"Breathing is truly a strange phenomenon of life, caught midway between the conscious and unconscious and peculiarly sensitive to both."

Dickenson Richards, M.D.
Columbia University College of Physicians and Surgeons
Nobel Laureate in Medicine, 1956

Goals and objectives for the pulmonary section: II

- Understand gas exchange in health and disease
  - Alveolar air equation and calculation of alveolar-arterial (A-a) gradient
    - $P_AO_2 = P_IO_2 - (PCO_2/R)$
  - Oxygen delivery to tissues
    - Oxyhemoglobin dissociation curve
    - $DO2 = CO \times CaO_2$
    - $CaO2 = ([Hgb] \times 1.39 \times \%sat) + (pO_2 \times .0036)$
  - Mechanisms of hypoxemia
    - Shunt
      - Does not correct with oxygen breathing
    - V/Q mismatch
      - Corrects with oxygen breathing
      - Exacerbated by exercise
    - Alveolar hypoventilation
      - Normal A-a gradient
      - Corrects with oxygen breathing
    - Diffusion limitation
      - Corrects with oxygen breathing
      - Exacerbated by exercise

Roses are red,
Violets are blue;
Without your lungs,
Your blood would be, too

Goals and objectives for the pulmonary section: III

- Understand symptoms and signs of pulmonary disease
  - Symptoms
    - Dyspnea
      - Onset
      - Severity
      - Triggers
      - Progression
  - Signs
    - Wheezing
    - Crackles (rales and rhonchi)
    - Diminshed breath sound
    - Hyperresonant breath sounds
- Understand use of diagnostic testing in pulmonary disease
  - Pulmonary function testing
    - Restrictive and obstructive physiology
  - Arterial blood gas analysis
  - Chest radiograph
  - Lung pathology
    - Major types and patterns of injury and abnormality

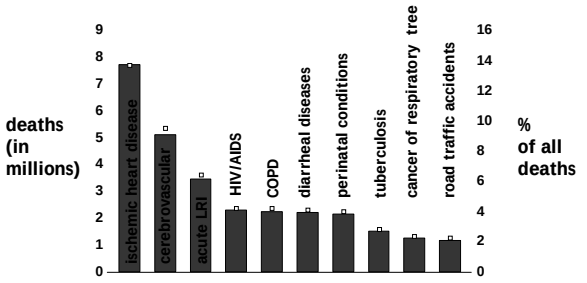
Goals and objectives for the pulmonary section: I

- Understand important categories and causes of lung disease in the United States and around the world
- Understand lung mechanics in health and disease
  - Lung mechanics determination efficiency of ventilation
    - Work of breathing
    - Compliance
      - $\Delta V/\Delta P$
    - Resistance
      - P_{alv}-P_{mouth}/ flow
    - PEEP and Auto-PEEP

Goals and objectives for the pulmonary section: IV

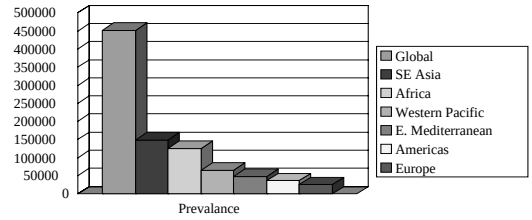
- Understand treatment approaches to patients with lung diseases
  - Symptomatic treatments
    - Oxygen therapy
    - Bronchodilators
    - Mechanical ventilation and PEEP
  - Disease specific treatments
    - Understand cellular and molecular basis of treatments for specific diseases
      - Steroids
      - Other immunosuppressives
      - Antibiotics
      - Anti-neoplastics
      - Pulmonary vasodilators

Leading causes of global mortality



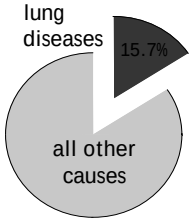
WHO, World Health Report, 2004

Yearly prevalence (in 000s) of acute respiratory infections (ARI), by WHO region



Source: WHO Global Disease Burden Report

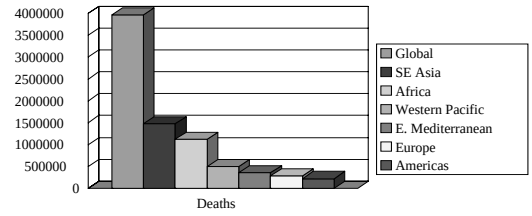
Impact of respiratory illness on global mortality



respiratory illnesses account for 8.43 million deaths per year, or 15.7% of total deaths in WHO member nations

