

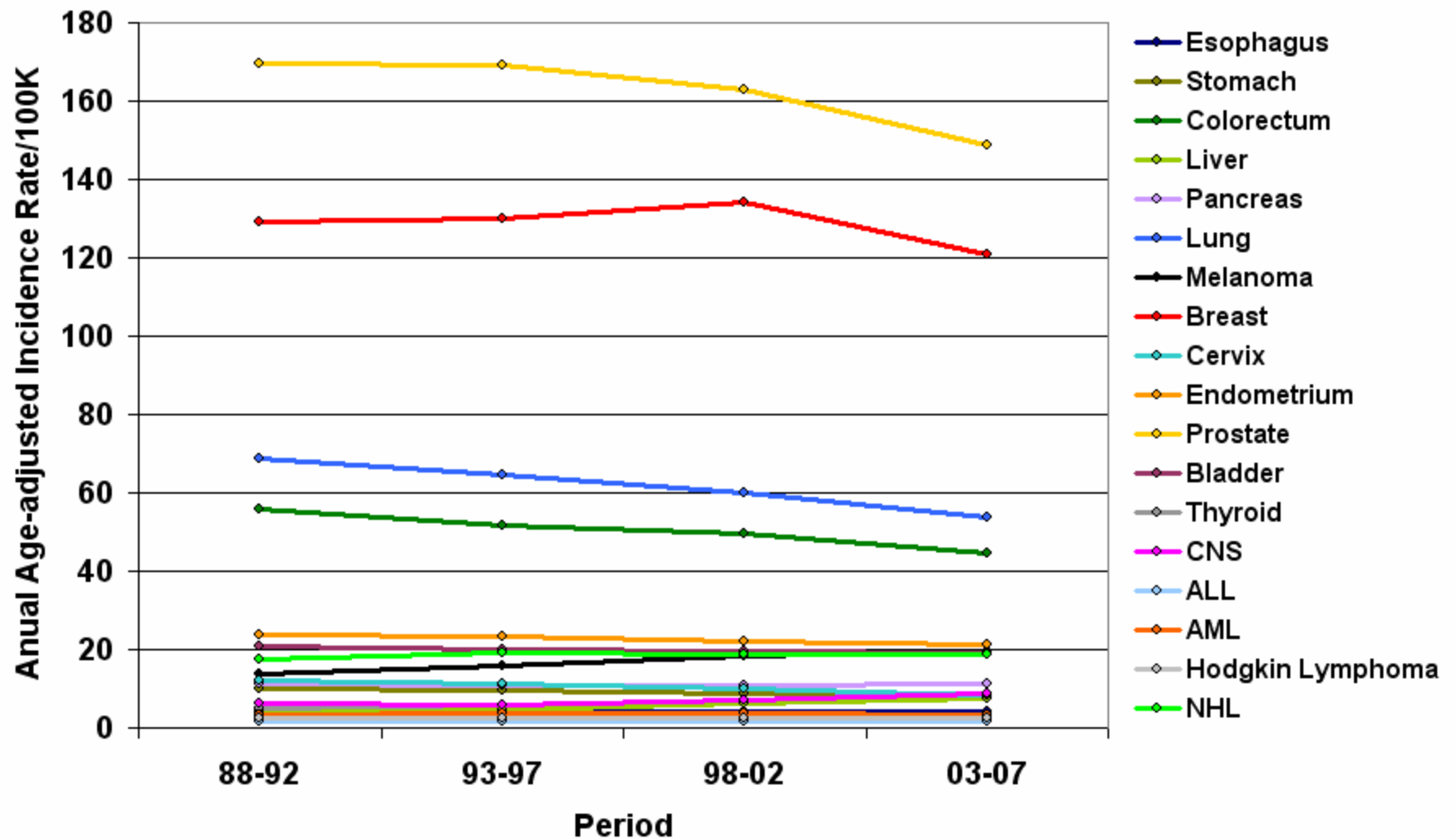
Cancer in Carlsbad

Thomas Mack, M.D., M.P.H.
Keck School of Medicine
University of Southern California

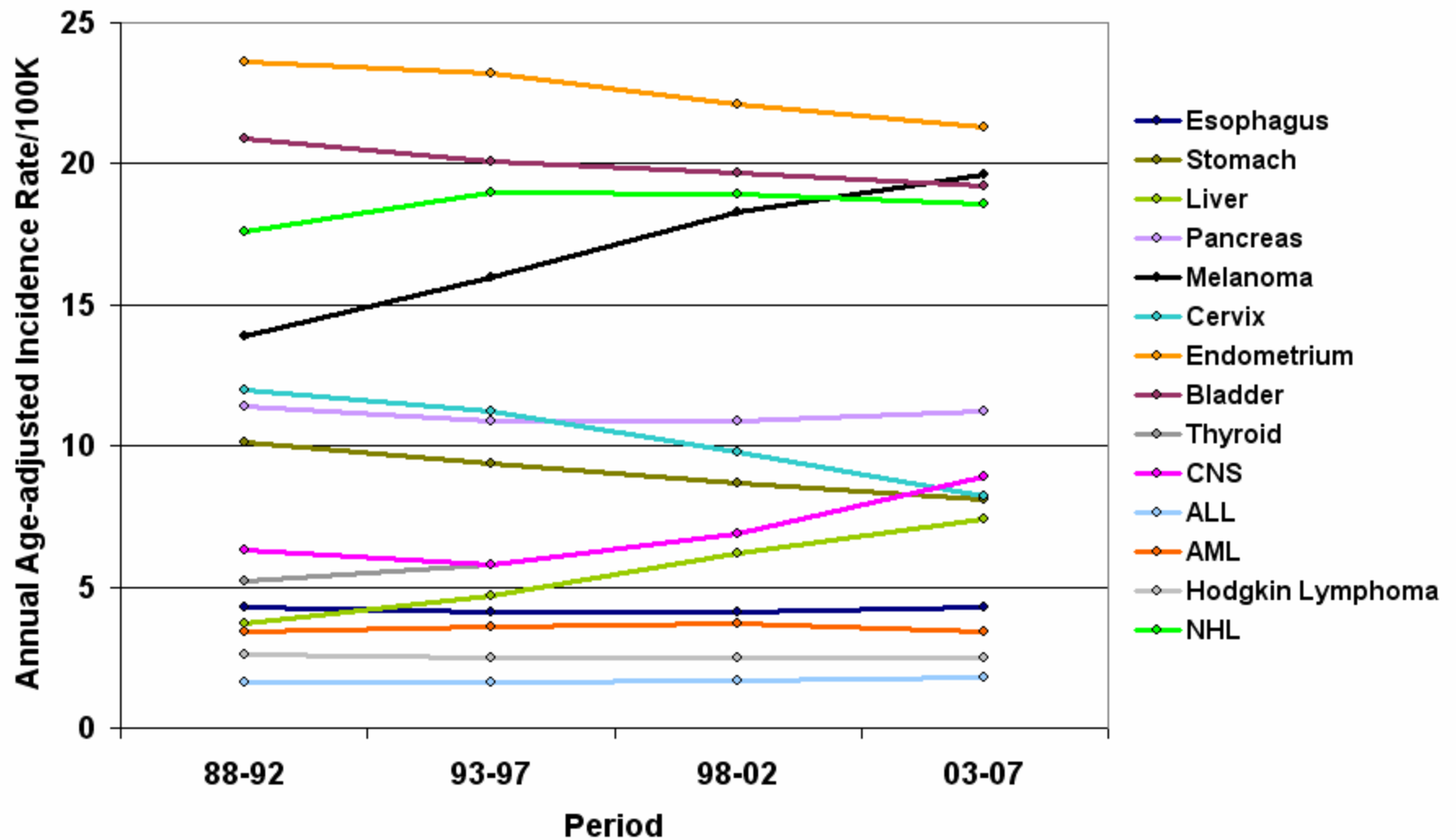
Outline

- **Carcinogens**
- **Detecting a real cancer excess**
- **Cancers in California**
- **Cancers in Carlsbad**
- **Prevention**

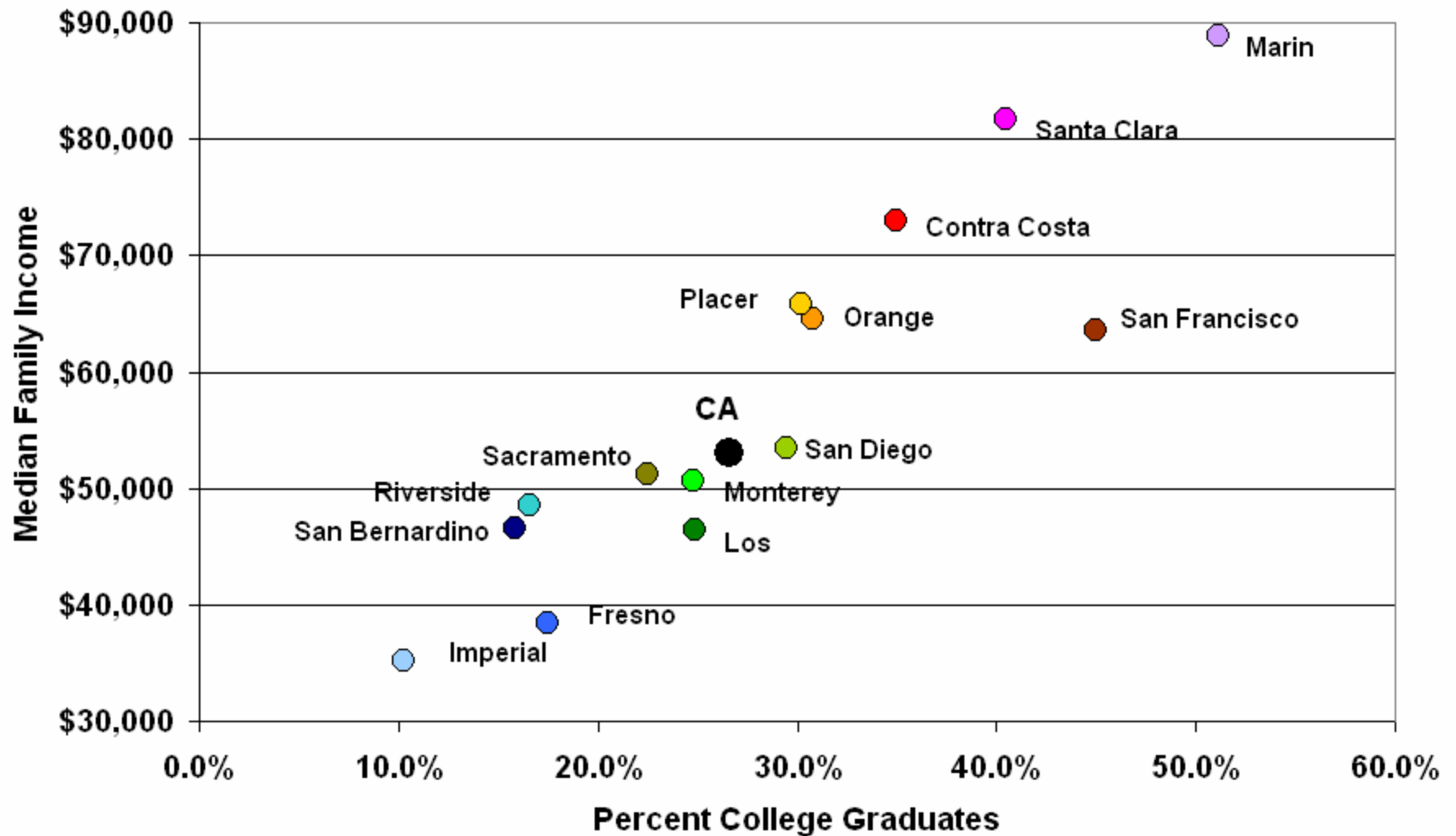
Trends in Incidence of Cancer in California by Cancer Site



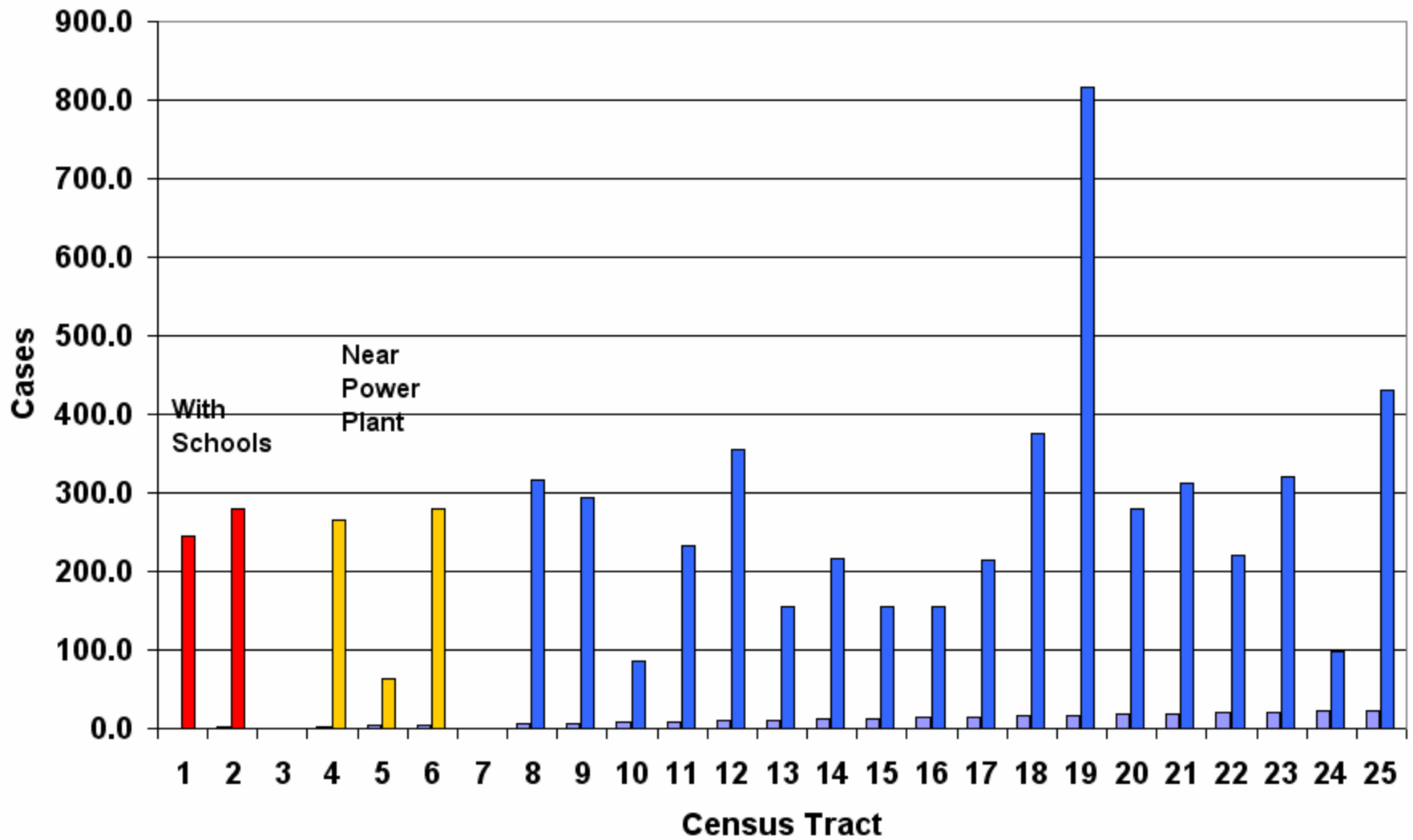
Trends in Incidence of Cancer in California by Cancer Site



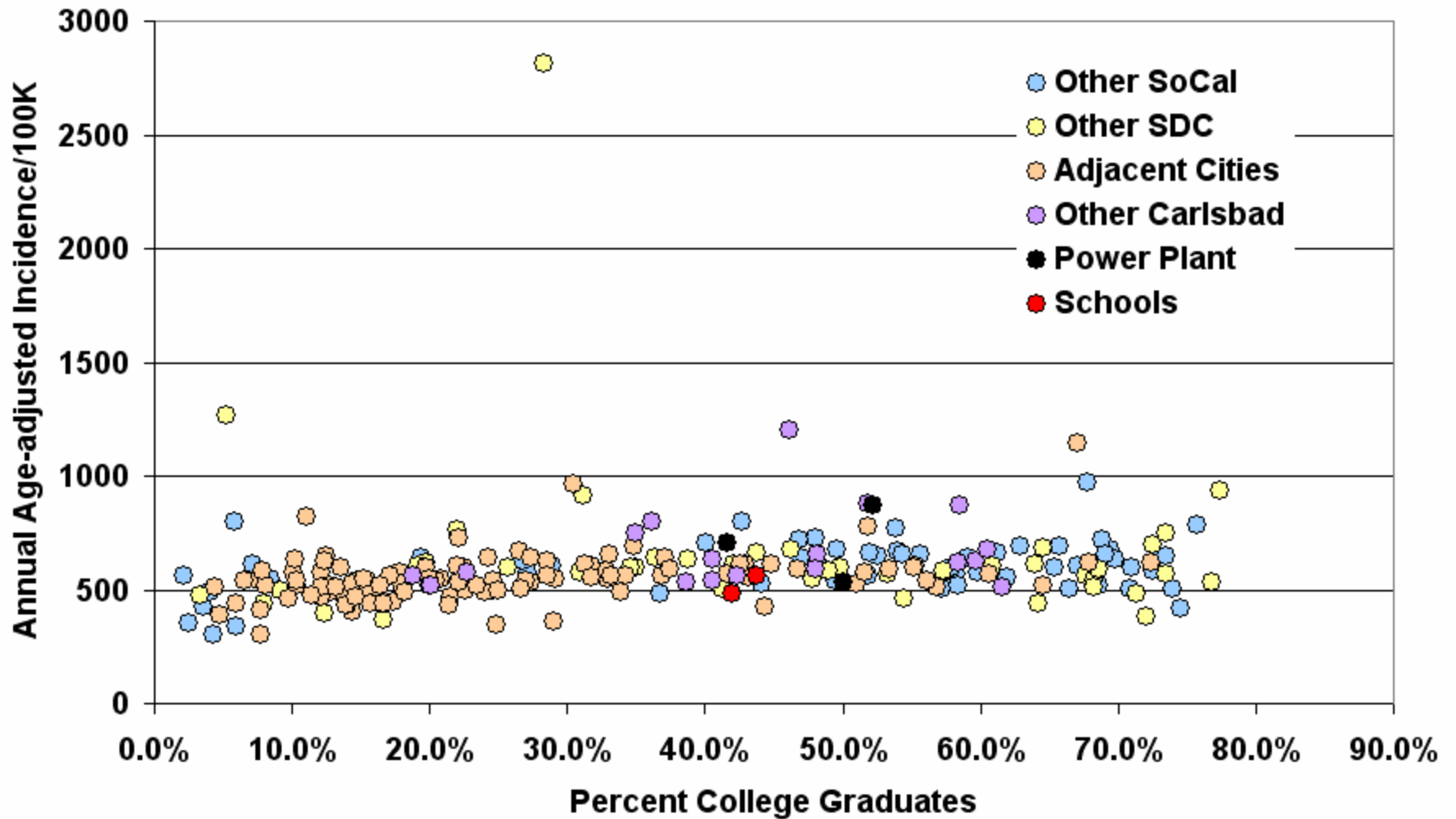
California County Median Family Income According to County Percent College Graduates



