Epidemiology

Translational Research in Clinical Oncology
October, 2016

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Division of Cancer Epidemiology and Genetics,
National Cancer Institute
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A Population Perspective
Cigarettes and culture
Decades of change
Epidemiology
DCEG
NIH epidemiology

National Cancer Institute

Division of Cancer Epidemiology and Genetics

Genetic Epidemiology Branch

We are INTRAMURAL
~ 85% $$ are extramural

Cancer ETIOLOGY

Other Branches focus on Nutrition, Hormones, Infection, Occupation, Statistics, Radiation
Division of Cancer Epidemiology and Genetics (DCEG)

• Identify the environmental and genetic causes of cancer in the population
• High quality, high impact, value-added research
• National and international in scope
• Scientific partnerships in molecular epidemiology across NCI and beyond
Major public health advances

Regulatory changes
- Drinking water
- Gasoline (less benzene)
- Workplace safety (diesel)
- Safer farming

Clinical practice
- Cancer susceptibility syndromes
- Second cancers among cancer survivors

Preventive interventions
- Safer CT scans
- Risk-reducing surgeries for individuals at high-risk
- Benefits of healthy weight and physical activity
- Efficacy of human papillomavirus vaccine for cervical cancer
- Eliminating indoor pollution
Collaborations

Collaborations around the world
DCEG
Cancer risk

Cancer risk assessment tools

Breast Cancer Risk Assessment Tool
An interactive tool to help estimate a woman's risk of developing breast cancer

Melanoma Risk Assessment Tool
An interactive tool to help estimate a person's risk of developing invasive melanoma

Colorectal Cancer Risk Assessment Tool
An interactive tool to help estimate a person's risk of developing colorectal cancer
Epidemiologists are ethically prohibited from doing experiments on people.

So, we observe large populations and see how their outcomes relate to what people do (i.e., smoke, drink, eat, etc.)

_This weakness of the ‘observational’ argument were exploited by tobacco companies to deny evidence linking cigarettes and cancer......_
Hierarchy of studies
Goals of Epidemiology
1. Identify the causes of cancer
2. Quantify risks/identify risk groups
3. Understand mechanisms
4. Public health and health services
5. Identify syndromes
6. Prevention
Epidemiologists emphasize prevention

Rationale:
Effective (think polio, smallpox, smoking cessation, clean water, HPV…)
Cheaper (compared to late stage interventions)
Public health orientation
Eliminate disease at the source

Downsides
Requires time to demonstrate effectiveness
Less dramatic than treatment
Can’t see disease you have prevented
Lives saved appear in statistics— not grateful patients
Less positive political impact (= funding)
Political opposition from powerful groups (Tobacco, Soft Drink Companies, Polluters, etc.)
No Nobel Prizes

Primary = directed to susceptibility stage
Example: Needle exchange to prevent AIDS, HPV vaccine

Secondary = directed to subclinical stage
Example: Screen for cervical cancer with Pap Smear

Tertiary = directed to clinical stage
Example: Treat diabetic retinopathy to prevent blindness
Epidemiologists worry about bias

Bias = systematic deviation from truth

Epidemiologists fret about PARTICIPATION RATES if too low.....

Study subjects not REPRESENTATIVE of the target populations

Results not be GENERALIZABLE to the general population

Selection Bias = subjects in the study are ‘selected’ and therefore nonrepresentative
Participation rate

Pilot studies: participation rate

<table>
<thead>
<tr>
<th>30%</th>
<th>49%</th>
<th>73%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phone</td>
<td>Invitation letter</td>
<td>New interviewers</td>
</tr>
<tr>
<td>Survey</td>
<td>Follow-up by phone</td>
<td>Physicians’ call</td>
</tr>
<tr>
<td></td>
<td>In hospital</td>
<td>Gas coupon</td>
</tr>
<tr>
<td></td>
<td>Advertisements</td>
<td>TV ads</td>
</tr>
<tr>
<td></td>
<td>Cash award</td>
<td>New invitation letter</td>
</tr>
<tr>
<td></td>
<td>Physicians’ letter</td>
<td>Mayor’s letter</td>
</tr>
<tr>
<td></td>
<td>Home/hospital</td>
<td>Toll-free phone line</td>
</tr>
</tbody>
</table>

Total number of subjects in pilot investigations:
156 Cases - 212 Controls

- Clinical data: 99%
- Questionnaires: 87%
- Biospecimens: 97%
Controls for epidemiologists

Epidemiologists worry about controls

Population controls
- Expensive
- Most representative (section bias still possible)
- Calculate ABSOLUTE risks (contract with RELATIVE risks)
- Increasingly difficult - RDD problematic!
- Defined in time and space
- Inclusion and exclusion criteria
- High response rate!