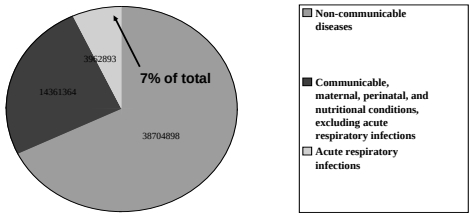
WHO, World Health Report, 2004

Deaths due to ARI, by WHO region



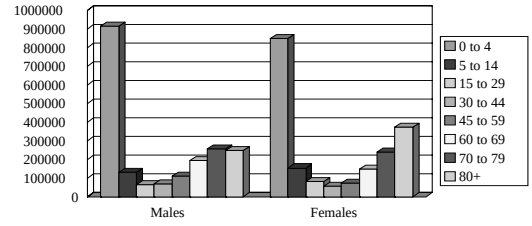
Source: WHO Global Disease Burden Report

Global deaths due to acute respiratory infections



Source: WHO Global Disease Burden Report

Deaths due to ARI, by age and sex, worldwide



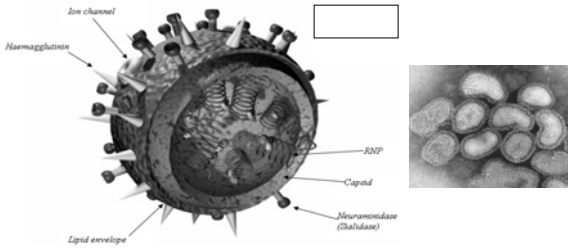
Source: WHO Global Disease Burden Report

Cause of death among children less than 5 years of age

Cause of Death	Africa	Global
	percent	
Acute respiratory infection	16	18
Diarrheal disease	14	15
Malaria	22	10
Measles	8	5
HIV or AIDS	8	4
Neonatal deaths	13	23
Other causes	19	25
	number	
All causes	4.5 million	10.9 million

Source: NEJM, WHO

Influenza



Serotypes of *S. pneumoniae* and *H. influenzae* in bacteremia-related isolates from Kenya

- *S. pneumoniae serotypes*
  - 1 (66 patients)**
  - 14 (39 patients)*
  - 6A (26 patients)
  - 6B (24 patients)*
  - 23F (21 patients)*
  - 18C (13 patients)*
  - 4 (11 patients)*
  - 3 (10 patients)
  - 19F (10 patients)*
- *H. influenzae*
  - 113/136 (83%) type B

*Serotype included in commercially available 7-valent conjugate pneumococcal vaccine

**Serotype included in 9-valent conjugate pneumococcal vaccine

Overall, 298/398 (75%) isolates were of serotypes covered by vaccines

Berkley, JA. N Eng J Med 2005; 352: 38-47

Influenza

- Roughly 20% of children and 5% of adults develop symptomatic influenza infections each year
- Infection is continuous in tropics, seasonal elsewhere
- Three types of influenza virus: A, B, C
- Only types A and B cause outbreaks
- Two major surface proteins:
  - Hemagglutinin: facilitates entry into host cells through sialic acid receptors
  - Neuraminidase: catalyzes cleavage of glycosidic linkages to sialic acid and assists in release of progeny virions from infected cells; drug target
- Influenza A:
  - 15 hemagglutinin subtypes
  - 9 neuraminidase subtypes

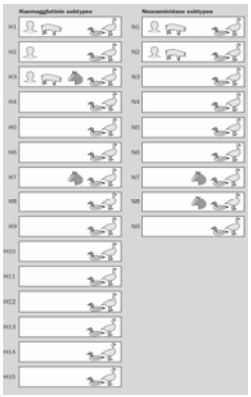
Notice of Prevnar Price Increase

Effective 9/25/04, Wyeth Pharmaceuticals will charge $326 for a 5 dose package (an increase of $5 per dose) of Prevnar (CPT 90669 pneumococcal conjugate vaccine, for children under 5 years, for intramuscular use).

