : Causal Mechanisms Affected by Deficiencies and Excesses

- Excess energy consumption, obesity and insulin resistance
- Deficient consumption of non-digestible fibers that affect rate of transport of mutagens and cancer-promoting chemicals in gastrointestinal tract

Obesity and Cancer
“Banish plump Jack , and banish all the world”

(King Henry IV, Part I)

- Dysfunctional disparity between energy intake (kilocalories), mechanisms controlling appetite, and energy expenditure (metabolic equivalents of physical activity) .
- In the year 2000, 35% of USA population was overweight, and 26% - 30% obese.
- If current trends are extrapolated, by the year 2010, more than 40 % of the population will be classified as obese .

Overweight, Obesity and Cancer Risk

- Endometrial (pre- and postmenopausal)
- Breast (postmenopausal)
- Kidney parenchymal (renal cell)
- Gallbladder
- Pancreas
- Adenocarcinoma : esophagus, gastric cardia
- Colon (and large adenomas)
- Prostate (association with invasive phenotype)

Obesity and Cancer
Metabolic and Neoplastic Sequelae

- Endogenous production of sex steroid hormones
- Hyperinsulinemia, alterations in production of insulin-like growth factor (IGF-1) and IGF-binding protein (IGFBP-3)
- Altered bile acid metabolism; cholelithiasis
- Dyslipidemia
- Central or intra-abdominal adiposity
- Increased production of proinflammatory cytokines

Reduction in risk of cancer associated with physical activity: The benefits of maintaining moderate or vigorous physical activity

Relative Risk	
0.76-0.90	0.51-0.75
Breast Endometrium	Colon*

*Physical activity appears to lower risk of large adenomatous polyps in the colon and potentially adenoma to carcinoma transformation

Source: Fulfilling the potential of cancer prevention and early detection
Institute of Medicine, 2003

Alleviating the Burden of Cancer Mortality: Modification of Behavioral Lifestyle Risk Factors

- Eliminating use of all forms of tobacco
  - 20% of global cancer mortality
  - 30% of USA cancer mortality
- Limiting consumption of alcohol—Joint hazard with tobacco resulting in greater than 50% of global deaths due to cancers of the upper aerodigestive tract
- Reducing tumorigenic effects of exposures to microbial agents—20-25% of cancer mortality in developing countries and 7-10% of cancer mortality in industrialized countries: immunization, antimicrobials, surveillance
- Avoid being overweight or obese, achieving balance between energy intake and energy expenditure from regular physical activity

Alleviating the Burden of Cancer Mortality (continued)

- Adherence to recommendations and guidelines by U.S. Preventive Services Task Force and American Cancer Society with respect to age-and risk factor-specific periodic screening for breast, uterine cervical and colorectal cancers.