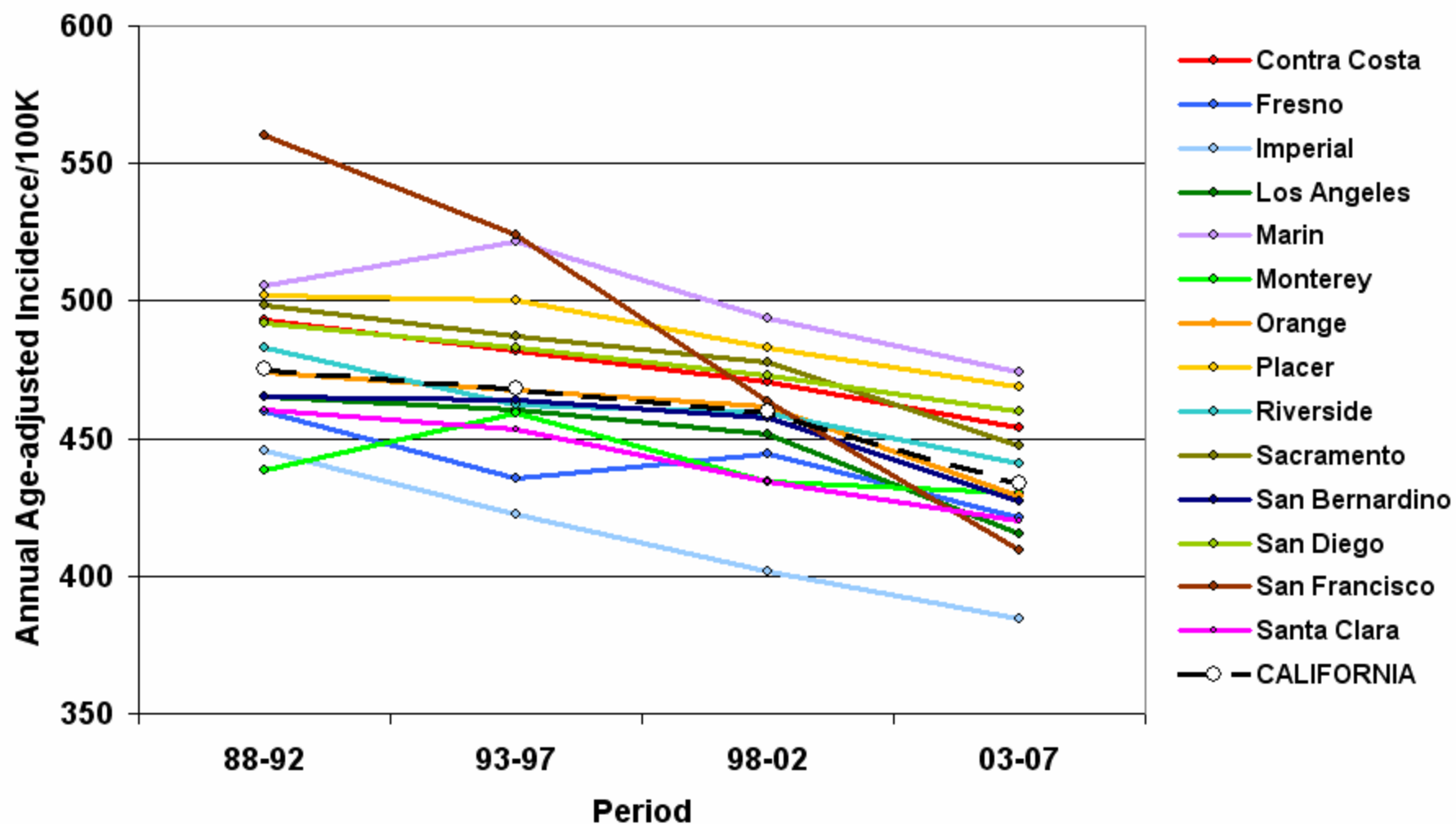
Number of Cancer Cases: 2000-2007, Carlsbad Census Tracts



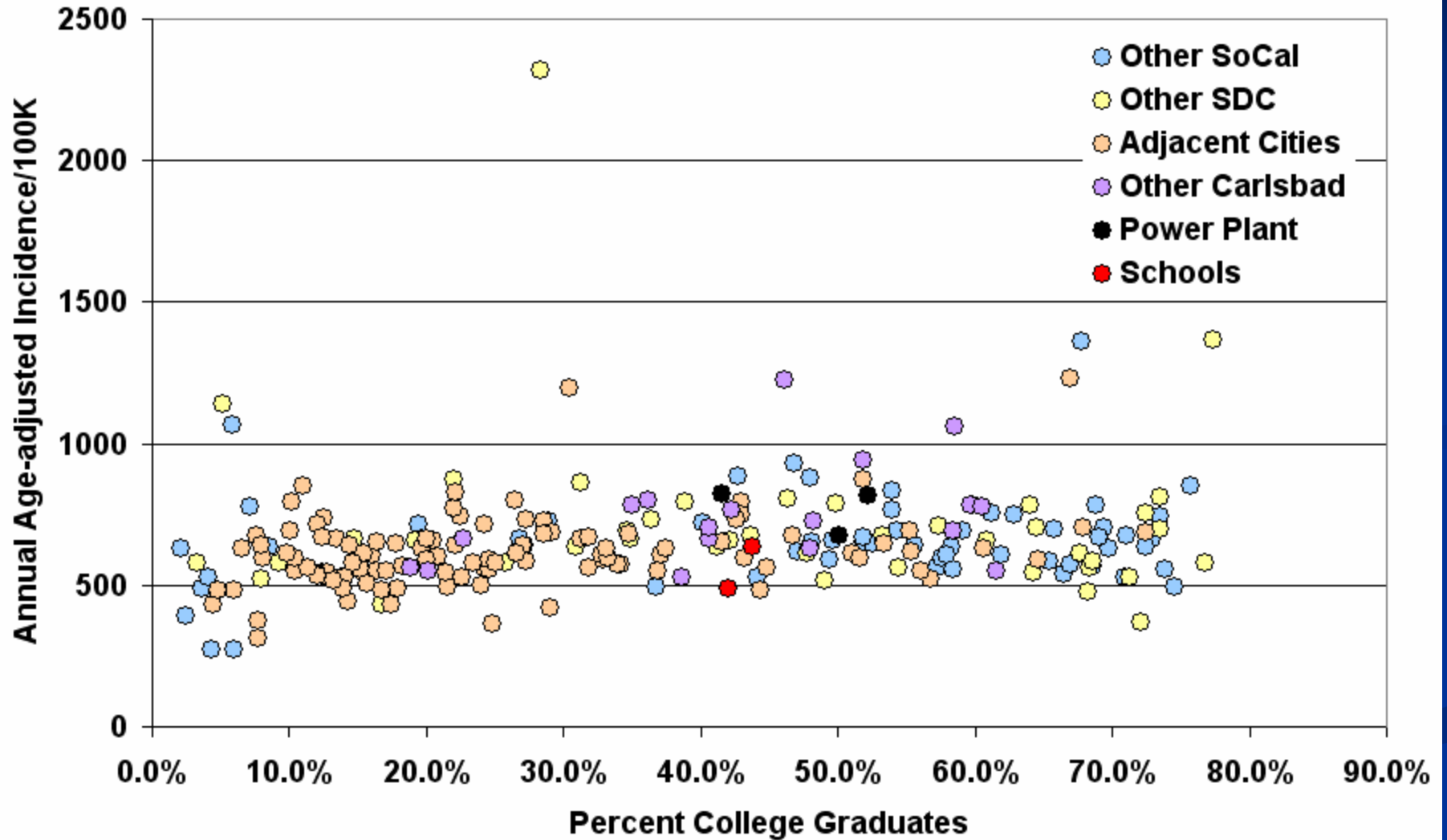
**2000-2007 Census Tract Occurrence of Cancer at All Sites
according to the Proportion of College Graduates**



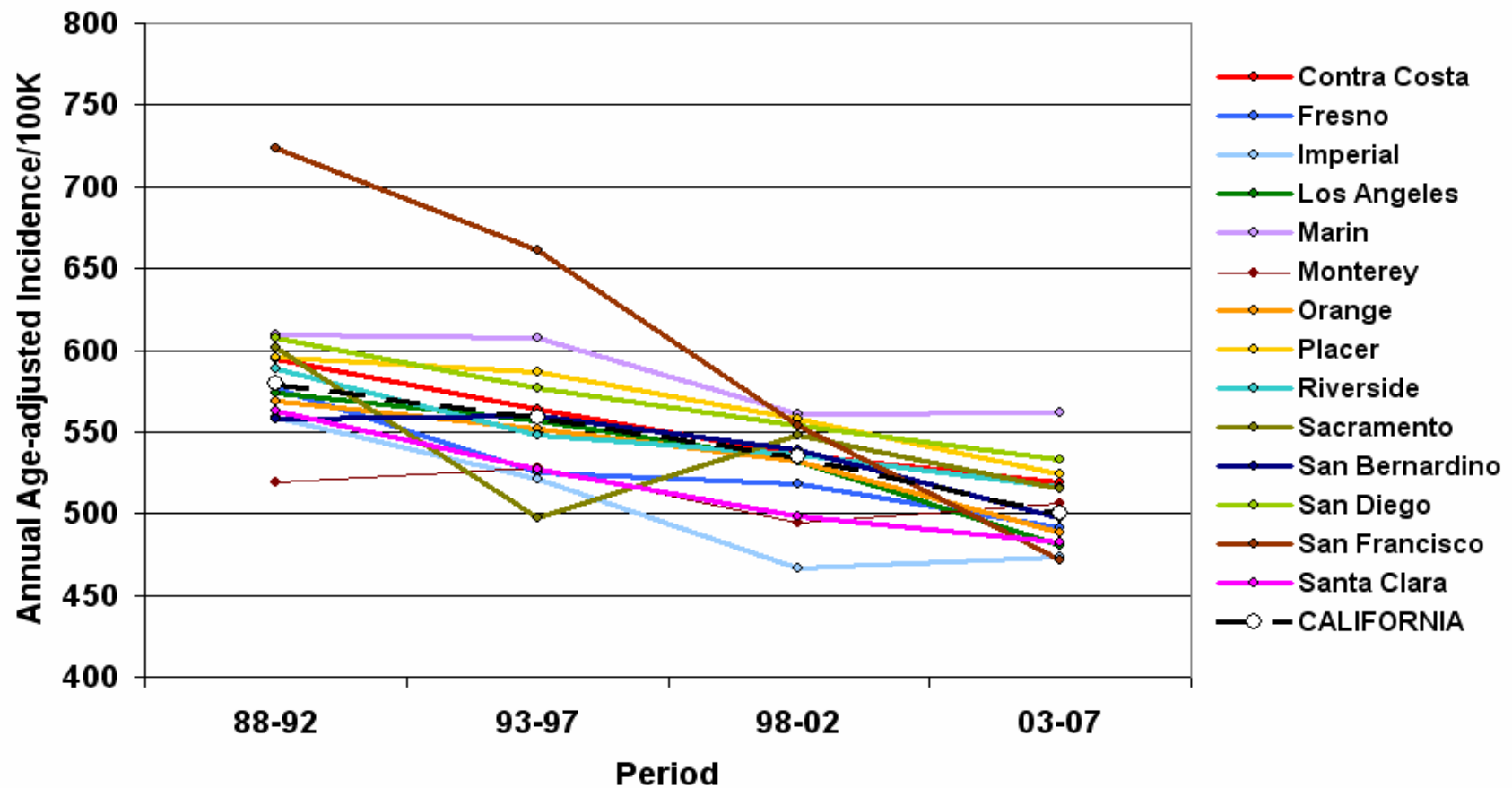
Trend in Occurrence of Cancer at All Sites in Selected California Counties



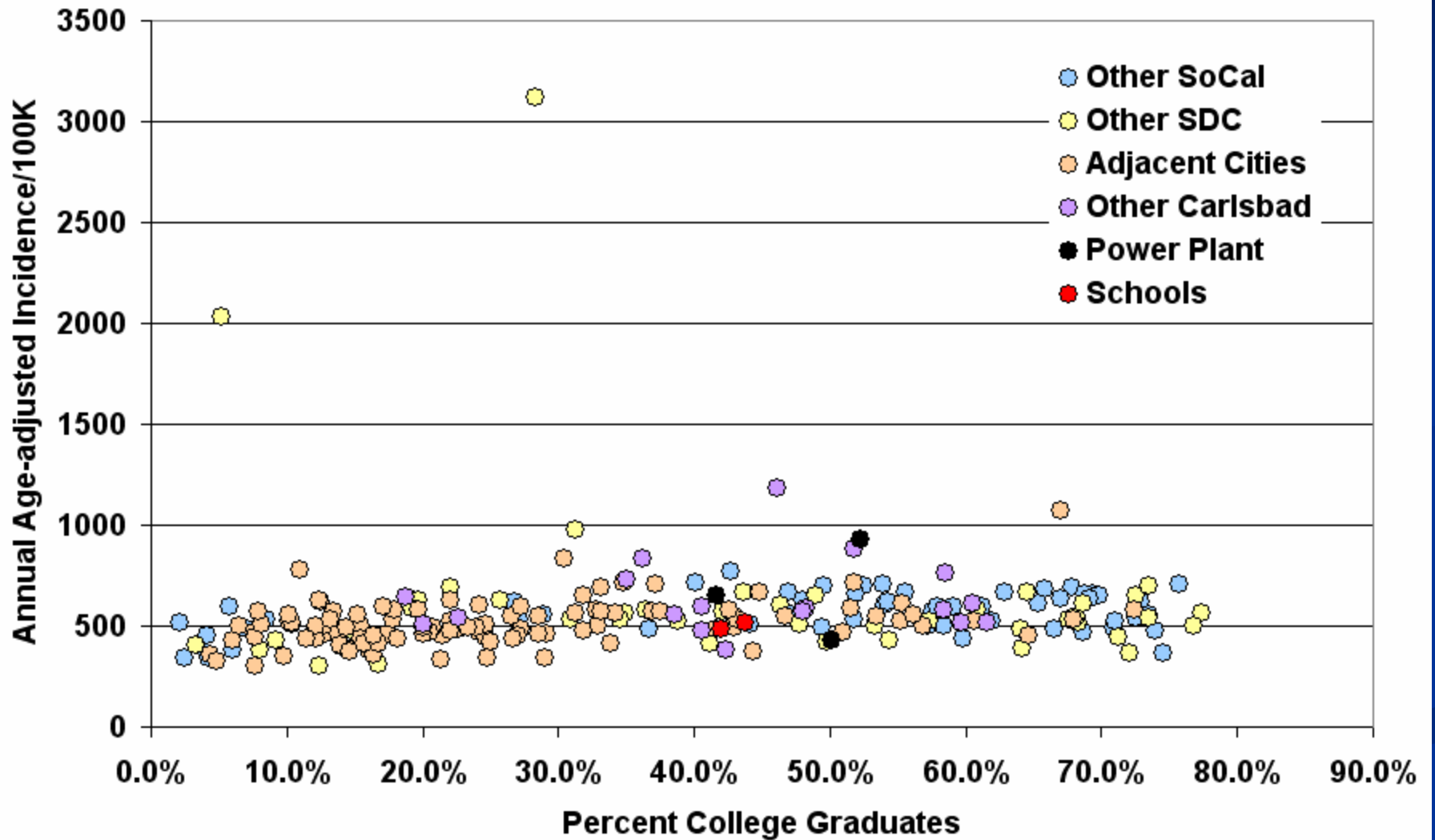
**2000-2007 Census Tract Occurrence of Male Cancer at All Sites
according to the Proportion of College Graduates**



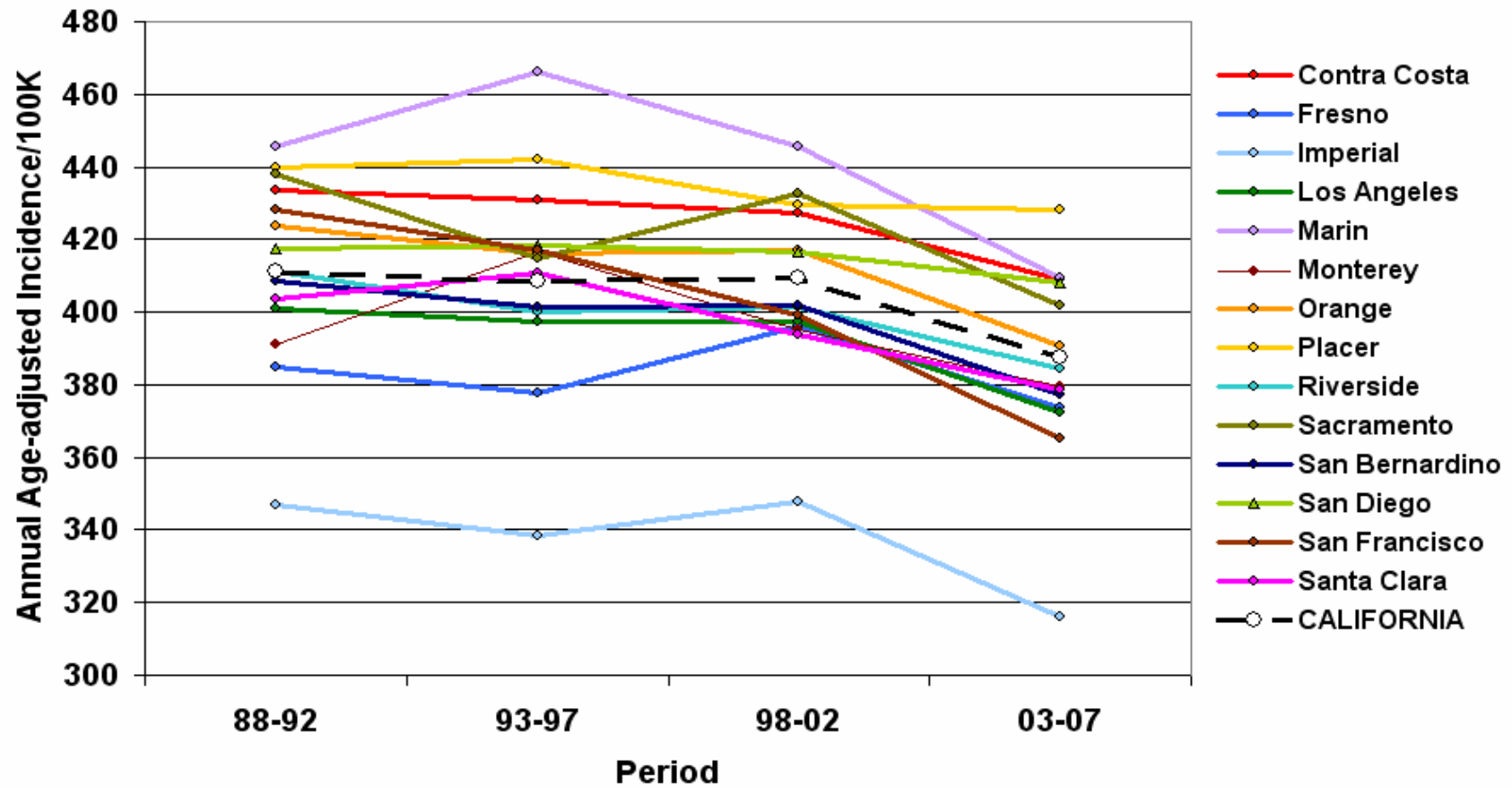
Trend in Occurrence of Male Cancer at All Sites in Selected California Counties



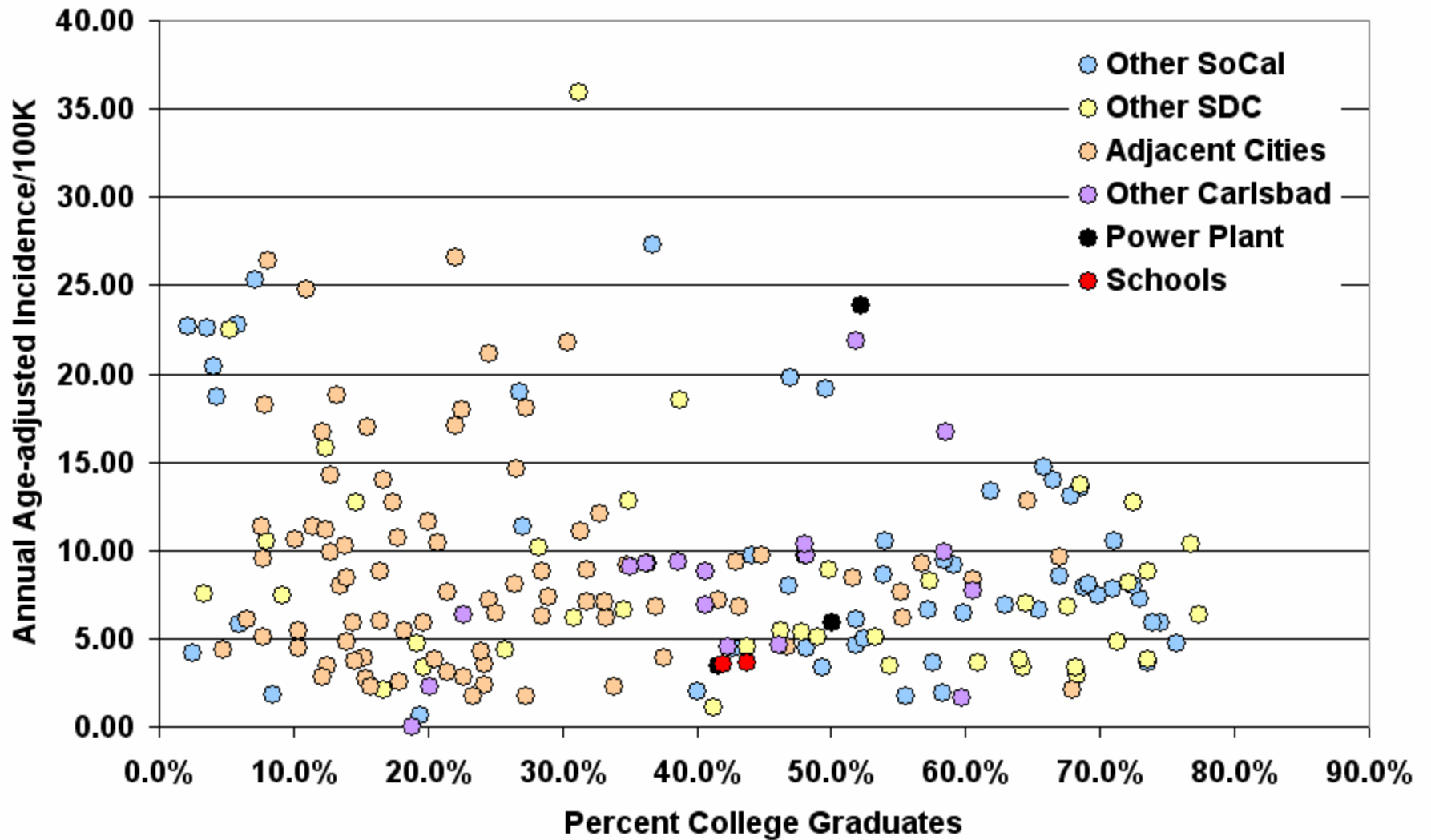
**2000-2007 Census Tract Occurrence of Female Cancer at All Sites
according to the Proportion of College Graduates**