American Academy of Pediatrics website

Natural hosts of influenza viruses

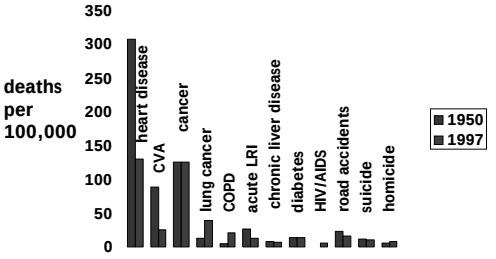
At present, only H1N1 and H3N2 are in circulation among humans



Pandemic influenza

- Caused by sudden appearance of a new subtype: antigenic shift
- 1918-1919
  - H1N1 "Spanish flu"
  - Arose in swine (?)
  - 20 million deaths in first year; 50 million deaths total
- 1957-1958
  - H2N2 "Asian flu"
  - Arose in fowl
  - Severe pandemic: 70,000 deaths in U.S.
- 1968-1969
  - H3N2 "Hong Kong flu"
  - Arose in fowl
  - Moderately severe: 34,000 deaths in the U.S.
- Future pandemics-
  - ?H5N1 ("Avian flu")
  - ? H7N7
  - Both are highly lethal, though little if any person-to-person transmission yet documented

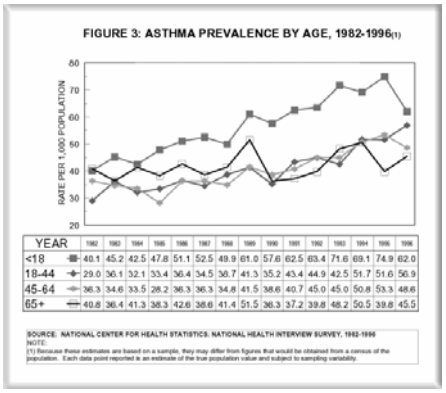
Trends in U.S. mortality for selected causes, 1950-1997



National Center for Health Statistics

Strategies for controlling influenza

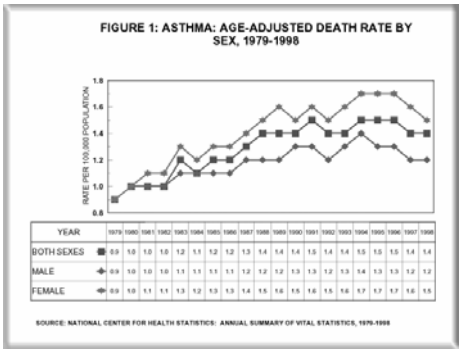
- Surveillance
- Vaccination
- Treatment



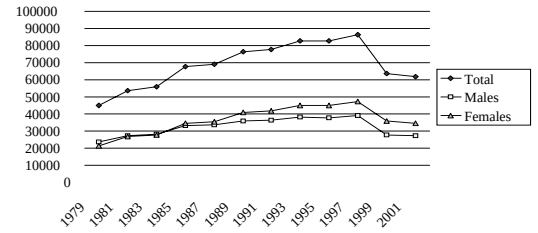
Leading causes of death in the U.S., 1980 and 1997

1980	1997
1. Heart disease	1. Heart disease
2. Cancer	2. Cancer
3. Cerebrovascular disease	3. Cerebrovascular disease
4. Unintentional injuries	4. COPD
5. COPD	5. Unintentional injuries
6. Pneumonia and influenza	6. Pneumonia and influenza
7. Diabetes	7. Diabetes
8. Chronic liver disease	8. Suicide
9. Atherosclerosis	9. Renal disease
10. Suicide	10. Chronic liver disease