‘Convenience’ controls are the least desirable
- Biased by differences in:
  - Age, risk factors, ethnicity, education,
  - participation rate, access to care, SES…. 

Gerstman, 2003
Epidemiologist as consultant

Questions the consulting epidemiologist will ask:
Your study design is…? 
Your controls came from….?
Did you collect key covariate data?
Did you consider bias, confounding?
What was the original hypothesis? (data dredging)
Have you done power calculations?
How did you validate your marker?

Epidemiologist is helpful when a question involves the population (as opposed to an individual, organ, cell, etc.)
Can you explain

The most common question epidemiologists get!

Can you explain why..............

My grandmother smoked all her life. her exercise was the TV remote, she never used a seat belt, she ate bacon and buttered toast for breakfast... she drank shots on her 90th birthday she outlived all her doctors......

The race is not to the swift or the battle to the strong, nor does food come to the wise or wealth to the brilliant or favor to the learned; but time and chance happen to them all. (Ecclesiastes)

Deterministic vs. Probabilistic
Cancer Maps

Cancer Mortality Rates by State Economic Area (Age-adjusted 1970 US Population)
Melanoma of Skin: White Males, 1950-69

US = 1.57/100,000
2.37-4.07 (highest 10%)
2.06-2.36
1.85-2.07
1.69-1.84
Geographic Information Systems

GIS

Geographic patterns of disease and exposure via satellite
Examples, used to estimate nitrate, pesticide levels (see, Ward et al., 2000)
SEER
Surveillance, Epidemiology, and End Results (SEER) Program
26% of US population incidence and survival, patient demographics, primary tumor site, tumor morphology and stage at diagnosis, first course of treatment, and follow-up for vital status
comprehensive source of population-based information
Welcome to the Surveillance, Epidemiology and End Results (SEER) Program, a premier source for cancer statistics in the United States. SEER collects information on incidence, survival, and prevalence from specific geographic areas representing 26 percent of the US population and compiles reports on all of these plus cancer mortality for the entire US. This site is intended for anyone interested in US cancer statistics or cancer surveillance methods.

You can use the tabs to find summarized statistics under Cancer Statistics; instructions for accessing and downloading the data and the software to analyze it under Accessing Datasets & Tools; reports, monographs and the SEER Bibliography under Publications; and data collection manuals, training, and resources under Information for Cancer Registrars.

- SEER Program Overview
- SEER Registries
- Research Activities
- Quality Improvement

Cancer Stat Fact Sheets
Get printouts of most recent statistics for each type of cancer.

Select a cancer type from the list:

—Choose a Cancer Site— Go
Cancer Incidence Rates

Cancer Incidence Rates*, All Sites Combined, All Races, 1975-2000

*Age-adjusted to the 2000 US standard population.
Cancer Rates for Men


Rate Per 100,000

- Prostate
- Lung
- Colon and rectum
- Urinary bladder
- Non-Hodgkin lymphoma

*Age-adjusted to the 2000 US standard population.

75% increase due to PSA screening
Cancer by sex and race

Cancer Incidence Rates* by Sex and Race, All Sites, 1975-2000

*Age-adjusted to the 2000 US standard population.
Cancer and Children

Cancer Incidence & Death Rates* in Children 0-14 Years, 1975-2000

*Age-adjusted to the 2000 Standard population.
Childhood Cancers

Childhood Cancers (< 14 ys)

* Incidence
  8,600 new cases/yr
  12,400 (0 – 19 ys)

* Mortality
  1,500 deaths/yr
  2,300 (0 – 19 ys)
  rates ↓ 50% since 1973

* Etiology -- poorly understood

Treatment Effective!
How do you prove a cause?