Trend in Occurrence of Female Cancer at All Sites in Selected California Counties



2000-2007 Census Tract Occurrence of Stomach Cancer according to the Proportion of College Graduates



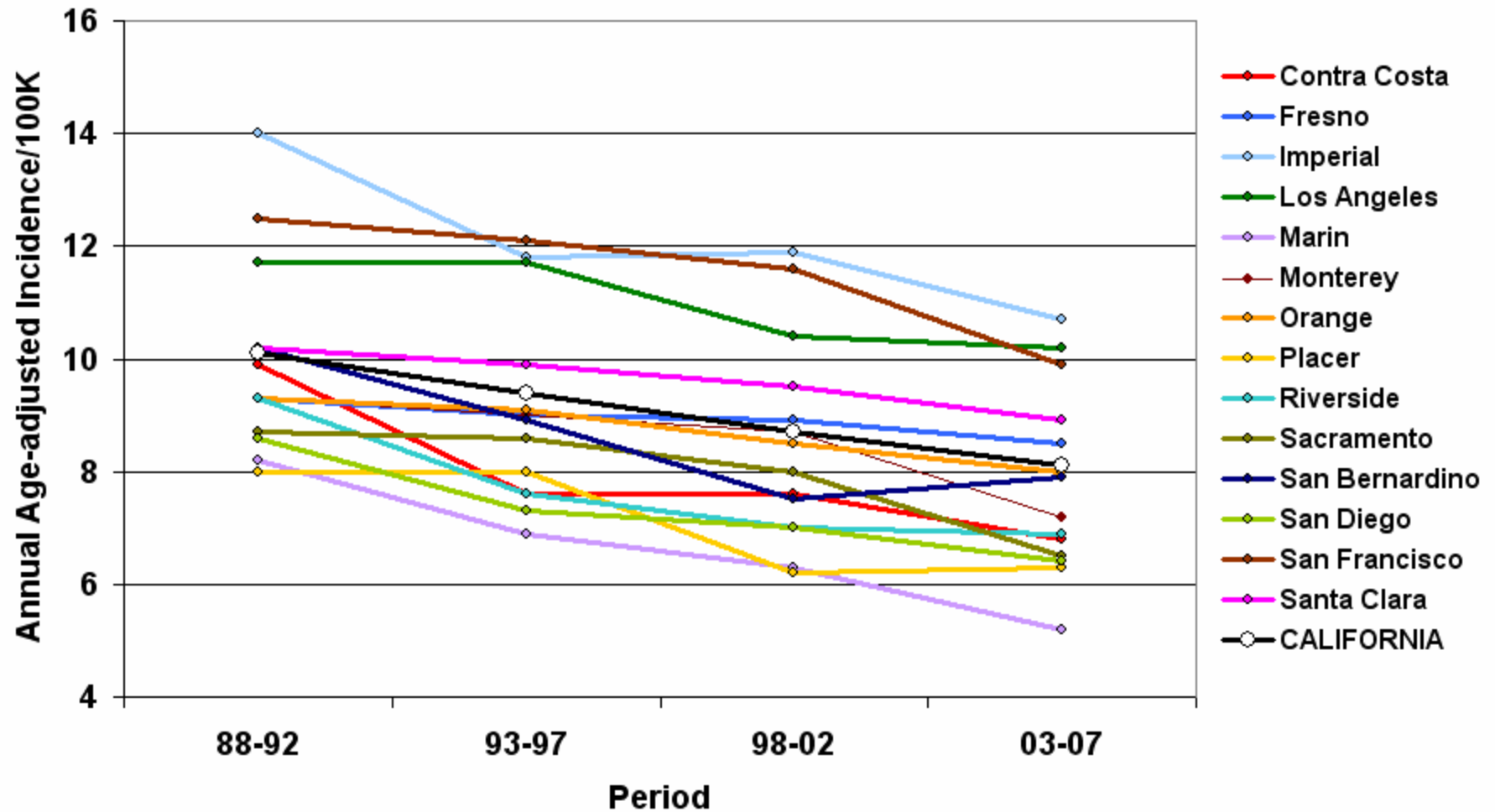
Stomach Cancer-Risk Factors

- Native of Latin America or East Asia
 - Children of such immigrants
- Working class persons generally
 - Multiple siblings
 - Decreasing trend

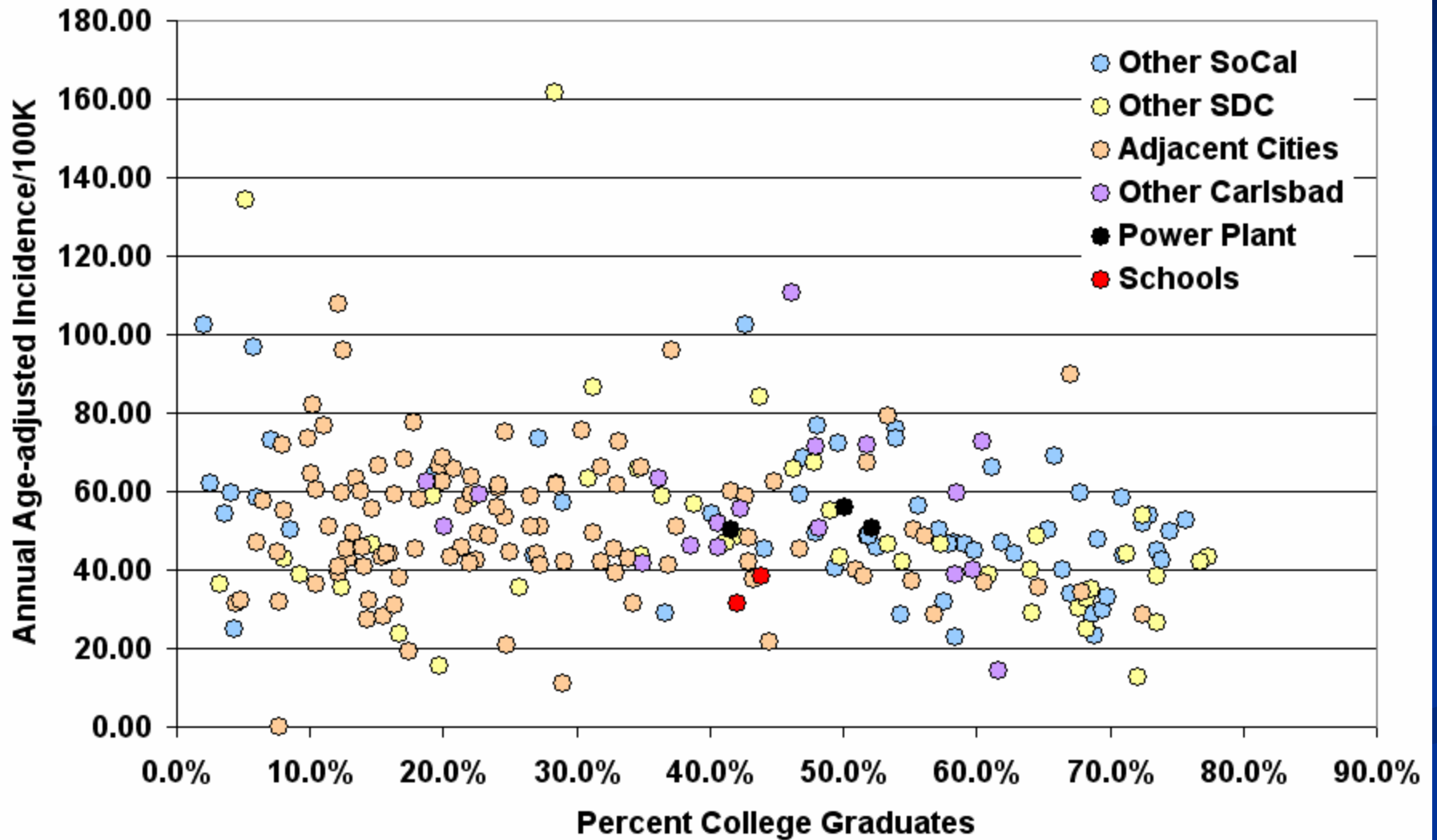
Stomach Cancer-Known Causes

- Helicobacter pyloris bacteria
 - Excessive dietary salt
 - Excessive dietary nitrates
- Few dietary vegetables and fruits

Trend in Occurrence of Stomach Cancer in Selected California Counties



**2000-2007 Census Tract Occurrence of Colorectal Cancer
according to the Proportion of College Graduates**



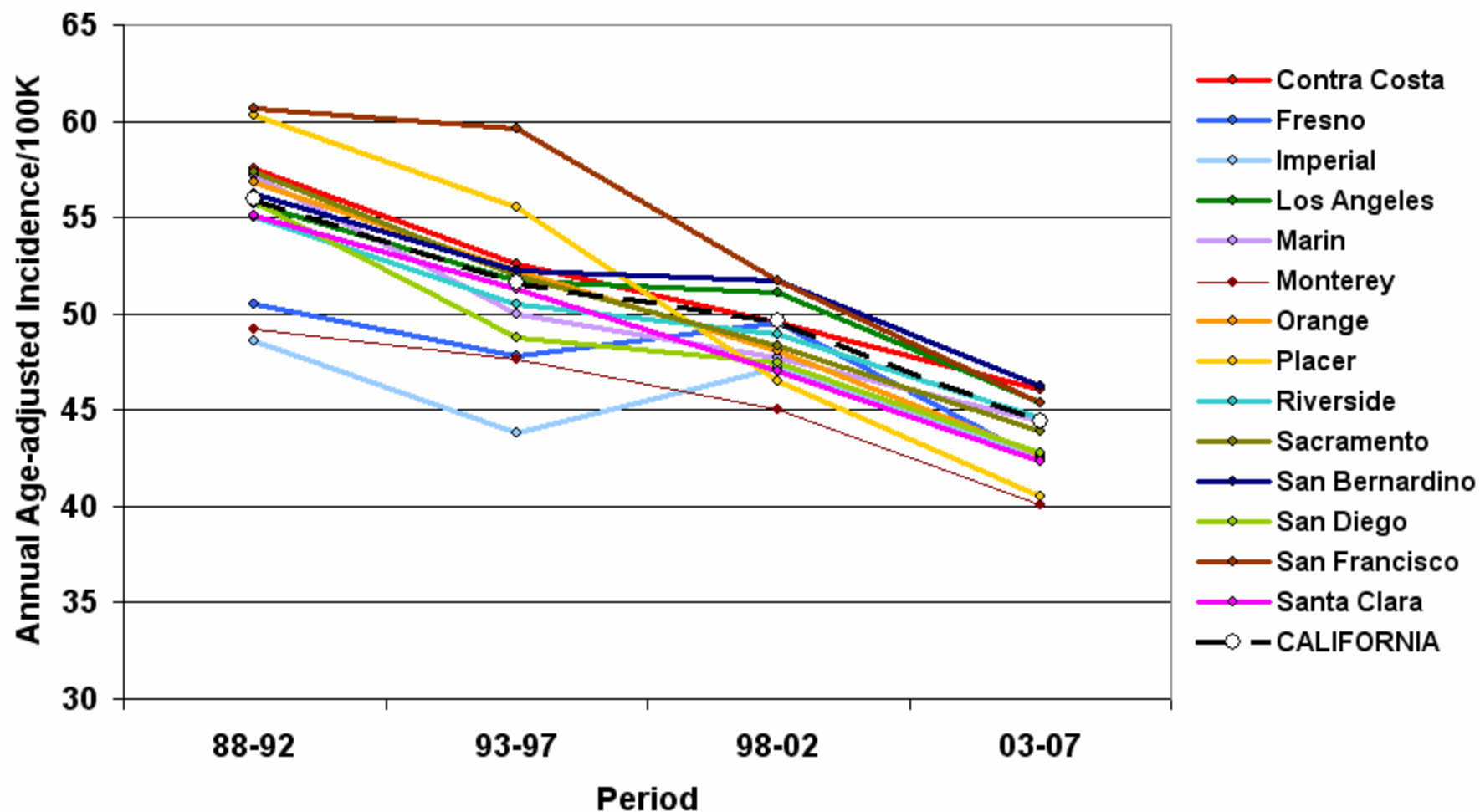
Colorectal Cancer-Risk Factors

- Resident of Developed Country
- Presence of colorectal polyps/adenomas
 - Family history of colorectal cancer
 - Sedentary occupation
 - Smoker

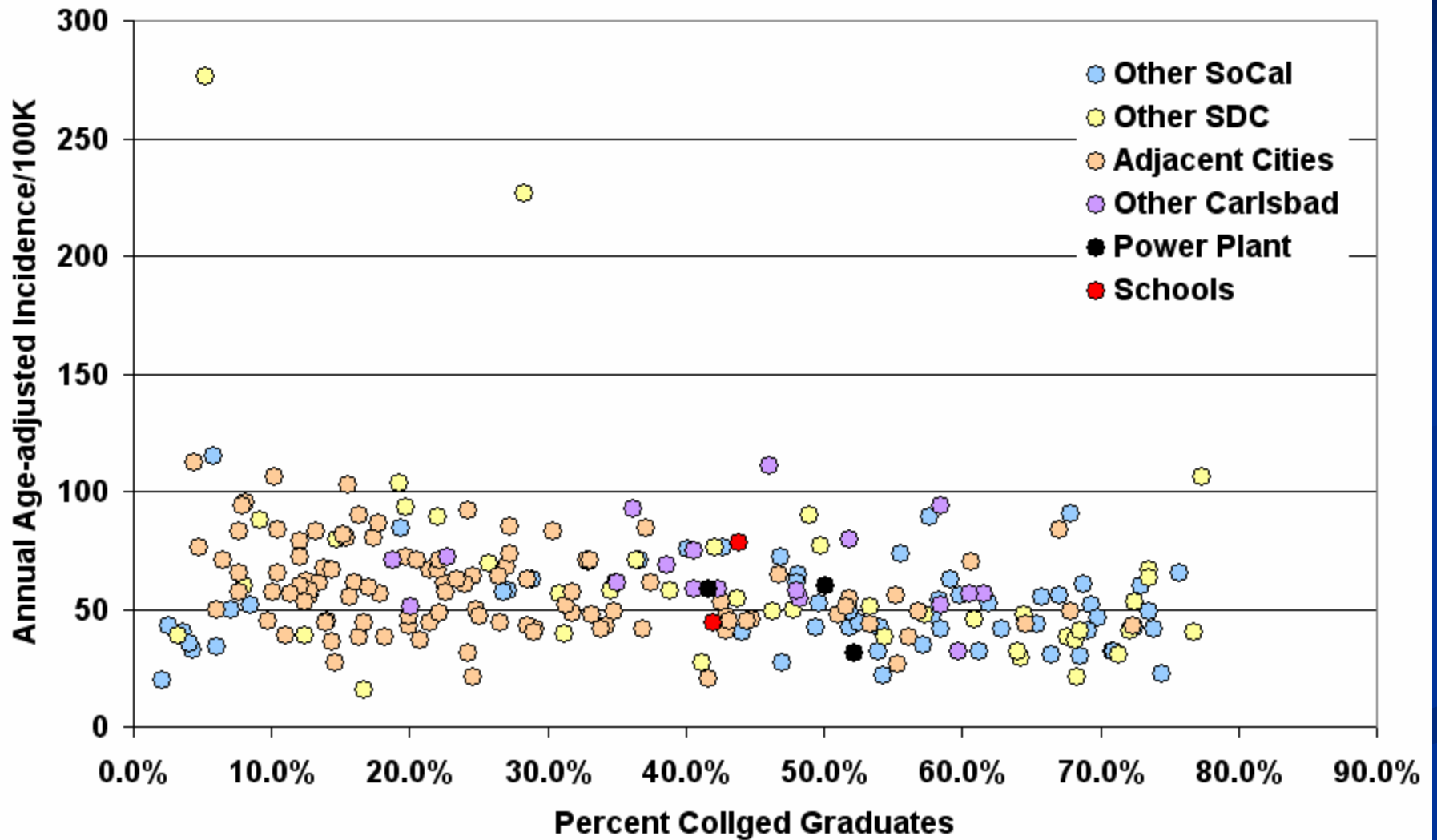
Colorectal Cancer-Known Causes

- Certain Genes
- Sedentary lifestyle
- Inflammatory Bowel Disease
 - Cigarette smoking

Trend in Occurrence of Colorectal Cancer in Selected California Counties



2000-2007 Census Tract Occurrence of Lung Cancer according to the Proportion of College Graduates



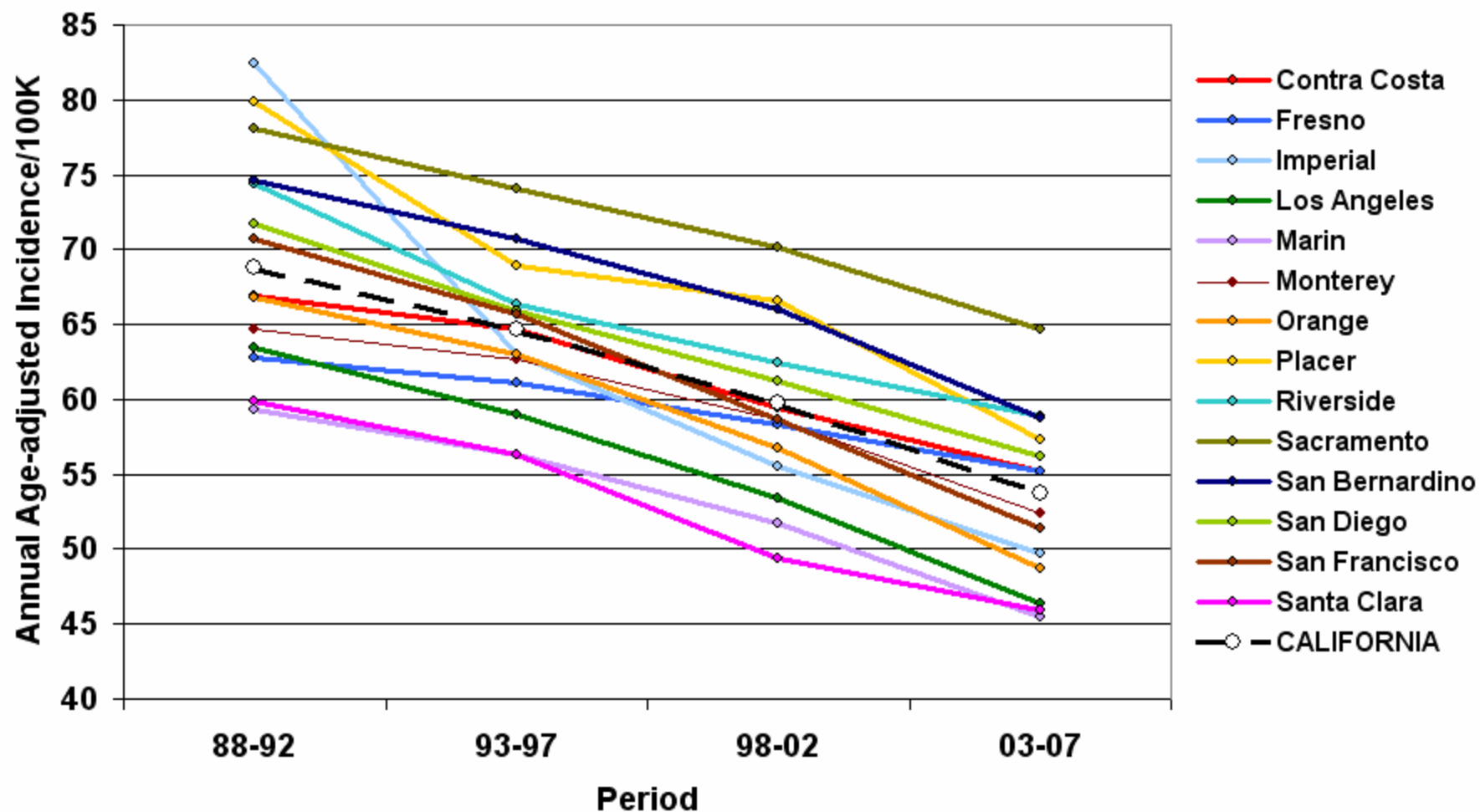
Lung Cancer-Risk Factors

- Male gender
 - African American (among men)
- Middle or lower social class (among men)
 - Higher social class (among women)