National Center for Health Statistics



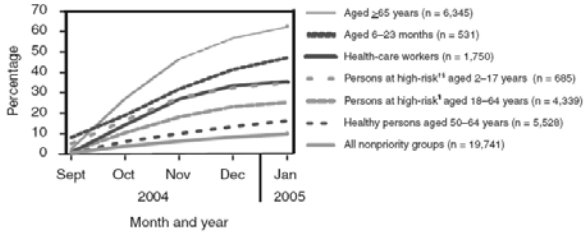
Deaths due to pneumonia and influenza, U.S., by year and sex



Source: National Center for Health Statistics

Influenza vaccine coverage, United States, 2004-2005

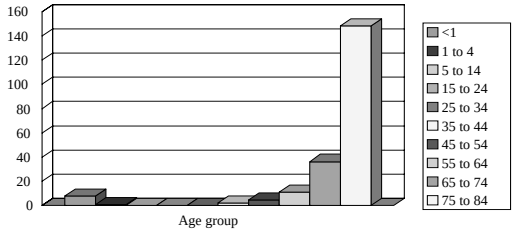
FIGURE. Monthly influenza vaccination coverage among selected priority populations, by month — Behavioral Risk Factor Surveillance System, United States, 2004–05 influenza season*



* Interviews were conducted during February 1–27, 2005.
† Does not include persons in households with infants aged <6 months, out-of-home caregivers of infants aged <6 months, or others with rare, high-risk conditions.
§ Asthma; other lung, heart, or kidney problems; diabetes; weakened immune system; anemia; or aspirin therapy for chronic conditions.
¶ Asthma; other lung, heart, or kidney problems; diabetes; weakened immune system; anemia; or pregnancy.

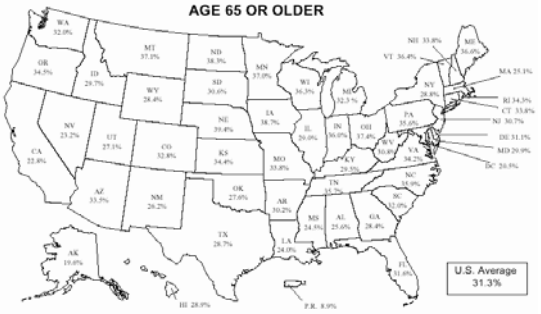
MMWR 2005; 54: 304-307

Age-specific mortality for ARI, US, 2001



Source: National Center for Health Statistics

FIGURE 9: PNEUMOCOCCAL VACCINATION STATUS SINCE 1991 OF MEDICARE BENEFICIARIES IN 1998 PERCENT OF ALL BENEFICIARIES AGE 65 OR OLDER

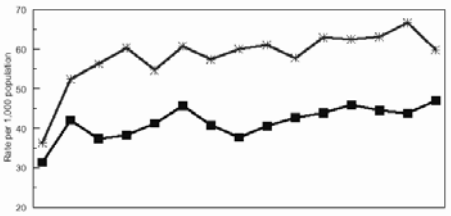


SOURCE: HEALTH CARE FINANCING ADMINISTRATION, 1998 INFLUENZA IMMUNIZATIONS PAID FOR BY MEDICARE, STATE AND COUNTY RATES, 1998

Risk factors for community acquired pneumonia

- Advancing age
- Tobacco use
- Air pollution
- Underlying chronic disease
- Malnutrition
- Alcohol use
- Chronic obstructive pulmonary disease
- Others including immunodeficiency, treatment with immunosuppressive drugs, malignancy, etc.

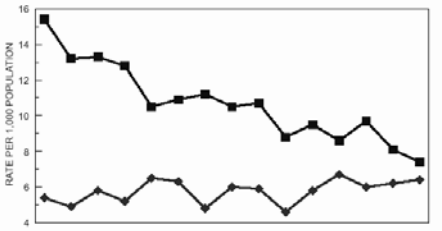
FIGURE 2: CHRONIC BRONCHITIS PREVALENCE, BY SEX, 1982-1996 (1)



YEAR	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996
MALE	31.4	42.0	37.4	38.3	41.2	45.7	40.8	37.7	40.6	42.7	43.9	45.9	44.5	43.8	47.0
FEMALE	36.3	52.4	56.3	60.3	54.7	60.7	57.4	60.0	61.0	57.7	62.9	62.4	63.1	66.6	59.8