(CLASSICAL)
1. It should confer high risk
2. It should be consistent
3. Dose response
4. Cause occurs first!
5. Biology makes sense

How do you prove a cause?
Causation
How do you prove a cause?
(TODAY)
1. Mendelian Randomization
2. Molecular Epidemiology
3. Mediation analysis
Lung Cancer and smoking
Lung cancer

The graph shows the annual number of cigarettes smoked per person per year and the annual deaths from lung cancer per 100,000 population from 1900 to 1980. The lines represent male smoking, male lung cancer, female smoking, and female lung cancer.
Lung cancer
Lung cancer
Lung cancer risks

Relative Risks of Lung Cancer According to Years Since Quitting Smoking among Males in Three Cohort Studies of Smokers

Years Since Quitting Smoking

<table>
<thead>
<tr>
<th>Years Since Quitting Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>20</td>
</tr>
</tbody>
</table>

Graph showing the relative risks of lung cancer over different years since quitting smoking.
Population Perspective
Accomplishments
Crisis communications over the decades

- Silicone breast implants
- Chernobyl accident
- Oral cancer and mouthwash (alcohol)
- Abortion and breast cancer
- Cell phones and brain tumors
- Fukushima disaster
What are the general risk factors for cancer?

- Increasing age
- Environmental factors
- Genetic factors
- Combinations of the above!
Most Cancer is due to the Environment

Dramatic differences in cancer rates by geography and over time are only compatible with extrinsic environmental causes.

Established by a vast body of descriptive, ecological, and analytical epidemiology.
## International Variation in Cancer Rates

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>H/L</th>
<th>highest</th>
<th>lowest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>155</td>
<td>Australia</td>
<td>Japan</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>100</td>
<td>Hong Kong</td>
<td>UK</td>
</tr>
<tr>
<td>Prostate</td>
<td>70</td>
<td>US (Blacks)</td>
<td>China</td>
</tr>
<tr>
<td>Liver</td>
<td>50</td>
<td>China</td>
<td>Canada</td>
</tr>
<tr>
<td>Cervix</td>
<td>28</td>
<td>Brazil</td>
<td>Israel</td>
</tr>
<tr>
<td>Stomach</td>
<td>22</td>
<td>Japan</td>
<td>Kuwait</td>
</tr>
<tr>
<td>Lung</td>
<td>19</td>
<td>US (Blacks)</td>
<td>India</td>
</tr>
<tr>
<td>Colon</td>
<td>19</td>
<td>US (Whites)</td>
<td>India</td>
</tr>
<tr>
<td>Bladder</td>
<td>16</td>
<td>Switzerland</td>
<td>India</td>
</tr>
<tr>
<td>Pancreas</td>
<td>11</td>
<td>US (Blacks)</td>
<td>India</td>
</tr>
<tr>
<td>Ovary</td>
<td>8</td>
<td>Maori (NZ)</td>
<td>Kuwait</td>
</tr>
<tr>
<td>Breast</td>
<td>7</td>
<td>Hawaii</td>
<td>Israel</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5</td>
<td>Canada</td>
<td>India</td>
</tr>
</tbody>
</table>
Cancer maps and exposure
Lung cancer mortality rate in Xuan Wei is among the highest in China.

County-specific female lung cancer mortality rates (per 100,000, 1973-75)
Cancer and prevention
Skull with cigarette
Tobacco and public health

major cause of preventable morbidity & mortality
1/5 US deaths (450,000 USA, 3M world/y)
10 million tobacco deaths/yr (2030, WHO)
30% of all cancer, 8 sites, all difficult to treat
tobacco related disease costs
Medicare/ Medicaid > $10B/yr each

In spite of widespread knowledge of the health consequences of smoking
- rates in US adults, 15% (2014)
- individual smoking cessation very difficult
Tobacco consumption

Per-Capita Consumption of Different Forms of Tobacco in The U.S. 1880-2003

Pounds of Tobacco Per-Capita

Year

Data Source USDA

Cigarettes
Cigars
Pipe/roll your own
Chewing
Snuff
Environmental Tobacco Smoke (ETS)
never-smoking women spouses of smokers at higher risk
then spouses of non-smokers (Hirayama, Trichopoulos, 1981)
NRC Report
Nonsmoking spouses have 30% increased risk
25% of cases in non-smokers due to smoking
~ 3000 deaths per year
ETS classified as Class A human carcinogen
Metanalyses conclude that ETS (both workplace and at home)
is a significant risk factor, e.g. Law, 1997
Summary:
Evidence implicating ETS suggests dose-response
extends to lowest exposures, i.e. no threshold
LITS
Smoking increases mortality
What are alcohol-associated cancers?
Oral
Pharynx
Esophagus
Larynx
Liver
Coffee drinking
Ionizing Radiation
Leukemia (AML, but not CLL*)
Breast
Lung
Thyroid
Head and neck cancer
Cancer risk