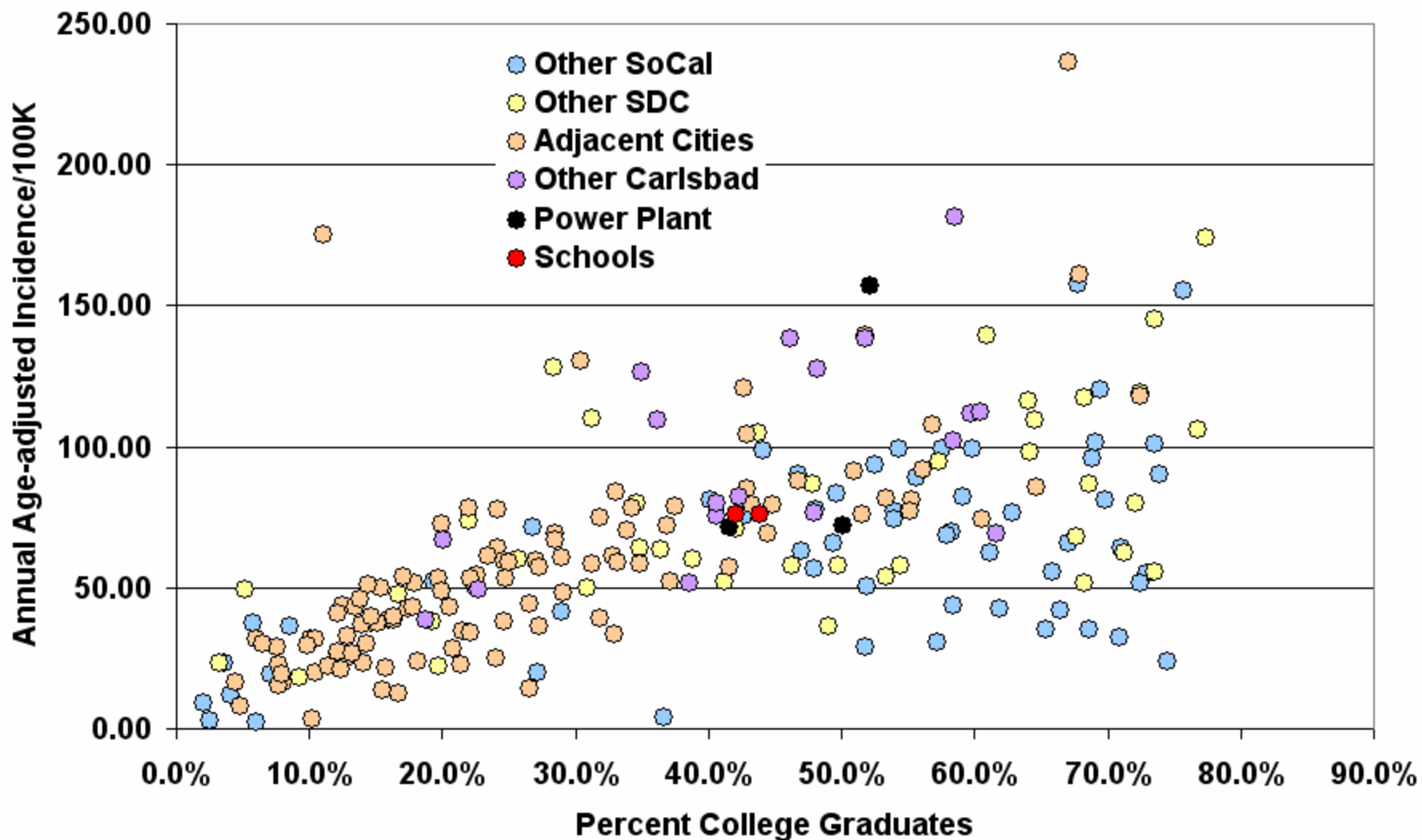
Lung Cancer-Known Causes

- Cigarette smoking
 - Arsenic dust
- Nickel and beryllium dusts/vapors
 - Lead and cadmium dusts
 - Hexavalent chromium
 - Chloromethyl ethers
 - Epichlorohydrin
 - Sulfuric acid mist
- Polycyclic aromatic hydrocarbons
 - Asbestos
 - Radon
- Other sources of incomplete combustion
 - Other organic material

Trend in Occurrence of Lung Cancer in Selected California Counties



**2000-2007 Census Tract Occurrence of Malignant Melanoma
according to the Proportion of College Graduates**



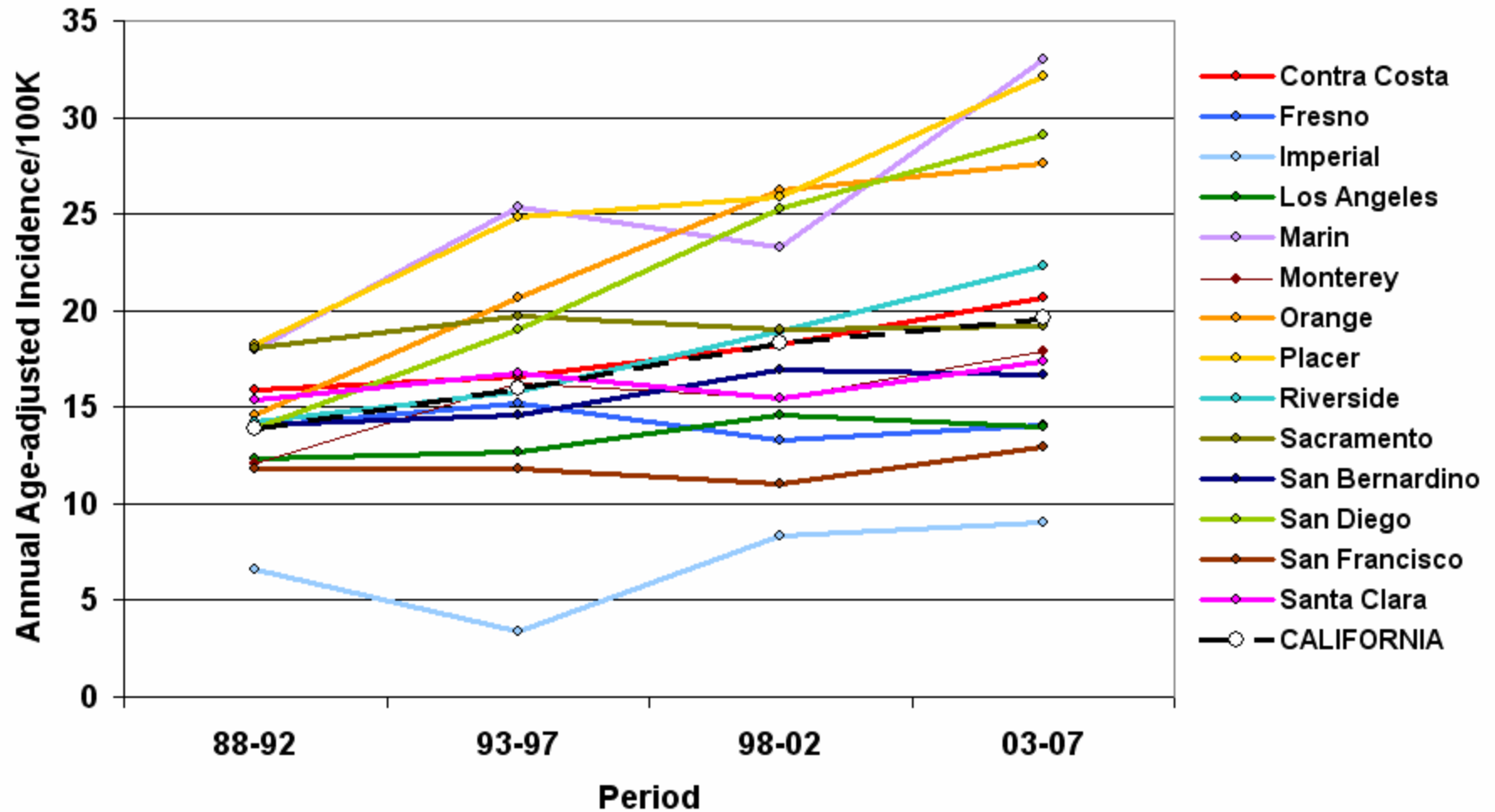
Malignant Melanoma-Risk Factors

- **Family History**
 - **European American**
 - **Light colored skin/hair**
 - **Red Hair and/or freckles**
- **Abundant ordinary moles (nevi)**
- **Early Intense exposure to sunlight**

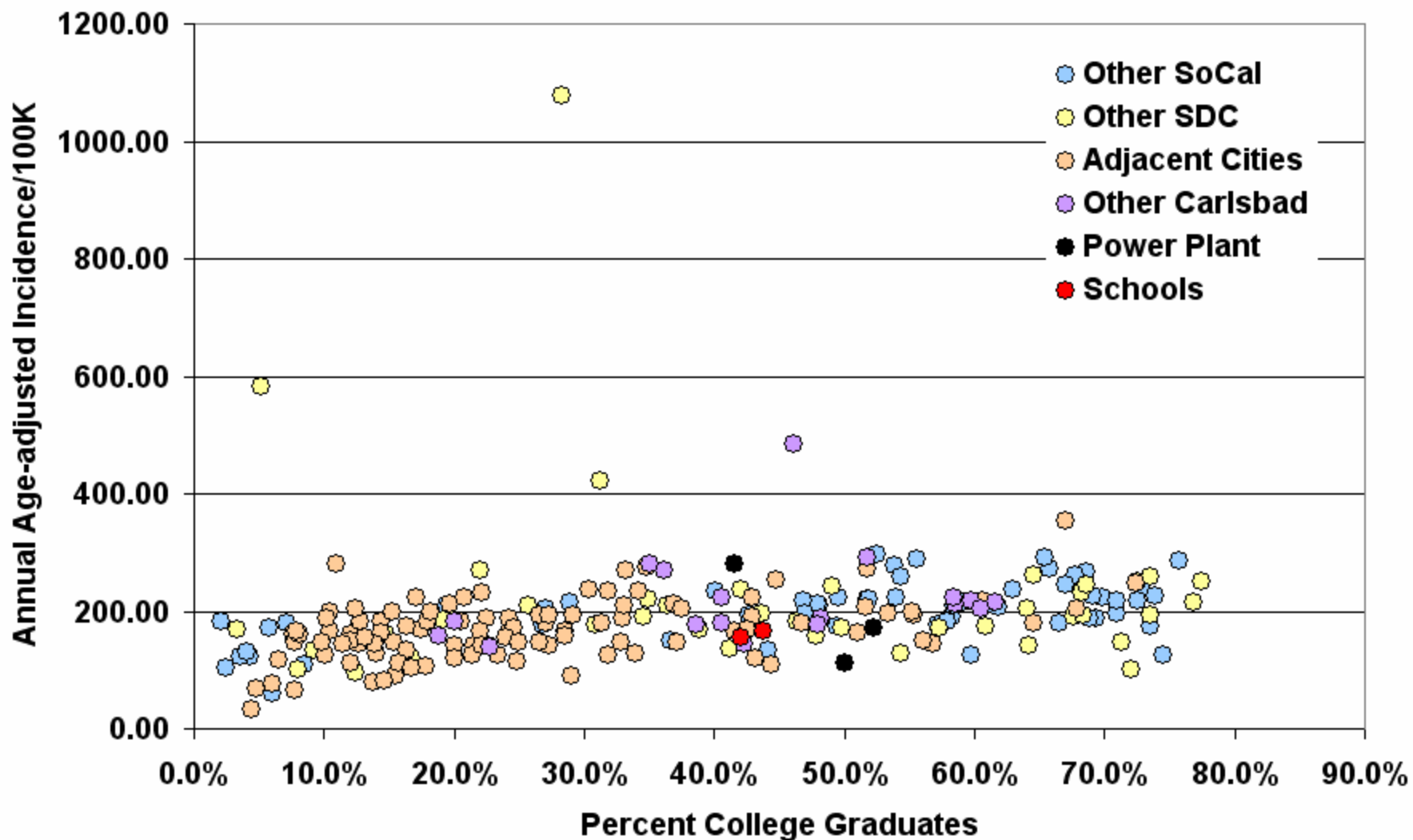
Malignant Melanoma-Known Causes

- Specific Genes
- Early/cumulative exposure to ultra-violet radiation

Trend in Occurrence of Malignant Melanoma in Selected California Counties



2000-2007 Census Tract Occurrence of Female Breast Cancer according to the Proportion of College Graduates



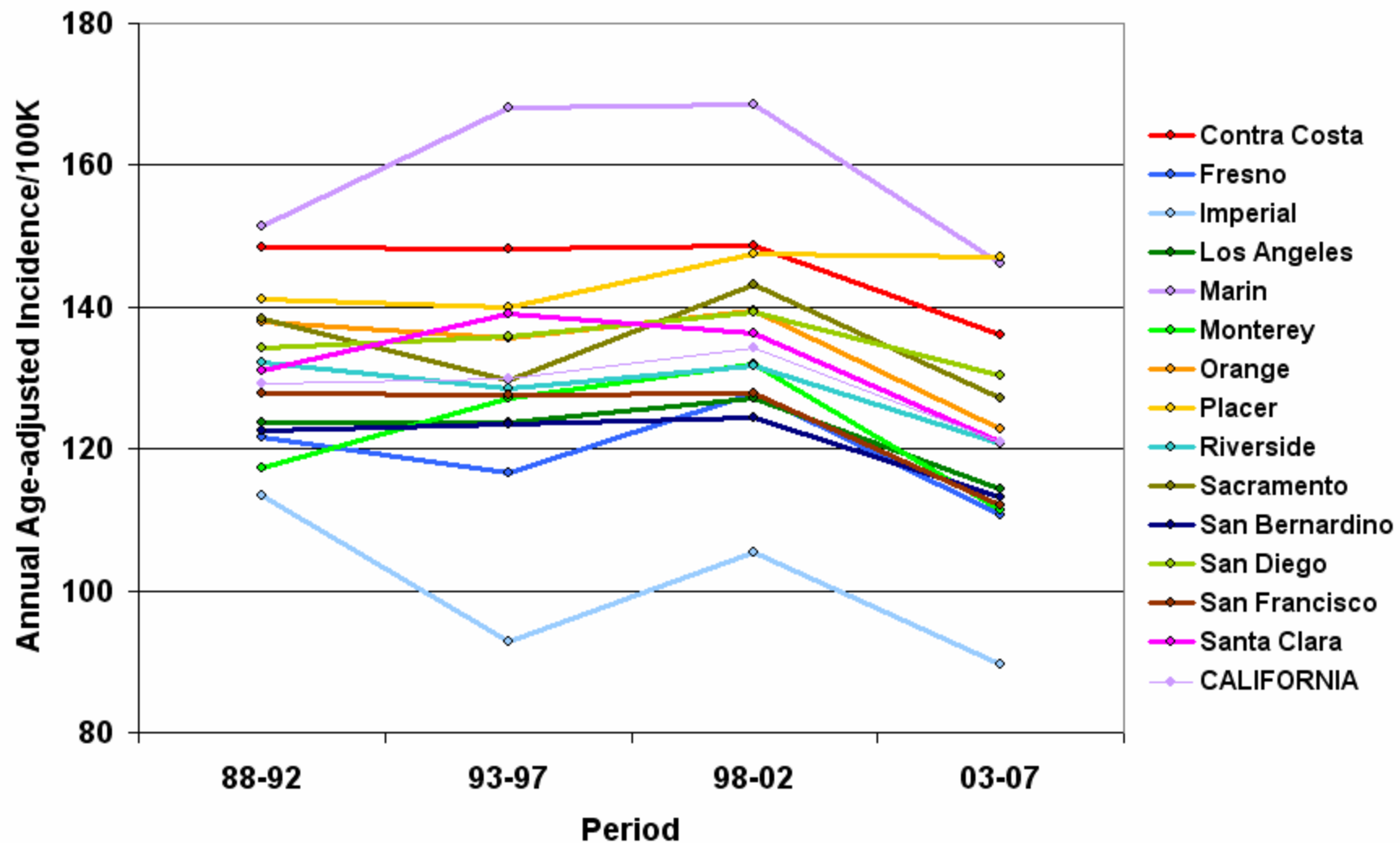
Breast Cancer-Risk Factors

- High level of education
 - Family History
 - Early menarche
- Late age at first full term delivery
 - Tall height/Obesity
- Repeated Chest x-rays/flourosocopy

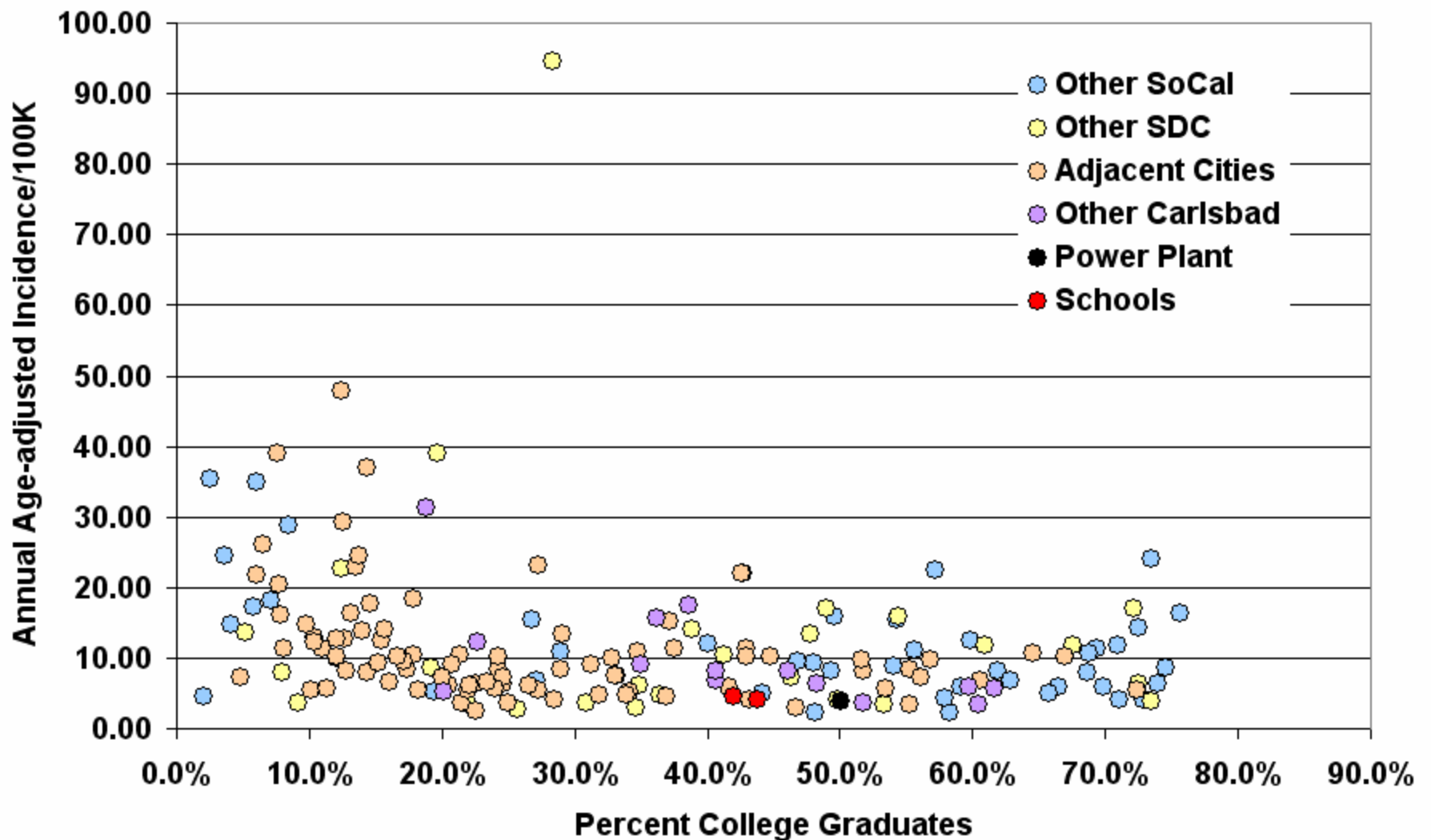
Breast Cancer-Known Causes

- Specific genes
- Ionizing Radiation
- Ovarian hormones
- Replacement hormones
- Chemotherapeutic agents
 - Alcohol consumption

Trend in Occurrence of Female Breast Cancer in Selected California Counties



2000-2007 Census Tract Occurrence of Cancer of the Cervix according to the Proportion of College Graduates