SOURCE: NATIONAL CENTER FOR HEALTH STATISTICS, NATIONAL HEALTH INTERVIEW SURVEY, 1982-1996

FIGURE 6: EMPHYSEMA PREVALENCE, BY SEX, 1982-1996 (1)



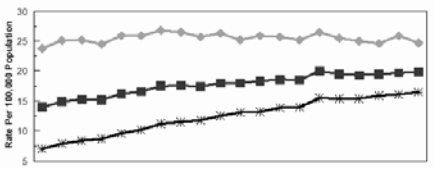
YEAR	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996
MALE	15.4	13.2	13.3	12.8	10.5	10.9	11.2	10.5	10.7	8.8	9.5	8.6	9.7	8.1	7.4
FEMALE	5.4	4.9	5.8	5.2	6.5	6.3	4.8	6.0	5.9	4.6	5.8	6.7	6.0	6.2	6.4

Estimated Deaths

Lung and Bronchus (31%)	Lung and Bronchus (25%)
Prostate (10%)	Breast (15%)
Colon and Rectum (10%)	Colon and Rectum (11%)
Pancreas (5%)	Pancreas (6%)
Non-Hodgkin Lymphoma (4%)	Ovary (5%)
Leukemia (4%)	Non-Hodgkin Lymphoma (4%)
Esophagus (4%)	Leukemia (4%)
Liver (3%)	Uterine Corpus (3%)
Urinary Bladder (3%)	Brain (2%)
Kidney (3%)	Multiple Myeloma (2%)
All Other Sites (22%)	All Other Sites (23%)

Ca 2003; 53:5--26

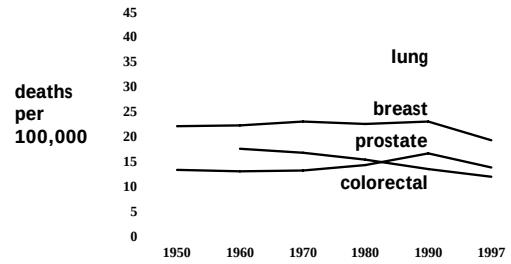
FIGURE 1: COPD AGE-ADJUSTED DEATH RATE, BY SEX, 1979-1998 (1)



	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998
BOTH SEXES	14.0	14.9	15.3	15.2	16.2	16.6	17.5	17.6	17.4	18.0	18.0	18.3	18.6	18.5	20.0	19.5	19.3	19.5	19.7	19.9
MALE	23.8	25.1	25.2	24.5	25.9	25.9	26.8	26.5	25.7	26.3	25.2	25.9	25.7	25.2	26.5	25.5	25.0	24.6	25.9	24.7
FEMALE	7.0	7.9	8.4	8.7	9.6	10.2	11.2	11.5	11.8	12.5	13.1	13.2	13.9	14.0	15.5	15.4	15.4	15.9	16.1	16.5

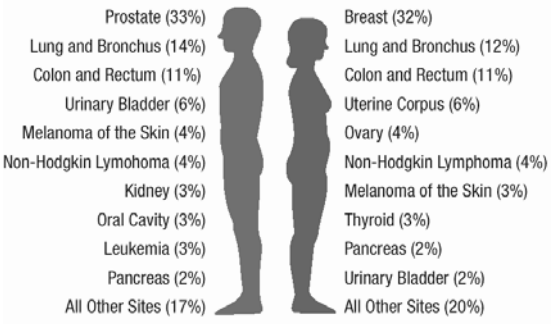
SOURCE: NATIONAL CENTER FOP HEALTH STATISTICS: ANNUAL SUMMARY OF VITAL STATISTICS, 1979-1998