Cancer Risks Following Chernobyl Accident

- I-131 dose-response for thyroid cancer significantly elevated (ERR=2.2/Gy) in residents <18 yrs
- Elevated risks persisted for 2 decades; no decrease to date

Brenner...Hatch...Lubin...Bouville...Ron.
Environ Health Perspect 2011

Dose-response similar for chronic lymphocytic leukemia (CLL) (ERR=4.1/Gy) and for non-CLL leukemia (ERR=2.7/Gy) in clean-up workers

Romanenko...Hatch...Bouville...Ron et al.
Radiat Res 2008
<table>
<thead>
<tr>
<th>Type of XRT Implicated</th>
<th>Study</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-Bomb</td>
<td>Japan</td>
<td>Breast, Leuk,</td>
</tr>
<tr>
<td>Gastric, Thy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A-Bomb</td>
<td>Marshall Island</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Medical</td>
<td>Breast/Mastitis</td>
<td>Breast</td>
</tr>
<tr>
<td>Medical</td>
<td>Hemangiaoma</td>
<td>Breast, Thyroid</td>
</tr>
<tr>
<td>Medical</td>
<td>Hodgkin’s</td>
<td>Breast, lung,</td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>TB-Flouroscopy</td>
<td>Breast</td>
</tr>
<tr>
<td>Radionuclides (Th-232)</td>
<td>Thorotrast</td>
<td>Leukemia, Liver</td>
</tr>
<tr>
<td>Radionuclides</td>
<td>Spondylytis</td>
<td>Bones (Ra-224)</td>
</tr>
<tr>
<td>Occupation</td>
<td>Radium Dial painters</td>
<td>Bone</td>
</tr>
<tr>
<td>Occupation</td>
<td>Rad Technicians</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Occupation</td>
<td>Chernobyl Cleanup</td>
<td>?</td>
</tr>
<tr>
<td>Environmental</td>
<td>Indoor radon</td>
<td>Lung</td>
</tr>
</tbody>
</table>
Skin cancer

Non-Ionizing Radiation (UV/sun)

1 Basal cell
2 Squamous cell
3 Melanoma

Tanning beds!
Skin damage

THE SUN YOU GET TODAY MAY NOT LOOK SO BEAUTIFUL TOMORROW.
## Infections and Cancer

<table>
<thead>
<tr>
<th>Infection</th>
<th>Cancer Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human papillomavirus</td>
<td>Cervical cancer</td>
</tr>
<tr>
<td></td>
<td>Vulvar/vaginal cancer</td>
</tr>
<tr>
<td></td>
<td>Anal cancer</td>
</tr>
<tr>
<td></td>
<td>Penile cancer</td>
</tr>
<tr>
<td></td>
<td>Oropharyngeal cancer</td>
</tr>
<tr>
<td>Hepatitis B &amp; C virus</td>
<td>Hepatocellular</td>
</tr>
<tr>
<td></td>
<td>Non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em></td>
<td>Gastric cancer</td>
</tr>
<tr>
<td>Liver flukes</td>
<td>Cholangiocarcinoma</td>
</tr>
</tbody>
</table>
## Newer infections

### Newer infectious hypotheses

<table>
<thead>
<tr>
<th>VIRUS</th>
<th>Human Cancer (hypothesized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>hepatocellular cancer</td>
</tr>
<tr>
<td>EBV</td>
<td>NHL</td>
</tr>
<tr>
<td>KSHV (HHV8)</td>
<td>NPC</td>
</tr>
<tr>
<td>HPV-16, -18, -33, -39</td>
<td>Hodgkin’s lymphoma</td>
</tr>
<tr>
<td></td>
<td>leiomyosarcoma</td>
</tr>
<tr>
<td>Polyomavirus</td>
<td>Kaposi’s sarcoma</td>
</tr>
<tr>
<td>HIV</td>
<td>Vulvo-vaginal cancer</td>
</tr>
<tr>
<td></td>
<td>Anal cancer</td>
</tr>
<tr>
<td></td>
<td>Penile cancer</td>
</tr>
<tr>
<td></td>
<td>Oropharyngeal cancer</td>
</tr>
<tr>
<td></td>
<td>Merkel cell virus/ <strong>CLL?</strong></td>
</tr>
<tr>
<td></td>
<td>NHL</td>
</tr>
</tbody>
</table>
Fusobacterium and colorectal carcinoma
Oropharynx cancers
# Occupational exposures