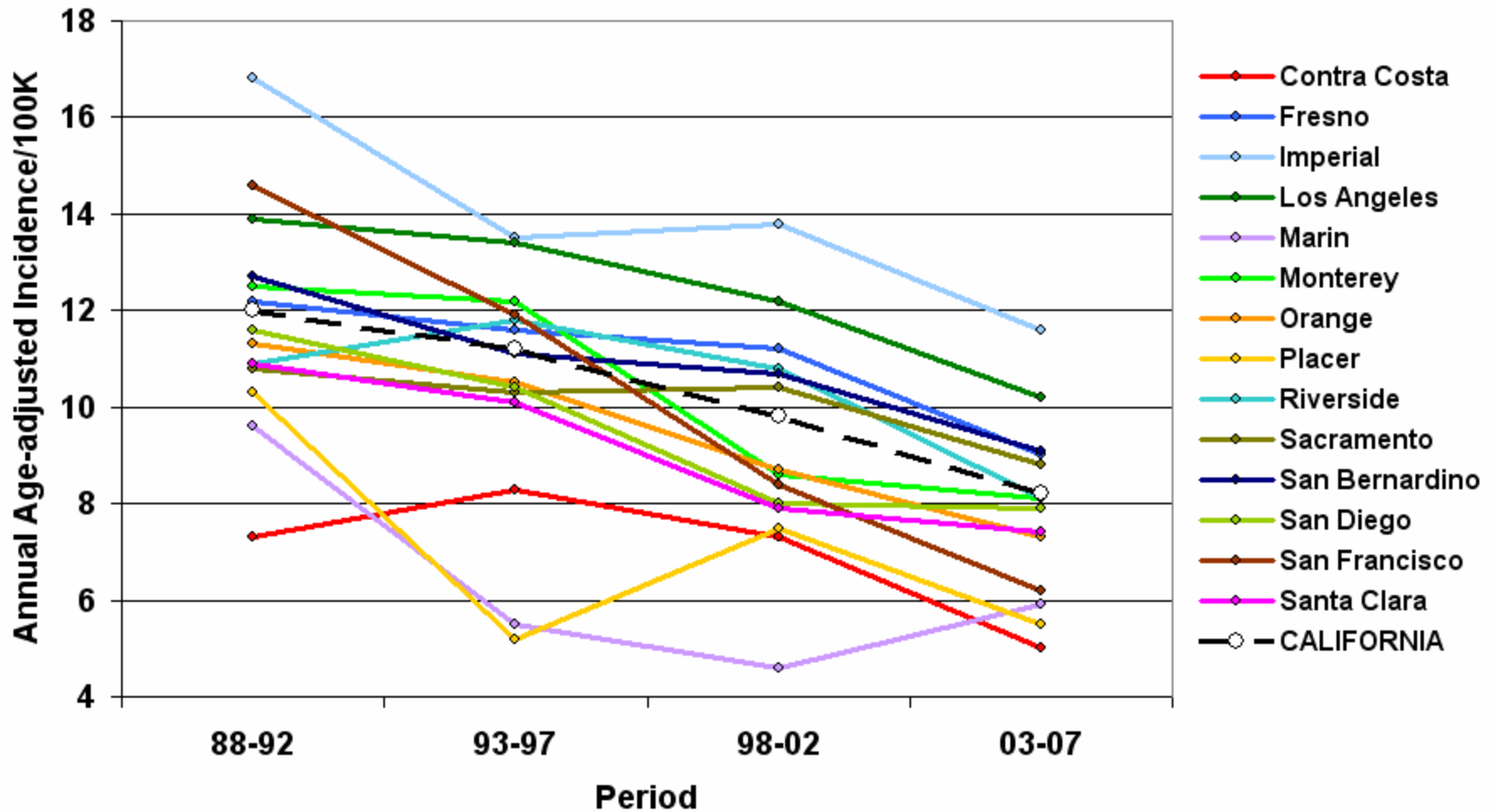
Cancer of the Cervix-Risk Factors

- Early sexual activity
- Multiple sexual partners
- Partners with multiple partners
- Genital condylomata (warts)

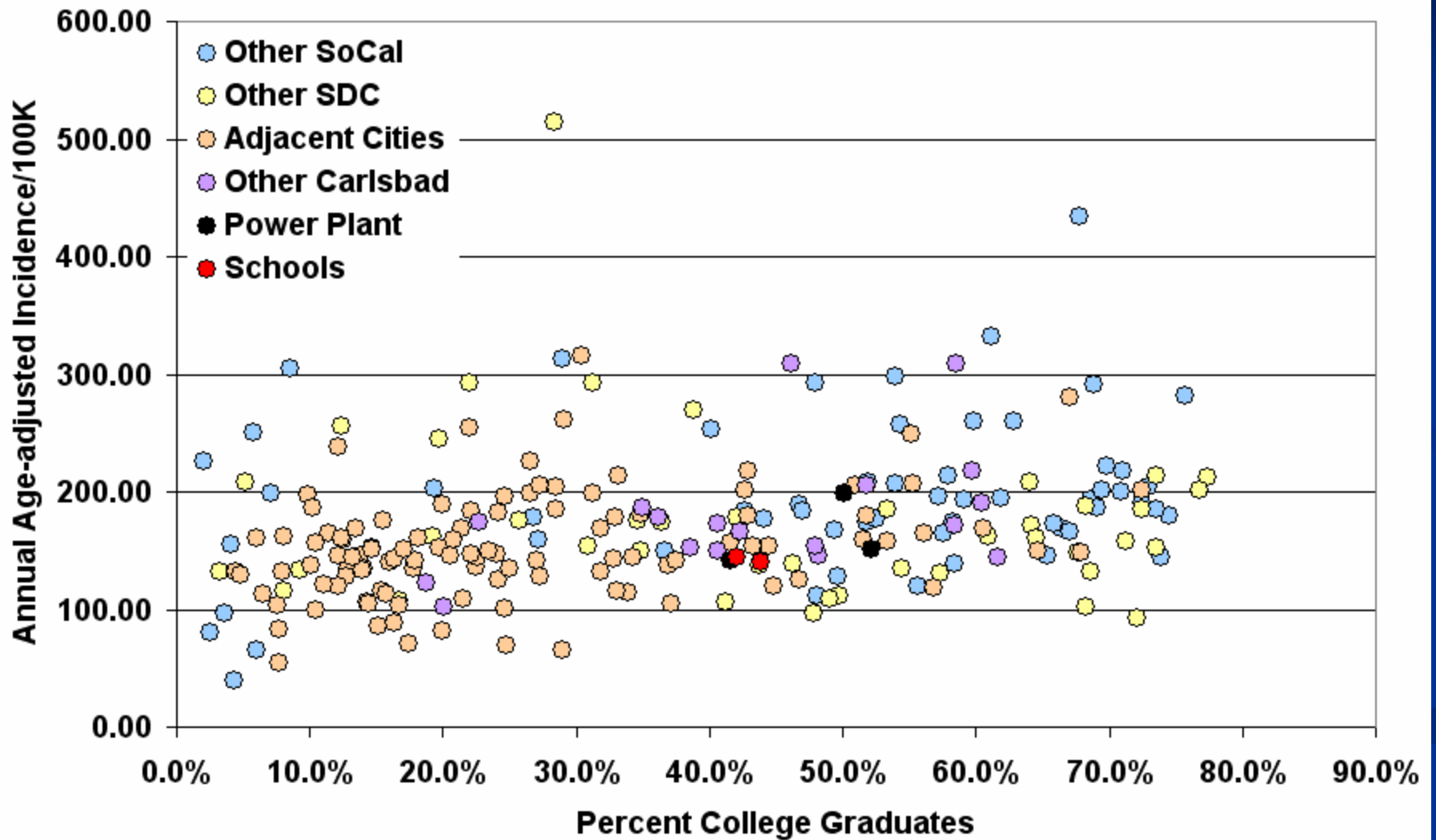
Cancer of the Cervix-Known Causes

- Human papilloma viruses
 - Smoking
- Lack of PAP screening
 - Immunosusceptibility
 - AIDS
 - Drugs for Transplantation

Trend in the Occurrence of Cancer of the Cervix in Selected California Counties



2000-2007 Census Tract Occurrence of Prostate Cancer according to the Proportion of College Graduates



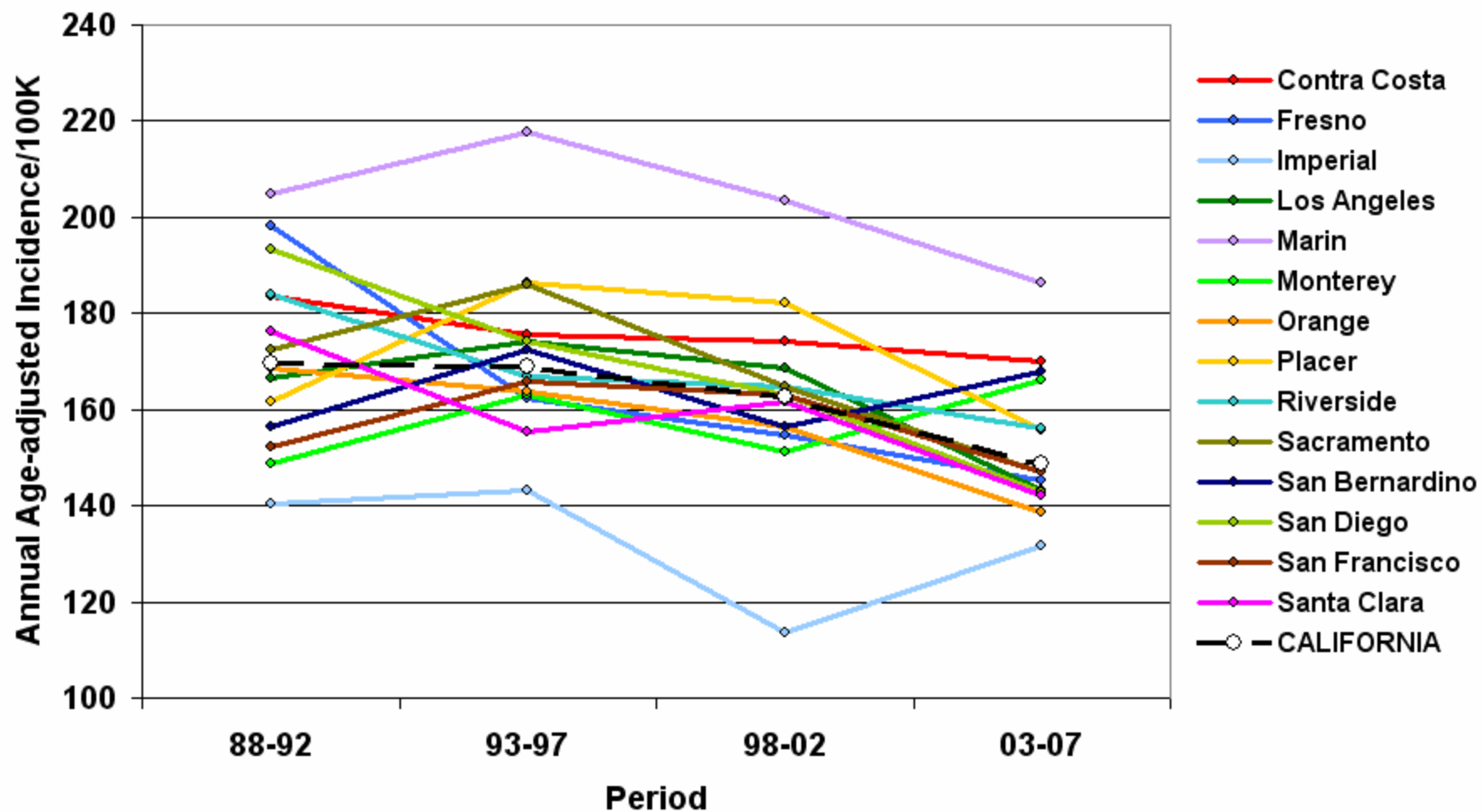
Prostate Cancer-Risk Factors

- African American Race
 - Family History
- Lower consumption of vegetables
 - Medical care for screening

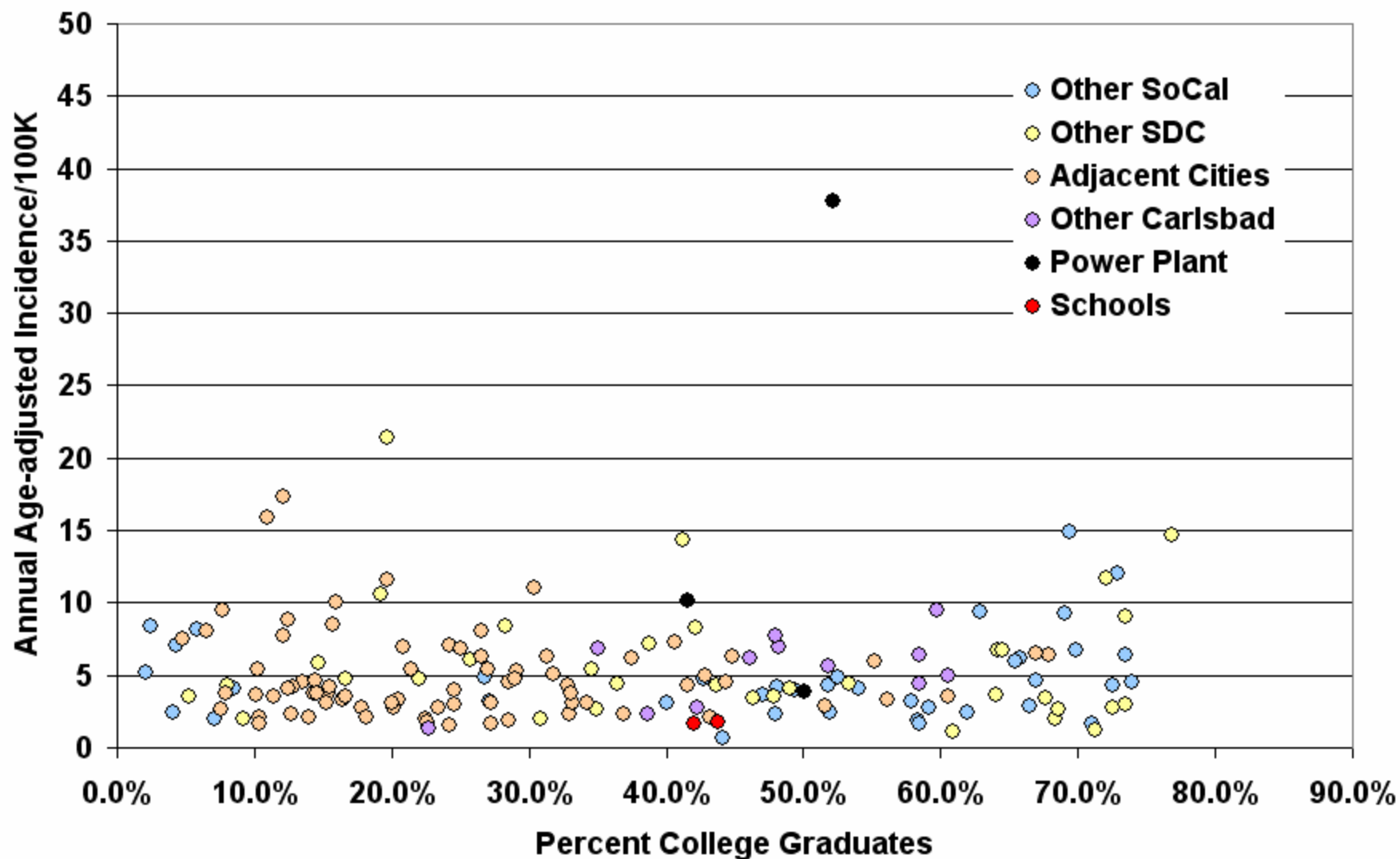
Prostate Cancer-Known Causes

- Specific Genes

Trend in Occurrence of Prostate Cancer in Selected California Counties



2000-2007 Census Tract Occurrence of Soft Tissue Sarcomas according to the Proportion of College Graduates



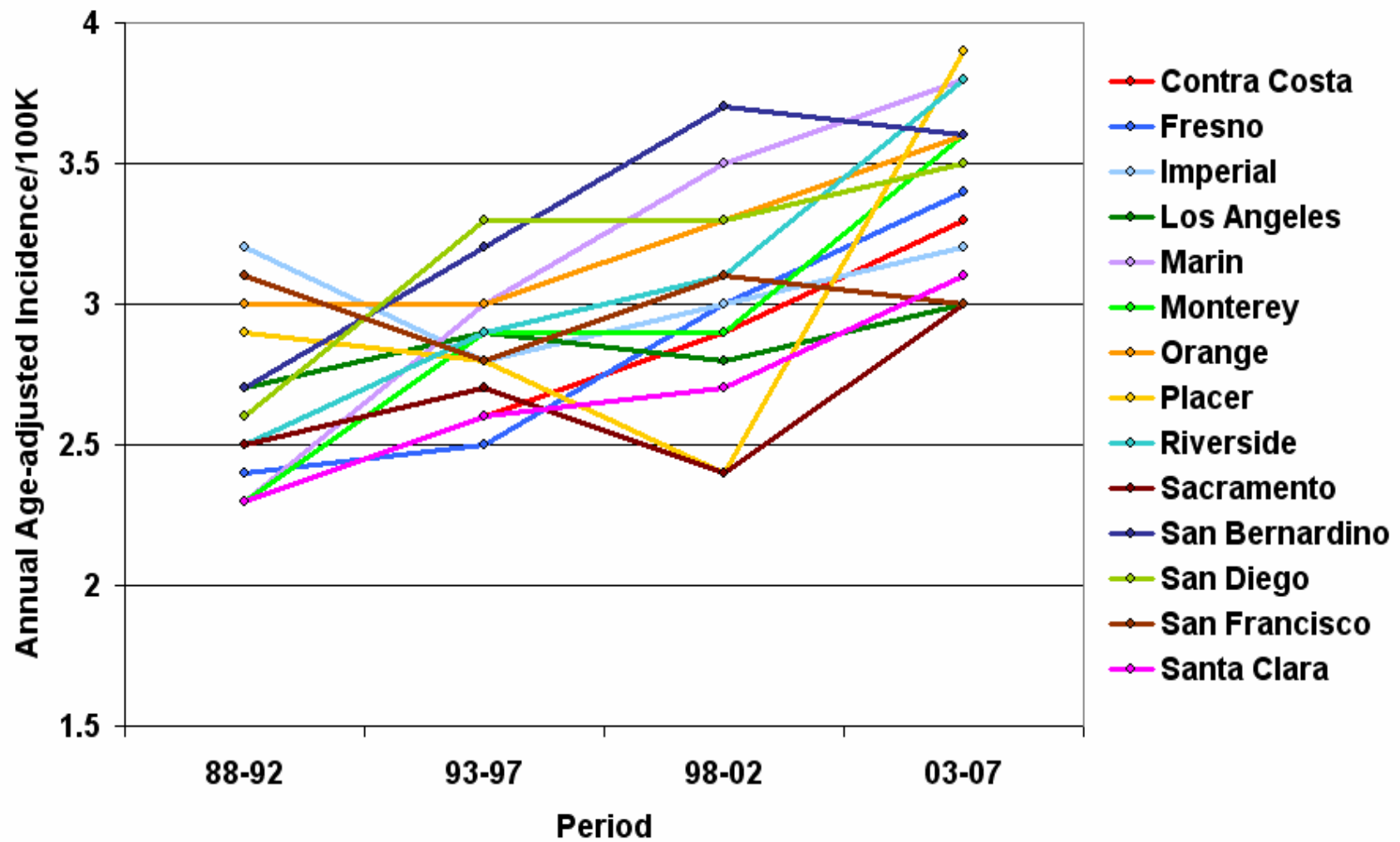
Soft Tissue Sarcoma- Risk Factors

- Age
 - Radiation Exposure
 - AIDS
- Auto-immune disease/treatment

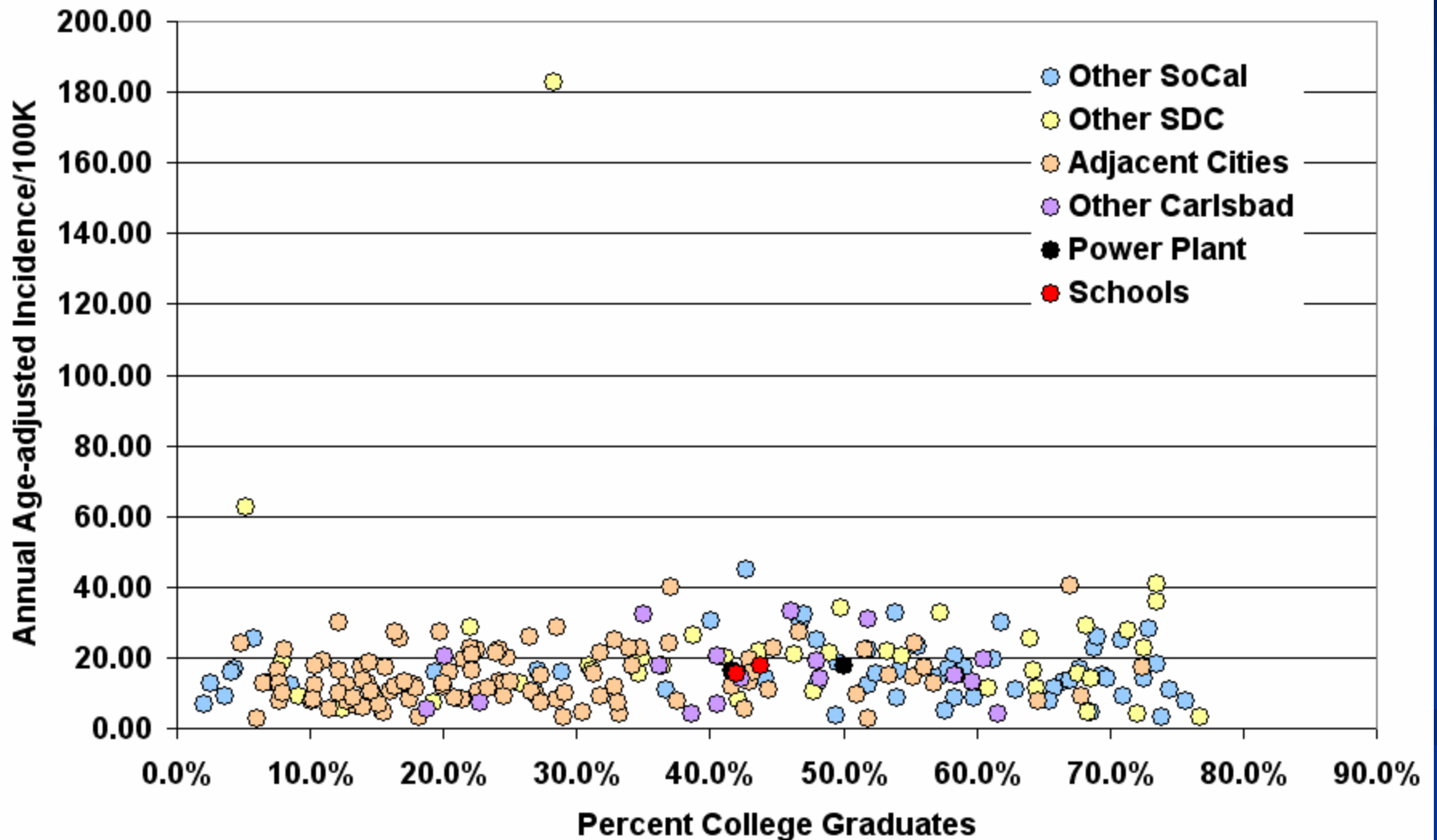
Soft Tissue Sarcoma- Known Causes

- Specific Genes
 - Radiation
- Immune deficiency/Immunosuppression
 - Dioxins/chlorophenols/herbicides
 - Exogenous hormones