Trends in cancer mortality in the U.S., 1950-1997



National Center for Health Statistics

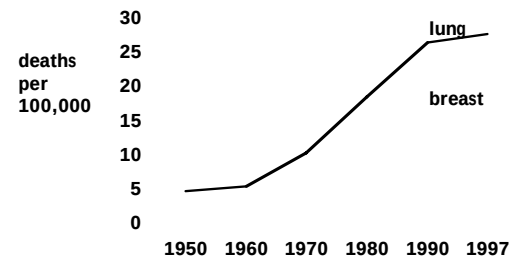
Estimated New Cases



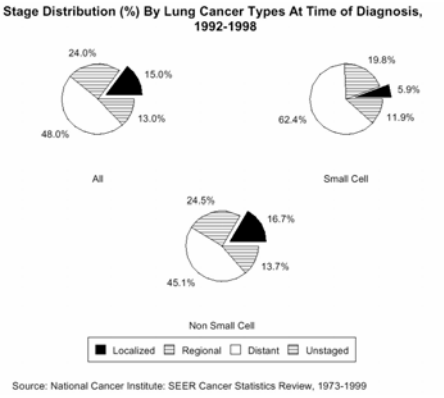
Prostate (33%)	Breast (32%)
Lung and Bronchus (14%)	Lung and Bronchus (12%)
Colon and Rectum (11%)	Colon and Rectum (11%)
Urinary Bladder (6%)	Uterine Corpus (6%)
Melanoma of the Skin (4%)	Ovary (4%)
Non-Hodgkin Lymohoma (4%)	Non-Hodgkin Lymphoma (4%)
Kidney (3%)	Melanoma of the Skin (3%)
Oral Cavity (3%)	Thyroid (3%)
Leukemia (3%)	Pancreas (2%)
Pancreas (2%)	Urinary Bladder (2%)
All Other Sites (17%)	All Other Sites (20%)

Ca 2003; 53:5--26

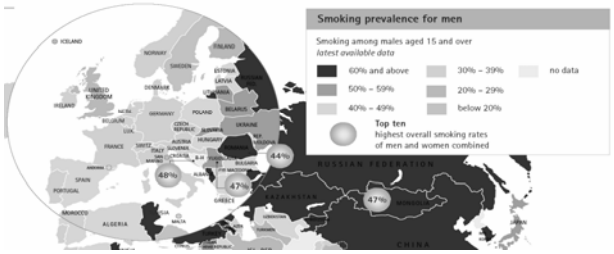
Trends in cancer deaths in U.S. women, 1950-1997



National Center for Health Statistics

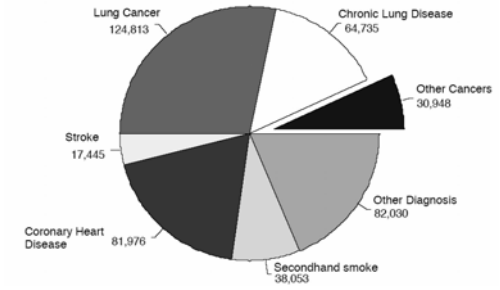


Smoking prevalence in Europe: men



Source: World Health Organization

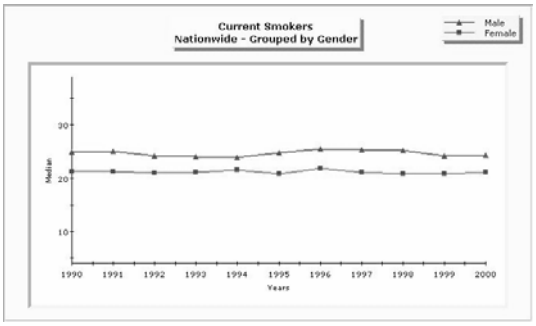
Tobacco-related deaths annually, U.S.



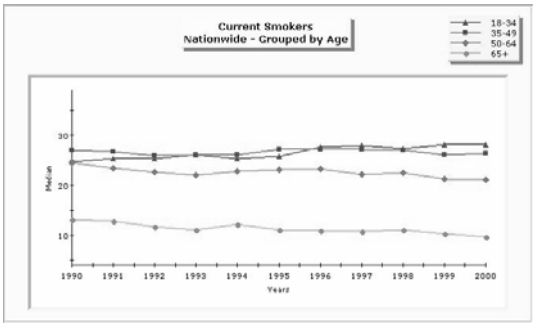
Source: CDC, ALA

Smoking prevalence in Europe: women

Source: World Health Organization

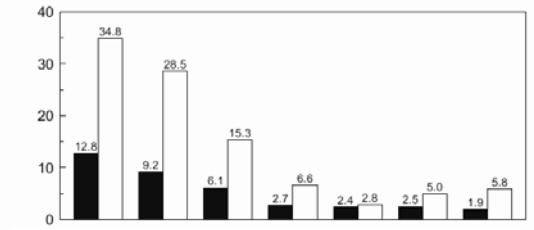


Source: CDC, National Center for Chronic Disease Prevention and Health Promotion, 2002