## OCCUPATIONAL EXPOSURES -- HUMAN CARCINOGENS

<table>
<thead>
<tr>
<th>EXPOSURE</th>
<th>SITE OF CANCER</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-Aminobiphenyl</td>
<td>Bladder</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Lung, skin</td>
</tr>
<tr>
<td>Asbestos</td>
<td>Lung, pleura, peritoneum</td>
</tr>
<tr>
<td>Benzene</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Benzidine</td>
<td>Bladder</td>
</tr>
<tr>
<td>beta-Naphthylamine</td>
<td>Bladder</td>
</tr>
<tr>
<td>Coal tars and pitches</td>
<td>Lung, skin</td>
</tr>
<tr>
<td>Mineral oils</td>
<td>Skin</td>
</tr>
<tr>
<td>Mustard gas</td>
<td>Pharynx, lung</td>
</tr>
<tr>
<td>Radon</td>
<td>Lung</td>
</tr>
<tr>
<td>Soot, tars, and oils (polycyclic hydrocarbons)</td>
<td>Lung, skin</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>Liver</td>
</tr>
<tr>
<td>Wood dusts (furniture)</td>
<td>Nasal sinuses</td>
</tr>
</tbody>
</table>
Diesel Exhaust in Miners Study
(OEEB, BB, NIOSH)

- Significant exposure-response based on quantitative historical exposure data, adjusting for smoking and other confounders (Silverman et al, JNCI, 2012)
- Played an influential role in IARC’s reclassification of diesel exhaust as a Group 1 carcinogen
A Population Perspective on Cancer
What is epidemiology?
What has epidemiology accomplished?
What can go wrong?
What can really go wrong?
What next?
A Population Perspective on Cancer
What is epidemiology?
What has epidemiology accomplished?
What can go wrong?
What can really go wrong?
What next?
Gaps in understanding
Chronic Lymphocytic Leukemia

- Most common leukemia of Western world.
- 30% of adult leukemia in USA
- Less frequent in Asia and Latin America.
- Male to female ratio is 2:1.
- Median age at diagnosis is 65-70 years.
- No extrinsic environmental causes known
- Family history is the most important risk factor
Gaps
Cancer and genetic changes
Genetic distinctions
gaps on the GENETIC side

New technologies have accelerated gene discovery but…

• Genes associated with common cancers confer minimal risk
• and explain only a small portion of the variation
• and do not help much with risk models
• How G and E work in concert is poorly understood

• Many cancer families- genes remain obscure
All Cancer is due to the Genetic changes
All cancer cells exhibit changes in their DNA that are passed on and maintain the ‘malignant phenotype’
GETTING ORIENTED

1. Germline or Somatic
   (inherited or in the tumor)
2. Family or Population
   (rare or common)
3. Candidate or Agnostic
   (candidate gene study or GWAS)
Rare Genes

To look for rare genes you need families..........

High risk kindreds like this likely harbor rare genes that confer high risk- if we knew what were they would be clinically important....
## Cloned Familial Tumor Suppressor Genes

<table>
<thead>
<tr>
<th>Disease</th>
<th>Gene</th>
<th>Chromosome</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinoblastoma</td>
<td>RB1</td>
<td>13q14</td>
<td>1986</td>
</tr>
<tr>
<td>Wilms’ tumor</td>
<td>WT1</td>
<td>11p13</td>
<td>1990</td>
</tr>
<tr>
<td>Li-Fraumeni syndrome</td>
<td>p53</td>
<td>17p13</td>
<td>1990</td>
</tr>
<tr>
<td>Neurofibromatosis 1</td>
<td>NF1</td>
<td>17q11</td>
<td>1990</td>
</tr>
<tr>
<td>Neurofibromatosis 2</td>
<td>NF2</td>
<td>22q12</td>
<td>1993</td>
</tr>
<tr>
<td>von Hippel-Lindau</td>
<td>VHL</td>
<td>3p25</td>
<td>1993</td>
</tr>
<tr>
<td>Familial melanoma 1</td>
<td>p16</td>
<td>9p21</td>
<td>1994</td>
</tr>
<tr>
<td>Familial breast 1</td>
<td>BRCA1</td>
<td>17q21</td>
<td>1994</td>
</tr>
<tr>
<td>Familial breast 2</td>
<td>BRCA2</td>
<td>13q12</td>
<td>1995</td>
</tr>
<tr>
<td>Basal cell nevus</td>
<td>PTC</td>
<td>9q22</td>
<td>1996</td>
</tr>
</tbody>
</table>
GWAS etiology hits