Trends in Occurrence of Soft Tissue Sarcoma in Selected California Counties



2000-2007 Census Tract Occurrence of Brain Cancer according to the Proportion of College Graduates



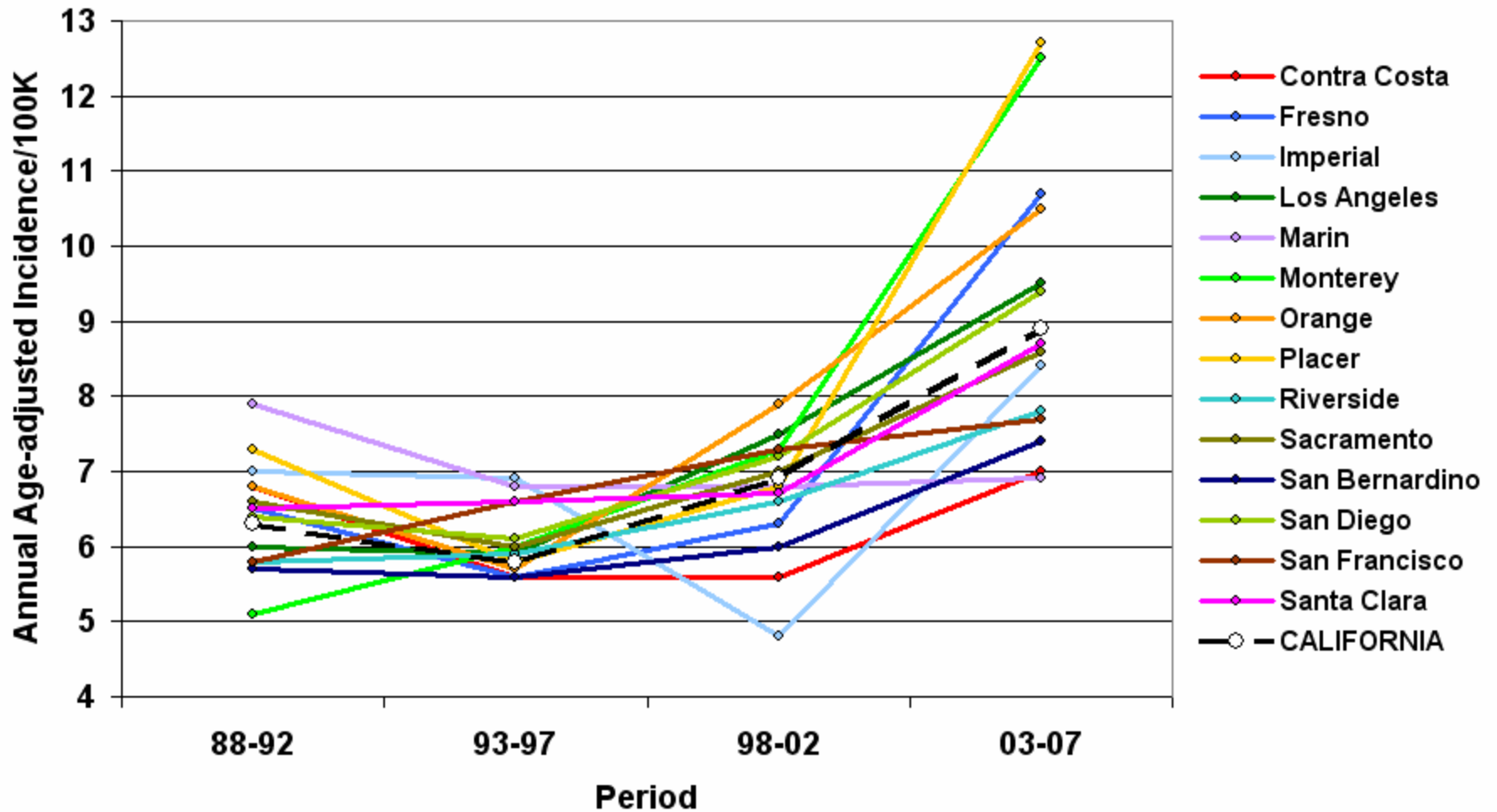
Brain/CNS Cancer-Risk Factors

- Family History
- Higher social class
- Trend is increasing

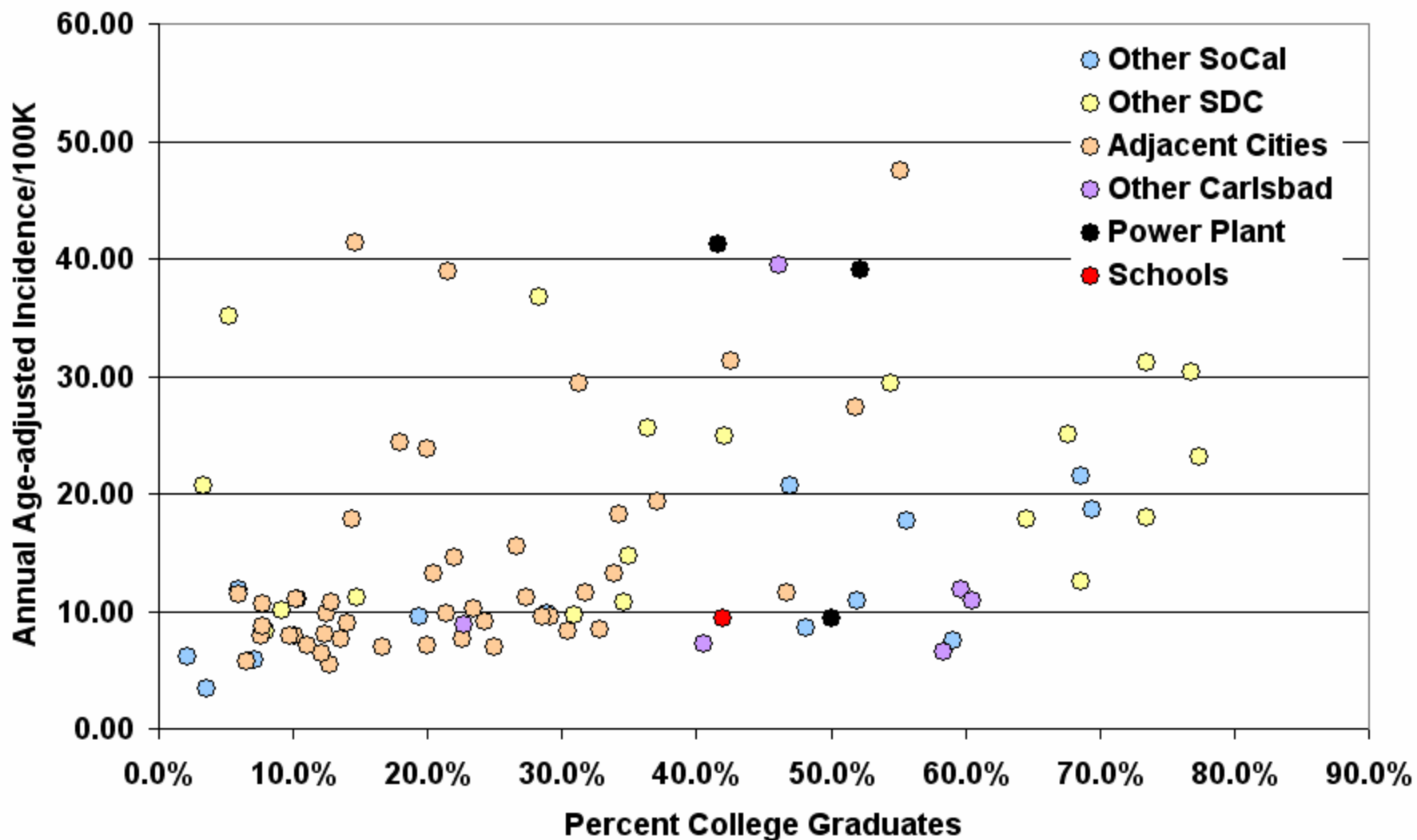
Brain/CNS Cancer- Known Causes

- Specific Genes
- Ionizing Radiation

Trend in Occurrence of Brain Malignancies in Selected California Counties



2000-2007 Census Tract Occurrence of Acute Lymphoblastic Leukemia according to the Proportion of College Graduates



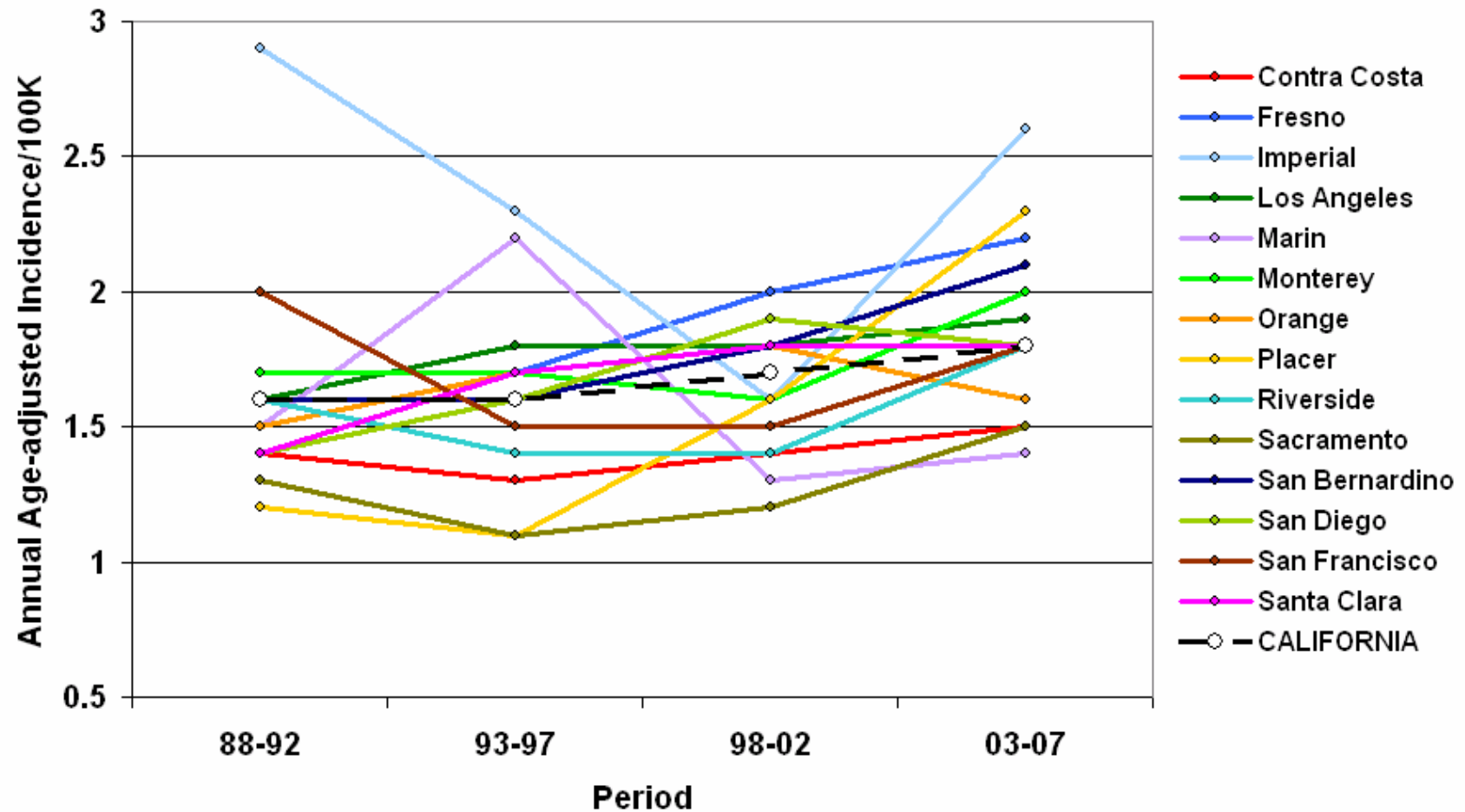
Acute lymphoblastic leukemia— Risk Factors

- Male gender
- Down's syndrome
 - Latino heritage
 - Age 0-5
- Relative Isolation from others after birth

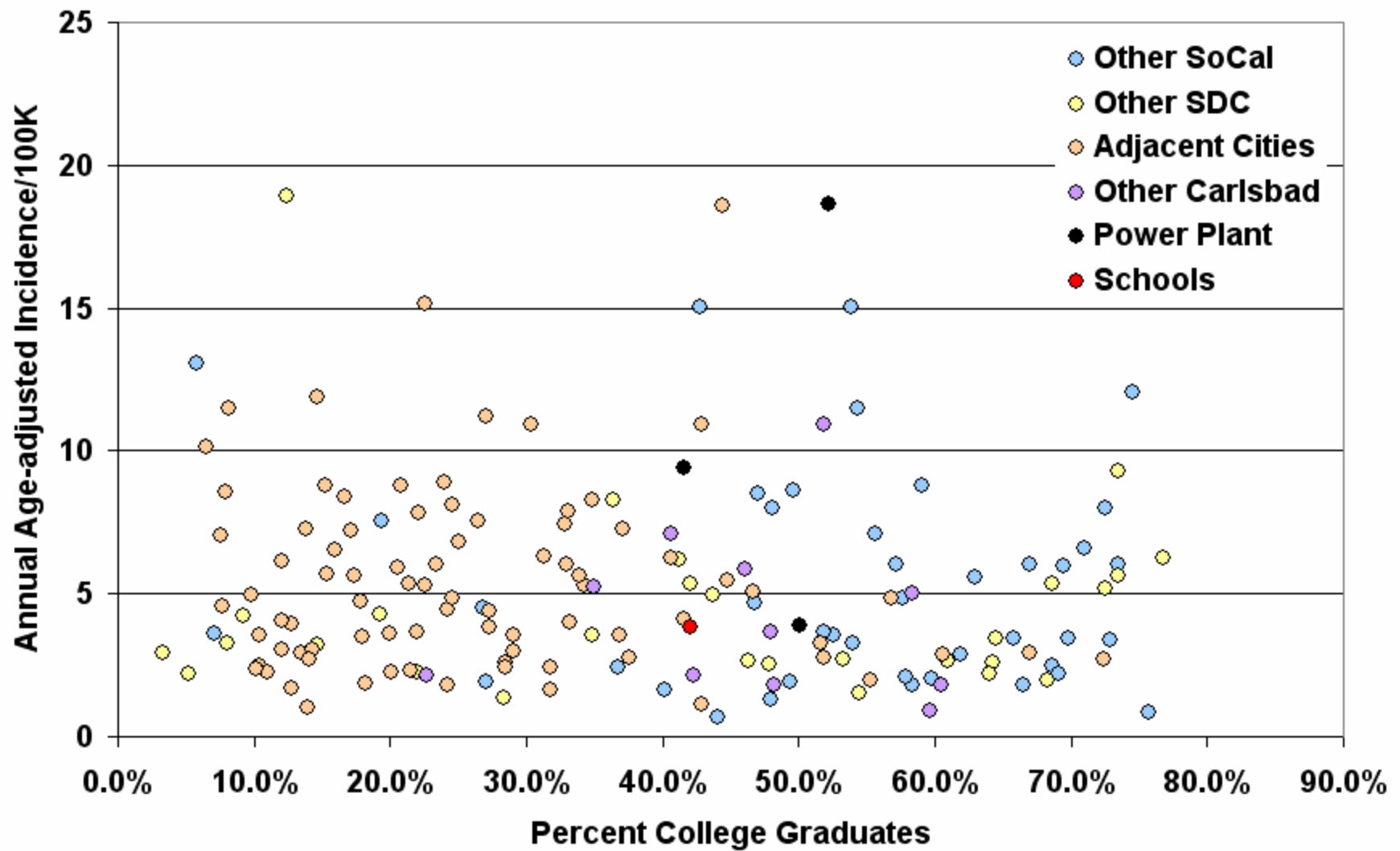
Acute lymphoblastic leukemia— Known Causes

- Ionizing Radiation
- Chromosome abnormalities
 - An unknown virus

Trend in Occurrence of Acute Lymphoblastic Leukemia in Selected California Counties



2000-2007 Census Tract Occurrence of Acute Myelogenous Leukemia according to the Proportion of College Graduates



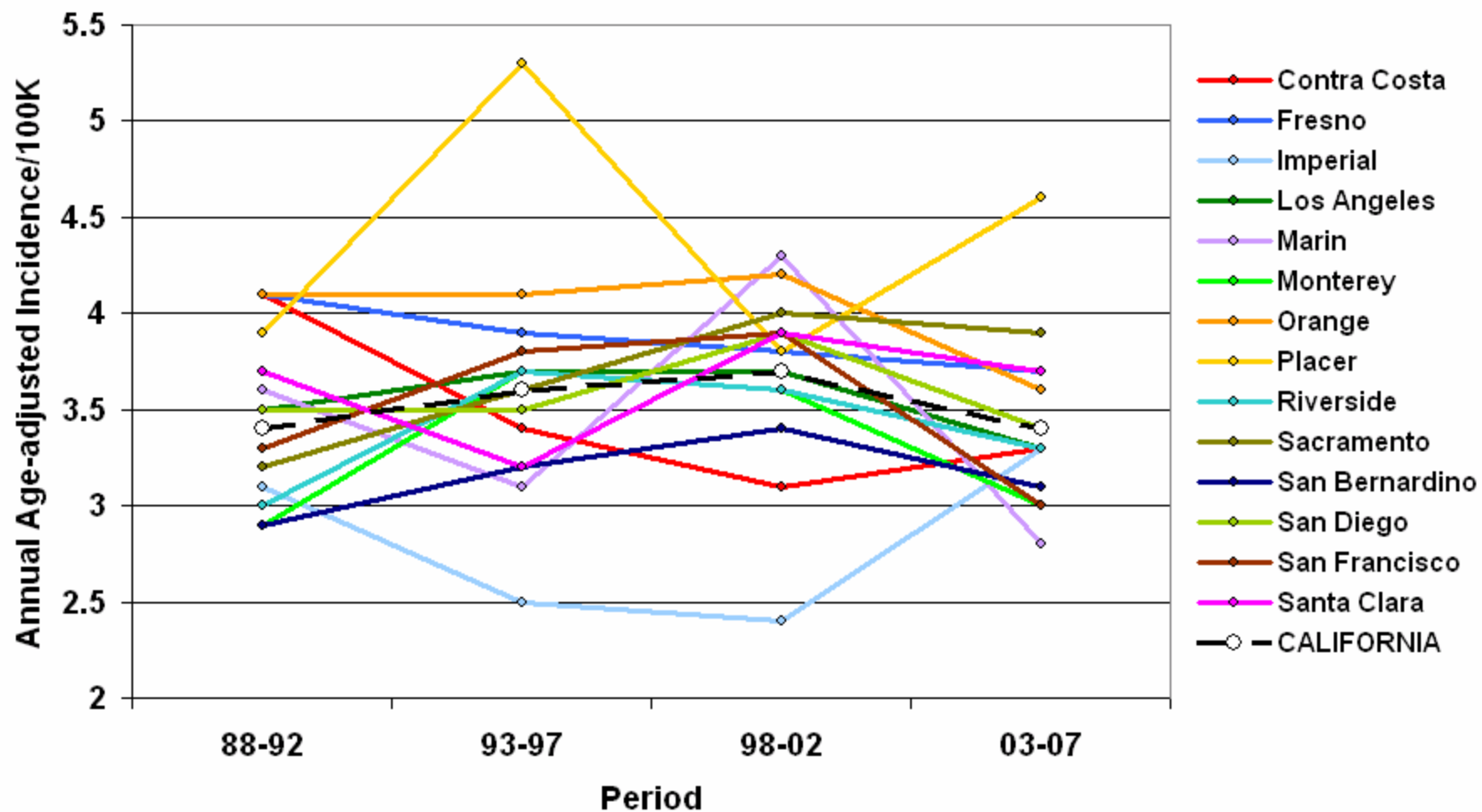
Acute Myelogenous leukemia— Risk Factors

- **Certain Occupations**
 - Radiation exposure
 - Chemotherapy
 - Family History