Source: CDC, National Center for Chronic Disease Prevention and Health Promotion, 2002

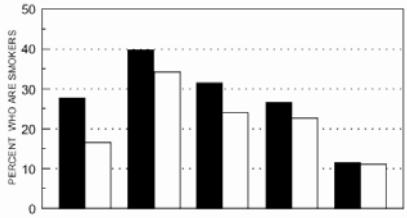
FIGURE 7: PERCENTAGE OF MIDDLE AND HIGH SCHOOL STUDENTS WHO ARE CURRENT USERS OF TOBACCO, BY TYPE - NATIONAL YOUTH TOBACCO SURVEY, 1999



	Any Tobacco	Cigarette	Cigar	Smokeless Tobacco	Pipe	Bidi	Kretek
Middle School ■	12.8	9.2	6.1	2.7	2.4	2.5	1.9
High School □	34.8	28.5	15.3	6.6	2.8	5.0	5.8

Source: Youth Tobacco Surveillance - MMWR Vo. 49, No. SS-10

FIGURE 5: CURRENT CIGARETTE SMOKING AMONG ADULTS, BY LEVEL OF EDUCATION, 1998



Level of Education	<8 Yrs.	9-11 Yrs.	12 Yrs.	13-15 Yrs.	16+ Yrs.
MALE ■	27.7	39.7	31.5	26.6	11.5
FEMALE □	16.7	34.3	24.1	22.8	11.2
ALL	21.9	36.8	27.4	24.6	11.3

Summary

It is important to know as much as possible about teenage smoking patterns and attitudes. Today's teenager is tomorrow's potential regular customer, and the overwhelming majority of smokers first begin to smoke while still in their teens. In addition, the ten years following the teenage years is the period

Because of our high share of the market among the youngest smokers, Philip Morris will suffer more than the other companies from the decline in the number of teenage smokers. For at least the next decade, however, the population trends will have a much more powerful influence, and in this regard we would appear to be the least vulnerable of all the companies, as will be discussed later in this report.

Philip Morris Co. memorandum, March 31, 1981

Limiting morbidity and mortality from tobacco use

- **Medical model**
  - **Smoking cessation**
  - **Early detection and treatment of smoking related illness:**
    - **Lung cancer screening**
    - **Prevention and treatment of COPD**
- **Public health model**
  - **Limiting access to tobacco**
    - **Raising cigarette tax**
    - **Enforcing age limits for purchase**
    - **Smoking restrictions in workplaces and public facilities**
  - **Discouraging use of tobacco**
    - **School-based initiatives**
    - **Counter advertising**

RJR
July 18, 1980

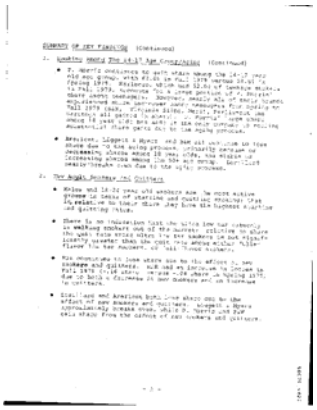
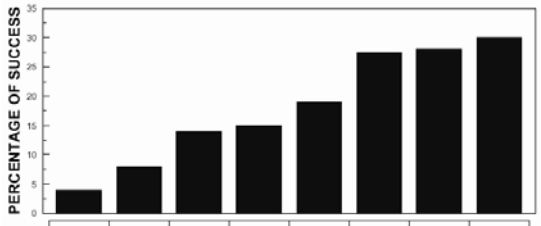