Published Cancer GWAS Etiology Hits: 8.10.12

~240 Disease Loci marked by SNPs
1 Locus marked by a CNV
Lung cancer challenge

**The lung cancer challenge....**

1- Drives overall cancer mortality in the US and worldwide
2- **Treatment** and screening pose challenges
3- Lung cancer is paradigm for genetics of complex disease
4- Clearest example of environment and gene in cancer
5- The clearest example of a genetically influenced behavior associated with the leading public health problem in the world

### 2009 Estimated US Cancer Deaths*

<table>
<thead>
<tr>
<th>Site</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>30%</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>9%</td>
<td>15%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>25%</td>
<td>25%</td>
</tr>
</tbody>
</table>

### Trends in Five-year Relative Survival (%) Rates, US, 1975-2004

<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>50</td>
<td>54</td>
<td>66</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>75</td>
<td>79</td>
<td>89</td>
</tr>
<tr>
<td>Colon</td>
<td>52</td>
<td>59</td>
<td>65</td>
</tr>
<tr>
<td>Leukemia</td>
<td>35</td>
<td>42</td>
<td>51</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>13</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>Melanoma</td>
<td>82</td>
<td>87</td>
<td>92</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>48</td>
<td>53</td>
<td>65</td>
</tr>
<tr>
<td>Ovary</td>
<td>37</td>
<td>40</td>
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</tr>
<tr>
<td>Pancreas</td>
<td>3</td>
<td>3</td>
<td>5</td>
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<tr>
<td>Prostate</td>
<td>69</td>
<td>76</td>
<td>99</td>
</tr>
<tr>
<td>Rectum</td>
<td>49</td>
<td>57</td>
<td>67</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>74</td>
<td>78</td>
<td>81</td>
</tr>
</tbody>
</table>
Molecular epidemiology
Traditional epidemiology

Exposure: Tobacco → Disease: Lung Cancer
Integrative epidemiology
Lung cancer case control
Integrative epidemiology

**Instruments**
- Fagerstrom Nicotine Dependency
- DSM-IV Nicotine Dependency
- Hospital Anxiety and Depression
- Eysenck Personality Inventory
- CESD- Depression
- Attention Deficit Inventory
- Attitudes and Knowledge about Smoking
- Intention to Quit Smoking

**Diagram:**
- B → E → ID → EBE → ASF → ED → D → O
- Exposure → Internal dose → Early biological effect → Altered structure or function → Early disease → Disease → Outcome

**Treatment:**
- Survival
- Prognostic and Clinical
Population perspective
Population perspective
Consortia
PhenX… approach to expand data collection and reduce misclassification
A Population Perspective on Cancer
What is epidemiology?
What has epidemiology accomplished?
What can go wrong?
What can really go wrong?
What next?
A Population Perspective on Cancer
What is epidemiology?
What has epidemiology accomplished?
What can go wrong?
What can really go really go wrong?
What next?
Paradigm change
Obesity rates
Obesity in the world and US
Diabetes trends
Diabetes in US
Obesity worldwide
Being overweight
Obesity causes
What causes obesity?
Dietary habits
Food pyramid
Institutional investment
Standard American diet
Obesity food
Dietary recommendations
Nutritional epidemiology
Food questionnaire
Challenges
Low fat trials
Obesity rates
Sugar
Late at night
Insulin resistance
Insulin resistance
Metabolic factors
Population perspective
Population perspective
Technology features
Lung cancer risk factors
Sleep
Sleep and obesity/smoking
Physical Activity

X
Vital Signs

Vital signs

Heart rate
Heart rate variability
Arrhythmias
Max and min
Relation to diet/exercise

Examples:
- Polar line of ‘watches’
- FitBit
- Adidas, Nike, etc.
- newer Apple, Samsung
Circadian variation

Internal body time is related to:
disease susceptibility
chronotherapy

Internal body time determined by 2 blood samples

Also can be determined by activity/sleep/food cycles

Human body metabolite timetable indicates internal body time.

PNAS 11sept2012 Kasukawa T et al.
Oxygen saturation
Social data

Data on social factors often absent from epidemiologic study designs
Can quantitate:
contacts,
‘friends’,
indices of interaction,
relationships,
frequency of contact

Social networks

The Spread of Obesity in a large social network over 32 years.
Future applications
Virtual cohort