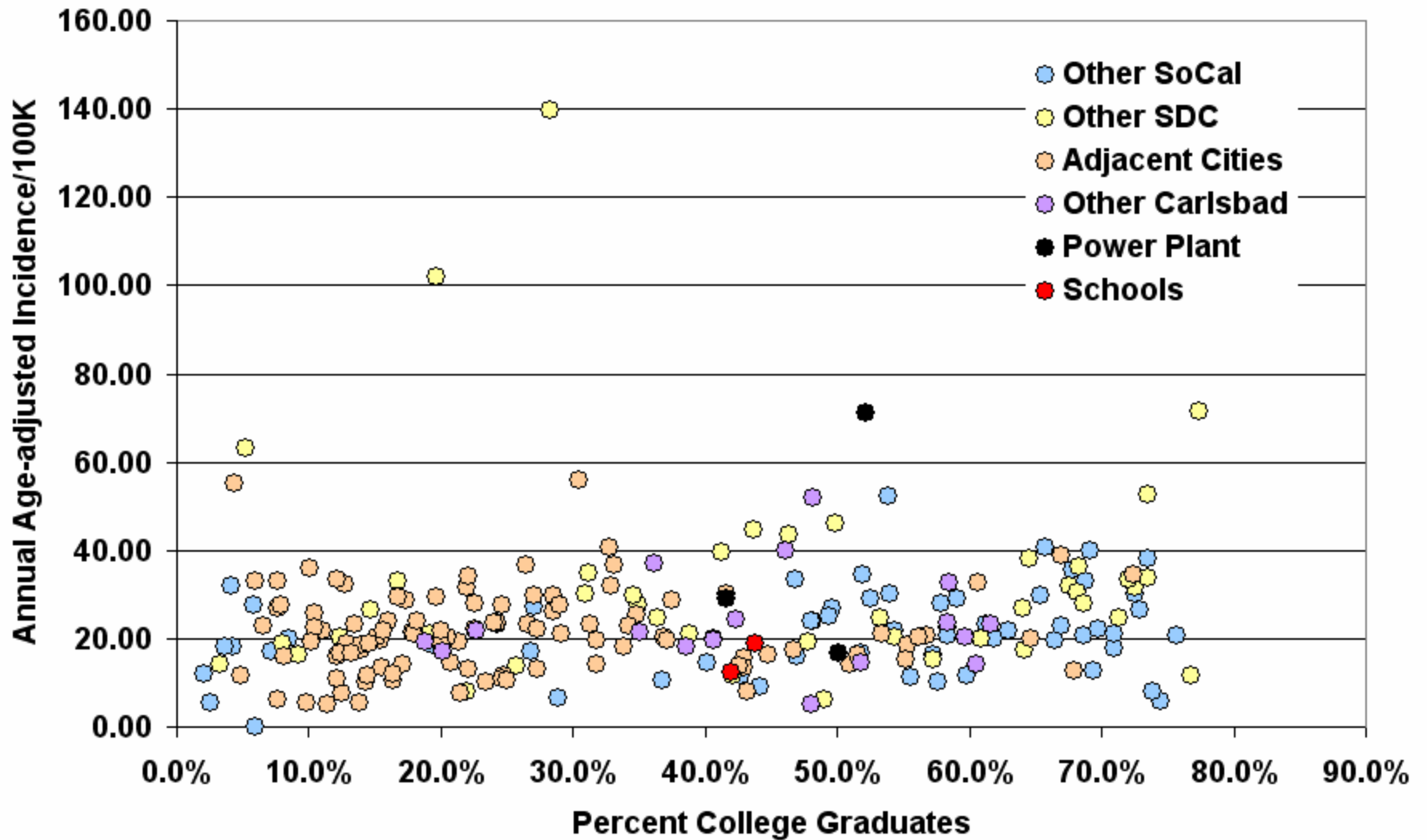
Acute Myelogenous leukemia— Known Causes

- Ionizing Radiation
- Chromosome abnormalities
 - Benzene
 - Chemotherapy
 - Specific genes

Trends in Occurrence of Acute Myelogenous Leukemia in Selected California Counties



2000-2007 Census Tract Occurrence of Non-Hodgkin Lymphoma according to the Proportion of College Graduates



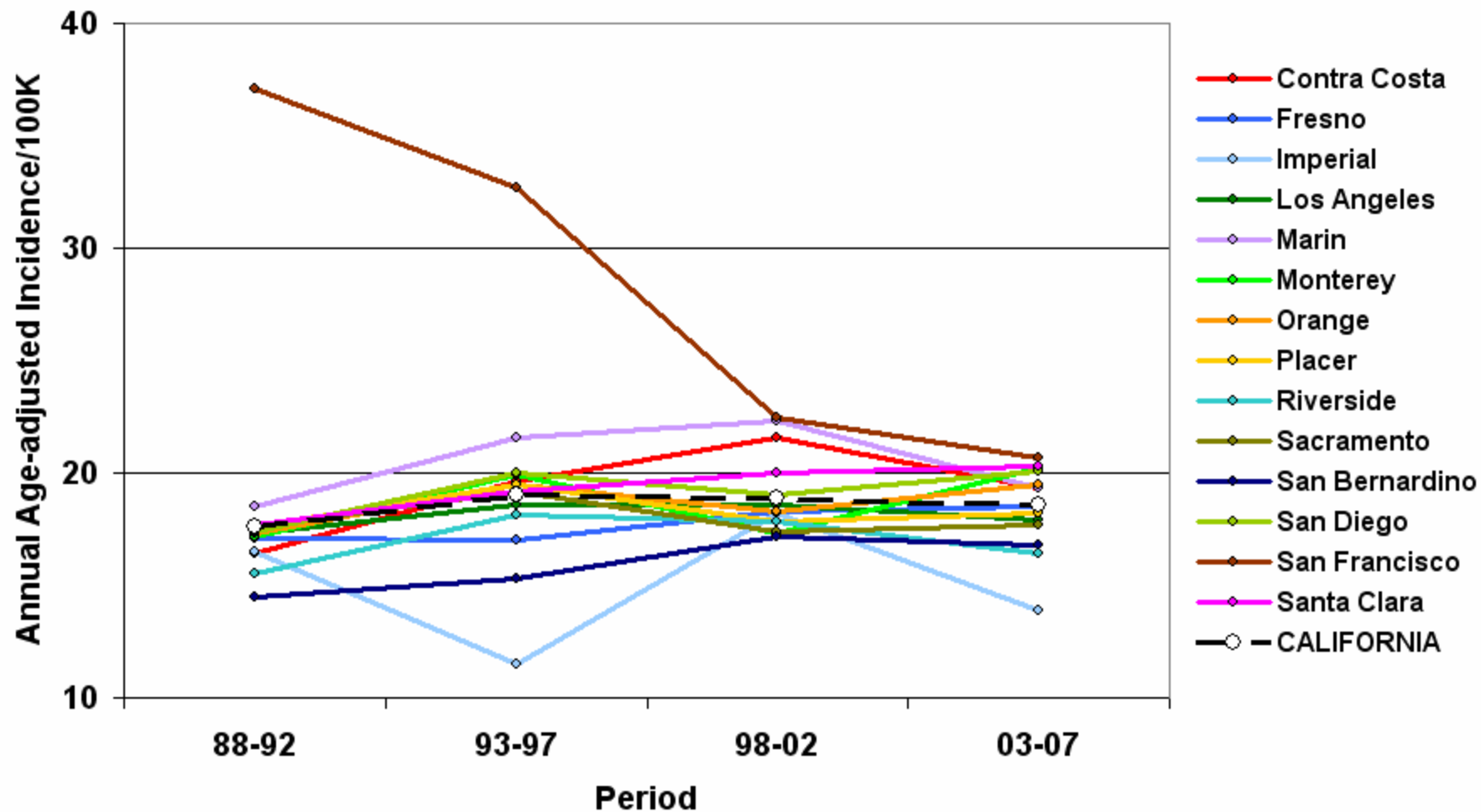
Non-Hodgkin Lymphoma- Risk Factors

- Recent transplantation
 - AIDS
 - Auto-immune disease
- Persons successfully treated for cancer
 - Farming (certain types of adult NHL)

Non-Hodgkin Lymphoma- Known Causes

- Specific auto-immune abnormalities (certain types)
 - HIV virus
 - Immunosuppressive Drugs
- Epstein-Barr Virus (certain types)
 - Hepatitis C
- Helicobacter pylori (certain types)
 - Multiple other infectious agents
 - Chemotherapeutic Drugs

Trend in Occurrence of Non-Hodgkin Lymphoma in Selected California Counties



Carcinogens are Cancer Causes

- Something that if eliminated, prevents cancer
- Genes or Environment
- Environment or *Environment*
- Workplace or Residence
- One's own choice or other people's litter

Genetic Factors (Causal genes)

- Play a role in virtually all forms of cancer
- Usually create susceptibility to environment
- Only a small proportion identified
- The single important factor for a few uncommon cancers

Finding Environmental Carcinogens

- Sources of Information
 - Clinical anecdotes
 - Lab *In vitro* mechanistic biology
 - Animal testing
 - Epidemiological Patterns
- These better for hypotheses than conclusions
- Definitive identification
 - Sound analytical Epidemiology
 - Often not feasible

All tools are imperfect

- Clinical and lab observations not definitive
 - Rarely well controlled or statistically sound
 - Human repair mechanisms are unaccounted for
- Animals are not like people
 - Don't live long enough for carcinogens to act
 - Have different anatomy and physiology
 - No clear basis for extrapolating results
- “Natural” epidemiologic observations are crude
 - Multiple exposures usual
 - Dosage speculative
 - But, like democracy, the worst except for the others

Analytical Epidemiological Studies

- Compare cancer cases to healthy people
- Compare exposed to unexposed people
- Rule out bad luck, biased counting, and other explanations

Formal Criteria designating carcinogens are needed to guide regulation

- THE CRITERION MODEL:
 - International Agency for Cancer Research
 - Definite, Probable, Possible, Unclassifiable
- EPA, FDA, NTP
- CANADA, OTHER COUNTRIES, STATES
- CALIFORNIA EPA: PROPOSITION 65

Our knowledge is limited

- Every kind of cancer has unique causes
- Every case has multiple causes
- No two cases have exactly the same set
- Our ignorance is profound, but varies by type
- Sometimes no patterns, anecdotes, or biological observations have panned out
- We should always test knowledge with reality
- An unexplained excess may give a lead

DEFINITE ENVIRONMENTAL CARCINOGENS

- >20 INDUSTRIAL CHEMICALS
- >15 INORGANIC PRODUCTS
- >15 METALS OR MINERALS
- >15 INDUSTRIAL PROCESSES
- 3 INSECTICIDES/HERBICIDES
- 5 FORMS OF RADIATION
- 10 INFECTIOUS AGENTS
- >30 PHARMACOLOGIC PRODUCTS
- 10 FOOD/DRINKS/HABITS

Carcinogenic exposures in the workplace endanger workers

- Airborne arsenic
- Airborne asbestos
- Other heavy metal dusts: chromium, nickel
- Products of incomplete combustion: soot, diesel exhaust
- Industrial inorganic chemicals: dioxins, PCB's, PBB's, vinyl chloride
- Refinery products like benzene and benzidene
- Solvents: carbon tetrachloride, TCE,
- Agricultural Pesticides: arsenic, chlordane, dieldrin

AIRBORNE CHEMICAL CARCINOGENS FROM INDUSTRY COMMONLY PRESENT IN RESIDENTIAL AIR

- Hexavalent Chromium
- Methylene Chloride
- Benzene
- Trichloroethylene
- Carbon Tetrachloride
- Vinyl Chloride
- Dioxins
- PCB'S, PBB'S

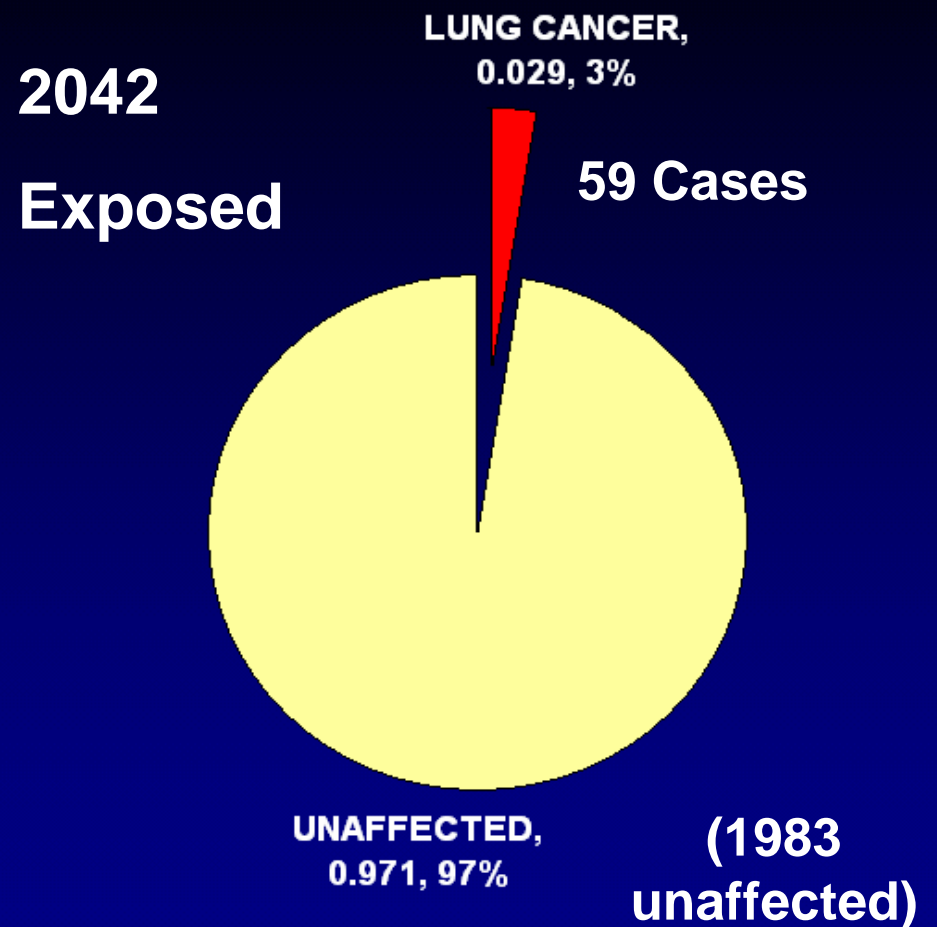
THE HISTORICAL RECORD

- No clear residential excess has ever been attributed to industrial emission of one of these volatile chemicals
- An occasional case could have been caused, but no excess has been identified

PROBLEM OF DOSE

- Workplace doses were high, residential doses low
 - Federal and State regulation is now fairly effective
 - Measurement technology picks up minute doses
 - Dose-response effects are presumed linear
 - Chemicals rapidly disseminate into open space
 - Dilution is proportional to the square or cube of distance from the emission point
-
- ANY SUCH CARCINOGEN COULD CAUSE CANCER, BUT NONE WOULD PRODUCE A NOTICABLE EXCESS OVER BACKGROUND

Effect of Industrial exposure to hexavalent chromium: Mean level 790 micrograms/cubic meter of air

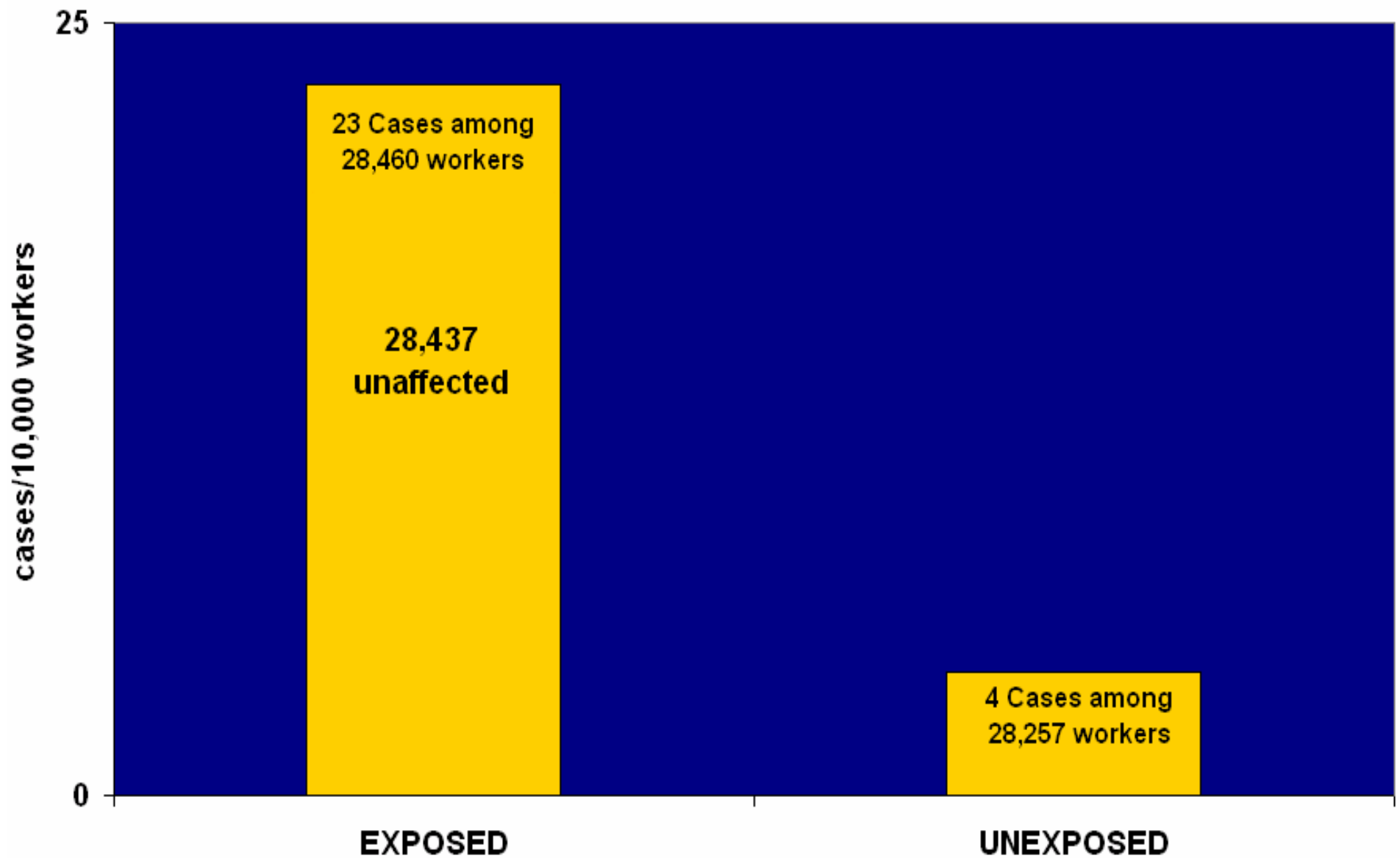


Projected effect of Strongest Community Exposure to Hexavalent Chromium

	Micrograms chromium ⁶ /m ³	Lung cancers /100,000
Workplace	790	1700
Community	0.04	0.09

Thus exposure at the point of the strongest known emission of carcinogen in California, about one extra case per million would appear (i.e. in the average census tract, one case every 200 years)

**Effect of industrial exposure to benzene:
Mean level 275 mg/cubic meter of air**



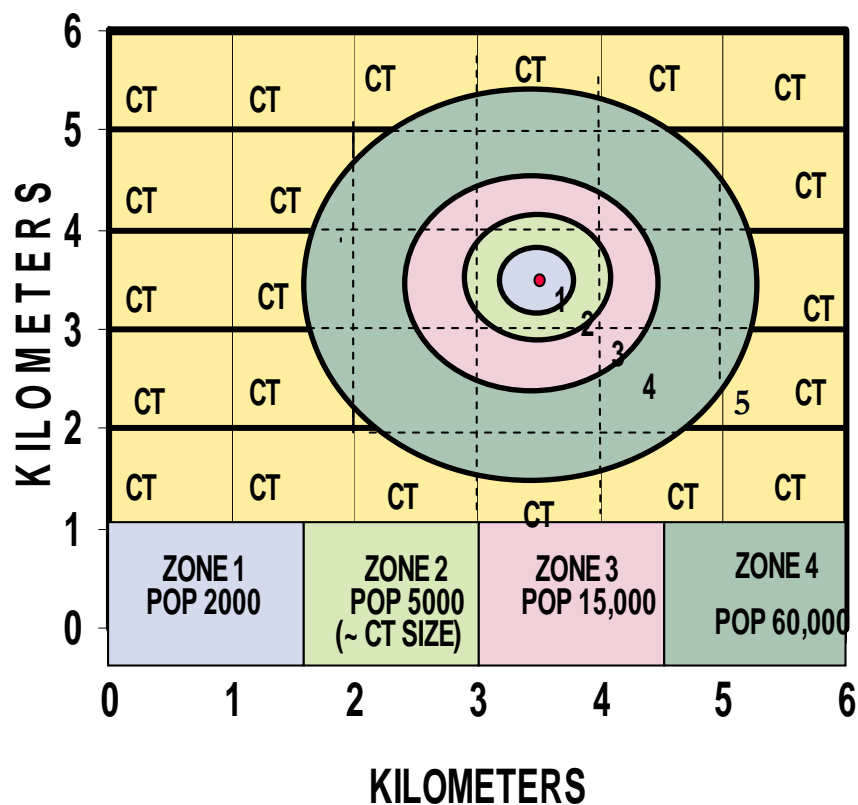
Projected effect of Community Exposure to Benzene