FIGURE 10: SUCCESS RATES FOR VARIOUS CESSATION METHODS, 1998



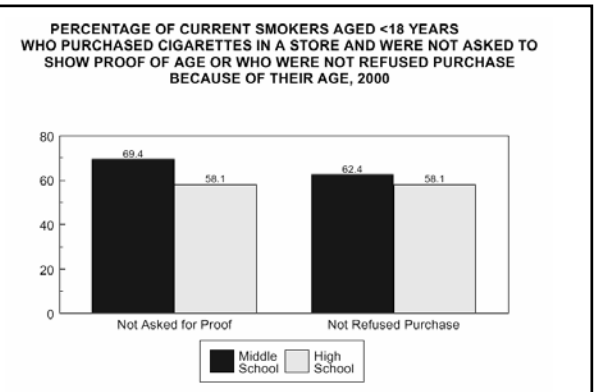
Self Help Only	Patch	Gum	Behavioral	Inhalers	Rplcmt + Bhvr	Prescriptions	Nasal Spray
4.0	8.0	14.0	15.0	19.0	27.5	28.0	30.0

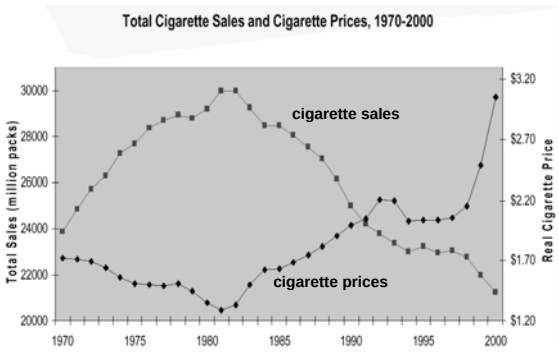
Source: CDC Office on Smoking & Health - Cessation Division

Hutchinson Smoking Prevention Project: Long-Term Randomized Trial of School-Based Tobacco Use Prevention

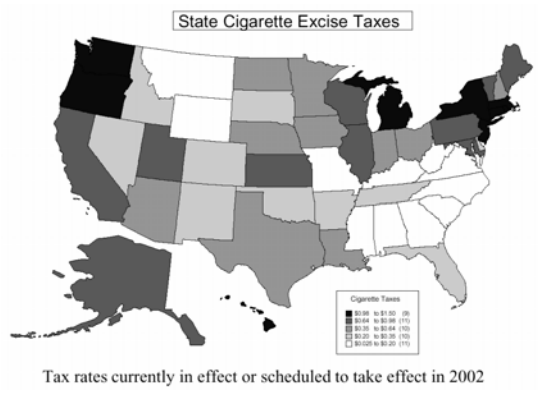
- 40 school districts in Washington State randomized to provide comprehensive anti-tobacco curriculum (based on CDC and NCI recommendations) in grades 3-12 or standard health curriculum
- Main study endpoints were smoking in grade 12 and 2 years after high school
- 8388 students entering third grade were subjects in the study; follow-up data available on 93%
- Prevalence of daily smoking at study conclusion: 24.66% in control districts, 24.41% in experimental districts

Peterson et. al., J Natl Can Inst 2000; 92: 1979-1991





APHA, 2002



APHA, 2002

Workplace smoking ban, Ireland

from McElvaney NG. NEJM 2004; 2231-2234

Smoke-Free Workplace Act of 2002 (NYC Local Law 47)

- Law took effect March 30, 2003
- Bans smoking in all indoor workplaces in New York City, including bars and restaurants of any size.
- Exemptions for 7 currently existing cigar bars.
- Exemptions for owner operated bars.
- Restaurants will be allowed to build completely enclosed, negative pressure ventilated smoking rooms into which no employee will be allowed until the last customer of the day has left. Clause sunsets after three years.
- New York State has adopted a similar law that covers the entire state

The New York Times

Legislators Pass Smoking Ban in New Jersey

By RICHARD LEZIN JONES and JOSH BENSON
Published: January 10, 2006

TRENTON, Jan. 9 - New Jersey lawmakers approved a far-reaching ban Monday on smoking in indoor public places that includes virtually all of the state's bars and restaurants but not the gambling areas of Atlantic City's 12 casinos.