	Milligrams benzene/m ³	New leukemias /100,000
Workplace	275	67
Community	0.2	0.04

Thus exposure to the highest level found in Southern California in 1963 (before current regulations) would produce about one extra case of leukemia per 2.5 million (i.e. in the average census tract, one case every 500 years)

Dispersion of carcinogen emissions

Point of carcinogen emission •



Impact of point source emission of a carcinogen known to double risk

	Population	Distance	Attributable Risk	# Cases
At Source	50	0.1 km	100/100,000	0.05
Zone 1	2000	0.3 km	11/100,000	0.22
Zone 2	5000	0.5 km	4/100,000	0.20
Zone 3	15,000	1.0 km	1/100,000	0.15
Zone 4	60,000	2.0 km	0.25/100,000	0.15
Zone 5	120,000	3.0 km	0.10/100,000	0.12

Thus, no more than a single additional case would be expected

Benzene-special concerns

- Reports of very high residential levels
 - From lawyers
- Component of gasoline
- Storage under gas stations
- Old refinery “tank farms” under housing
- Yet
 - No consistent excess among service station workers
 - No consistent excess among refinery workers

Solvents and Pesticides

- Mechanistic evidence suggests cancer risk
- Cancers are produced in animals, only by high and artificial doses
 - Forms do not correspond to human cancers
- Best evidence from risk to those heavily exposed
 - Dry cleaner workers exposed to TCE, carbon tetrachloride
 - Pesticide sprayers exposed to pesticides/herbicides
 - Arsenic, chlordane/heptachlor, dieldrin, methyl bromide
 - Neither commonly exposed to only one chemical
- In both cases small workplace increases
 - Inconsistent with respect to type and excess
 - “Healthy worker” effect confuses results
 - Regulators presume some danger to be safe
- No evidence to date of residential risk

Arsenic-special concerns

- Many industrial and agricultural uses
- When ingested, skin and GI cancers
- When inhaled, lung cancer
- No history of residential cases from inhalation

Additional Special Concerns

- Electromagnetic Radiation
 - Mobile phones
 - High tension wires
 - Electric blankets
 - Microwave radiation

RESIDENTIAL CARCINOGENS

- BRIEF EXPOSURE, BEHAVIORAL
 - INFECTIOUS AGENTS: Papilloma virus, Hepatitis B, Helicobacter pylori
- CHRONIC EXPOSURE, BEHAVIORAL
 - TOBACCO
 - ALCOHOL
 - HERITABLE OR ACQUIRED IMMUNODEFICIENCY
 - SOLAR RADIATION
 - DRUGS AND HORMONES
 - OBESITY/SEDENTARY LIFESTYLE
 - PHYSIOLOGIC OR THERAPEUTIC HORMONES
 - Foodborne remnants of burning (e.g. well done meat)

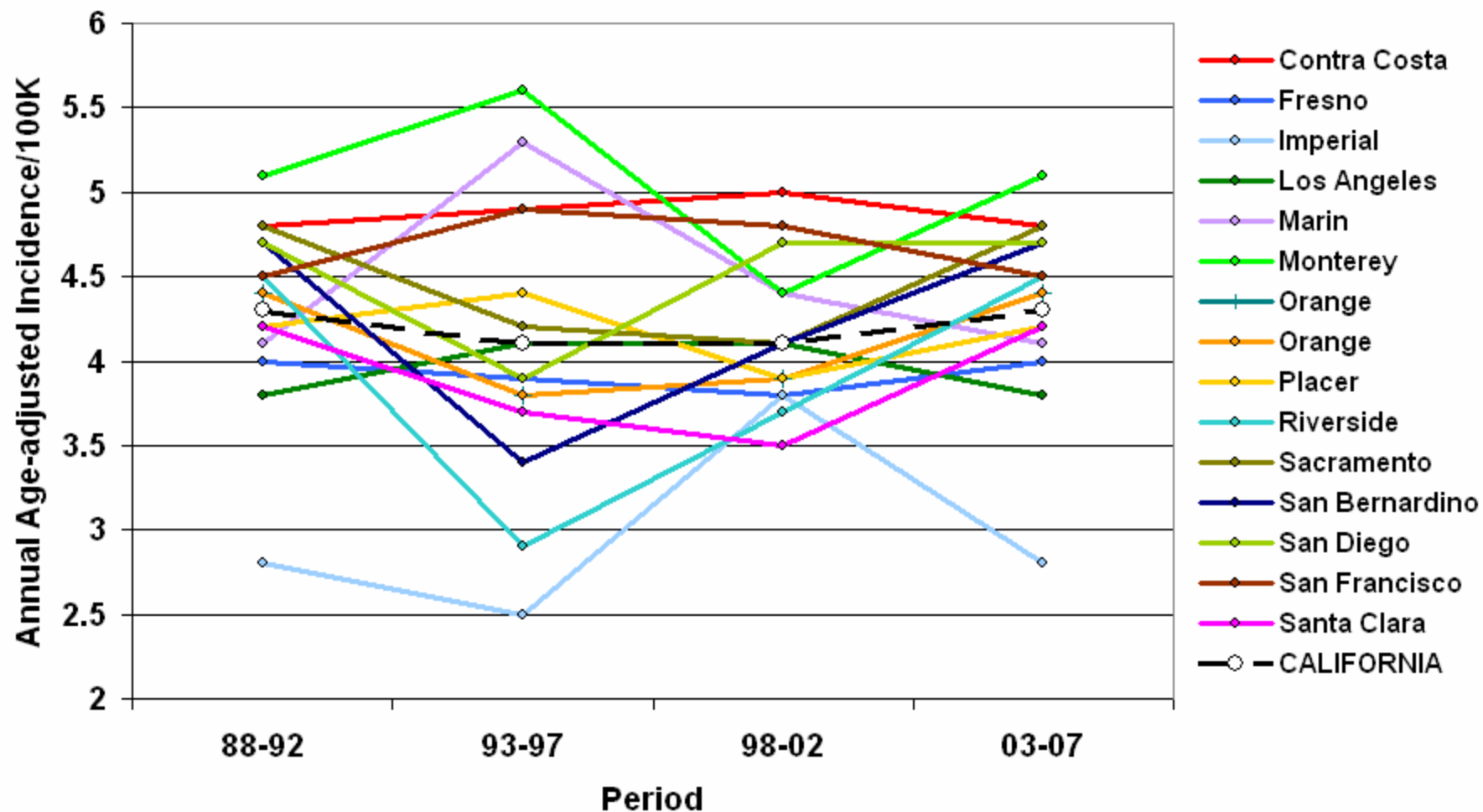
Cancer of the esophagus- Risk Factors

- Natives of Southern South America
 - Natives of northern Iran
- Natives of North Central China
 - Alcoholics

Cancer of the esophagus- Known Causes

- Cigarette smoking
- Alcohol consumption
- Few dietary vegetables and fruits
 - Consumption of very hot tea
 - Unknown food contaminants

Trends in Occurrence of Cancer of the Esophagus in Selected California Counties



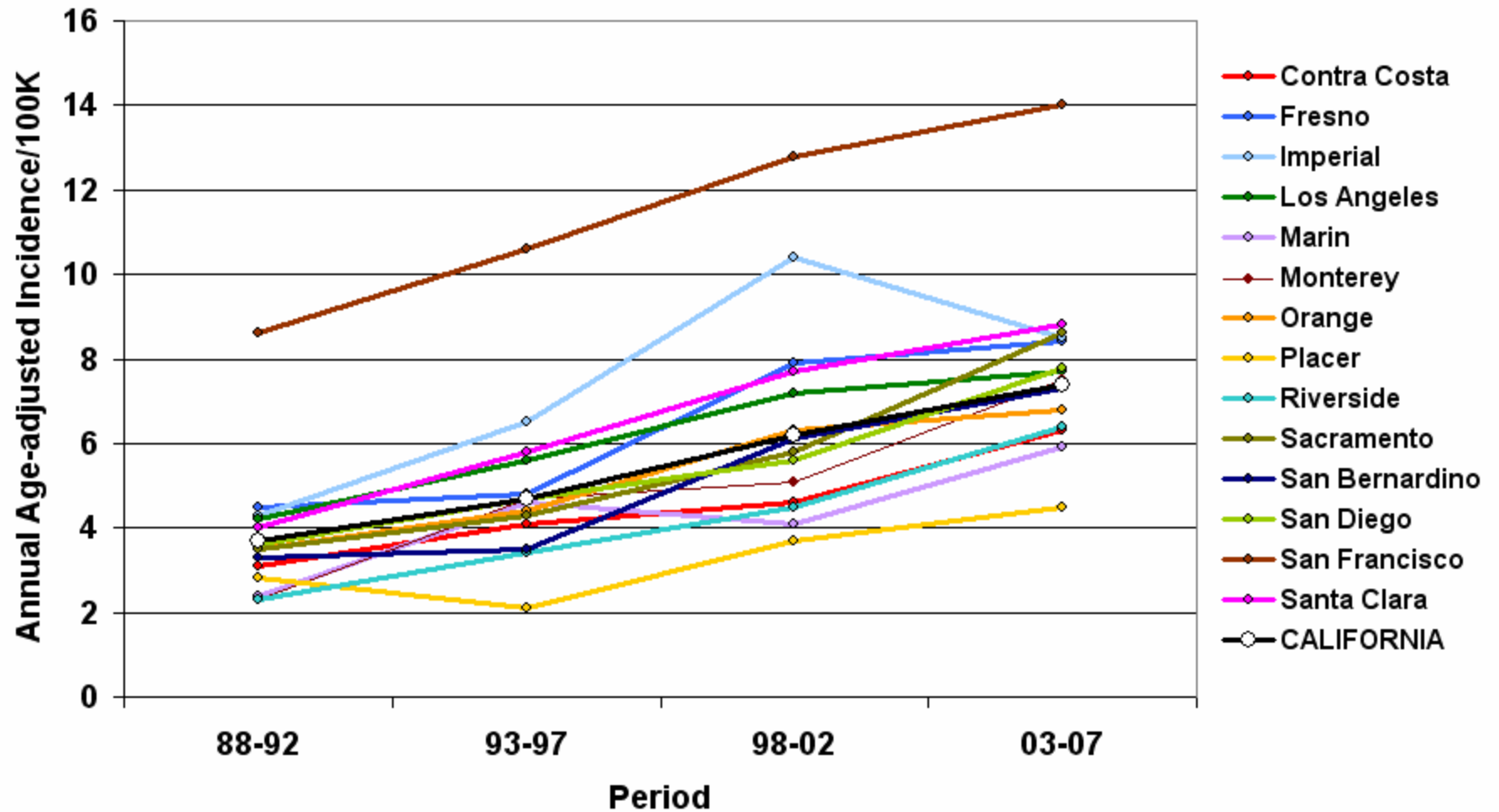
Liver Cancer-Risk Factors

- Native of West Africa or East Asia
 - History of Hepatitis B or C
 - Alcoholism
 - Other specific liver diseases

Liver Cancer-Known Causes

- Hepatitis B or C
- Aflatoxin-contaminated diet
 - Cirrhosis of the liver
 - Cigarette smoking
- Certain oral contraceptives
 - Schistosomiasis
 - Radioactive thorotrast
 - Hemochromatosis
- Certain other inherited metabolic diseases
 - Non-alcoholic fatty liver disease
 - Specific Genes

Trend in Occurrence of Liver Cancer in Selected California Counties



RESIDENTIAL CARCINOGENS

- BRIEF EXPOSURE, ENVIRONMENTAL
 - INFECTIOUS AGENT: UNKNOWN LEUKEMIA VIRUS
- CHRONIC EXPOSURE, ENVIRONMENTAL
 - ASBESTOS FROM CARS AND STRUCTURES
 - POLYCYCLIC HYDROCARBONS
 - FROM LOCAL SOURCES OF COMBUSTION
 - DIESEL EXHAUST FROM TRUCKS, SHIPS, ETC
 - AIRBORNE SOLID PARTICLES SETTLE, DON'T DISPERSE

CARCINOGENIC MEDIA

- TOXIC HAZARD, BUT NO CANCER EXCESS
 - LOVE CANAL
 - WOBURN MA: A CIVIL ACTION
 - HENLEY CA: ERIN BROCKOVICH
- NEITHER HAZARD NOR CANCER EXCESS
 - BEVERLY HILLS HIGH SCHOOL

WITH CHARACTERISTIC PATTERN

- Oropharynx CA
- Sq Esophagus
- Adenoca Stomach
- Upper Colon
- Hepatoma
- Gallbladder CA
- Larynx
- Squamous Lung
- Small Cell Lung
- Large Cell Lung
- Adenoca Lung
- Mesothelioma
- Kaposi Sarcoma
- NS Hodgkin's Dis
- Melanoma
- Breast Cancer
- Cervix Cancer
- Endometrial CA
- Prostate CA
- Anogenital Sq CA
- Squamous Bladder
- Papill. Thyroid CA
- Large B-cell NHL
- Immature C. NHL
- Sm.B/Mixed NHL
- Mult. Myeloma

NO CHARACTERISTIC PATTERN

- Mixed Salivary
- Stomach Cardia
- Small Bowel
- Sigmoid Colon
- Rectum
- Cholangio CA
- Biliary Tract CA
- Pancreas CA
- Nose/Sinuses
- Soft T. Sarcoma
- Angiosarcoma
- Osteosarcoma
- Ovarian CA
- Germ Cell CA
- Acute non-L Leuk.
- Bladder-Transit.
- Kidney CA
- Wilms Tumor
- CNS Malignancy
- Retinoblastoma
- Neuroblastoma
- Follicular Thyroid
- Mult End Neoplasm
- MC Hodgkin's L.
- Follicular NHL
- T-cell NHL
- ALL
- CLL
- CML
- Mixed Cell, Genitalia

Known Local Outbreaks of Cancer

- Acute Lymphoblastic Leukemia
 - British new towns, Fallon, NV
 - Probable introduction of virus from population influx to isolated community
- Sarcomas and possibly Lymphomas
 - Seveso, Italy
 - Dioxin spill from factory
- Bladder Cancer
 - Taiwan, Chile, Argentina, Bangladesh
 - Naturally occurring arsenic in the water supply
- Malignant Mesothelioma
 - Turkey, Italy, New Caledonia, Libby MT
 - Whitewash or building materials with asbestos
 - Tailings from asbestos-containing vermiculite mine

Causes of true, but non-environmental “clustering”

- Changes in Diagnostic technology or usage
 - New, more sensitive test
 - New convenient or cheap equipment
 - Change in public motivation
- Errors in the Census Denominator
 - Rapid post-census growth
 - Temporary residency for medical care
- Demographic Differences in Risk
 - Ethnicity
 - Social Class
 - Occupational History
 - Culture: Habits, Behaviors, etc

True excess: Fallon, NV 2000-2001

Acute Lymphoblastic Leukemia

Expected number of cases: 0.3

Observed number of cases: 16

Probably due to a virus introduction

Chance has several effects

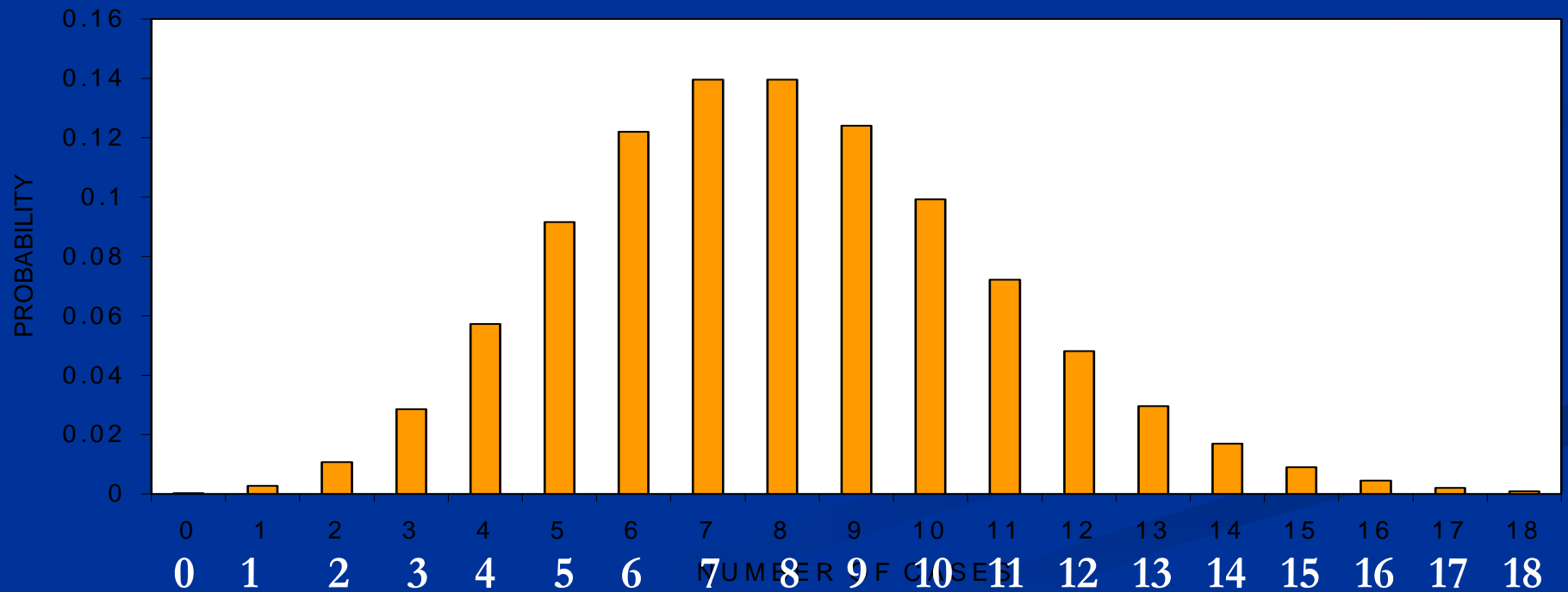


- Variation in population size at a given time
- Variation in baseline occurrence by chance
- Variable small number of added cases
- Large number of “clusters” from chance

Variation when 7-8 cases are Expected per census tract

Distribution of the number of cases
occurring by chance per tract
assuming the average is equal to μ

Number of Cases



The number expected rarely appears

- A toss of two dice, on average, should give a 7
 - Happens only one in 6 tries; otherwise half higher, half lower
 - When x cases are expected, very often more by chance

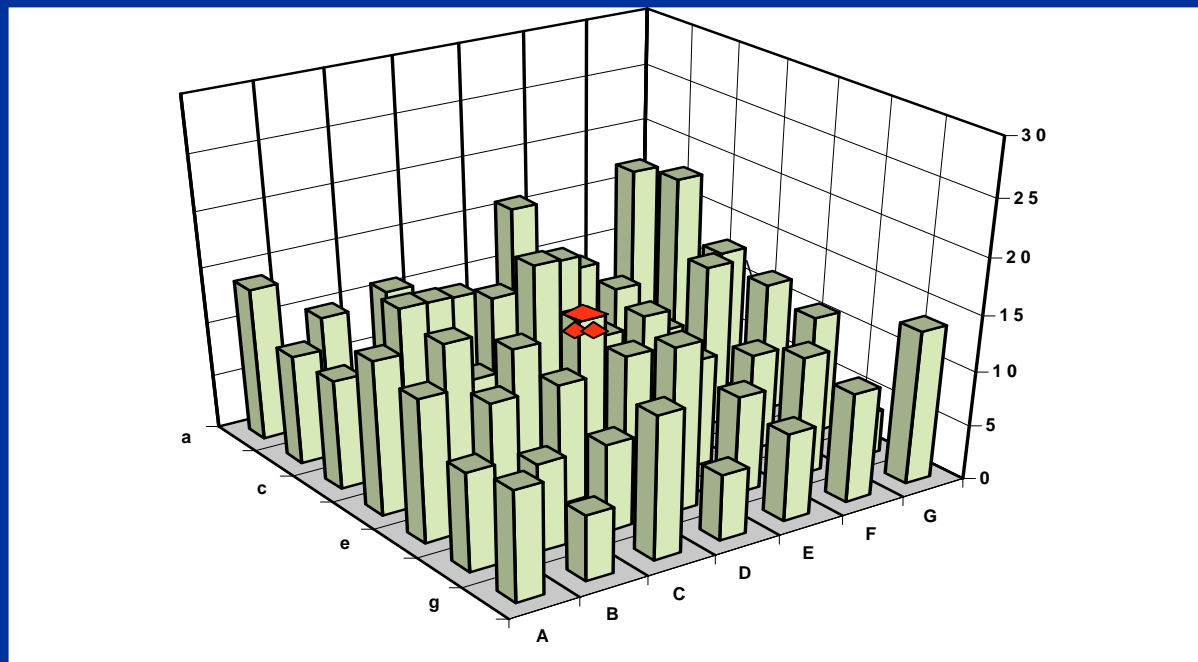
The number expected rarely appears

- Especially if the expected number is small
 - A specific card from a deck should appear twice out of 100 separate draws
 - If 100 separate sets of 100 draws are repeated, the card will appear twice in only 59%.
 - In 9% the card will not be drawn at all, and in 32% it will appear 3 or more times.

The number of tries matters

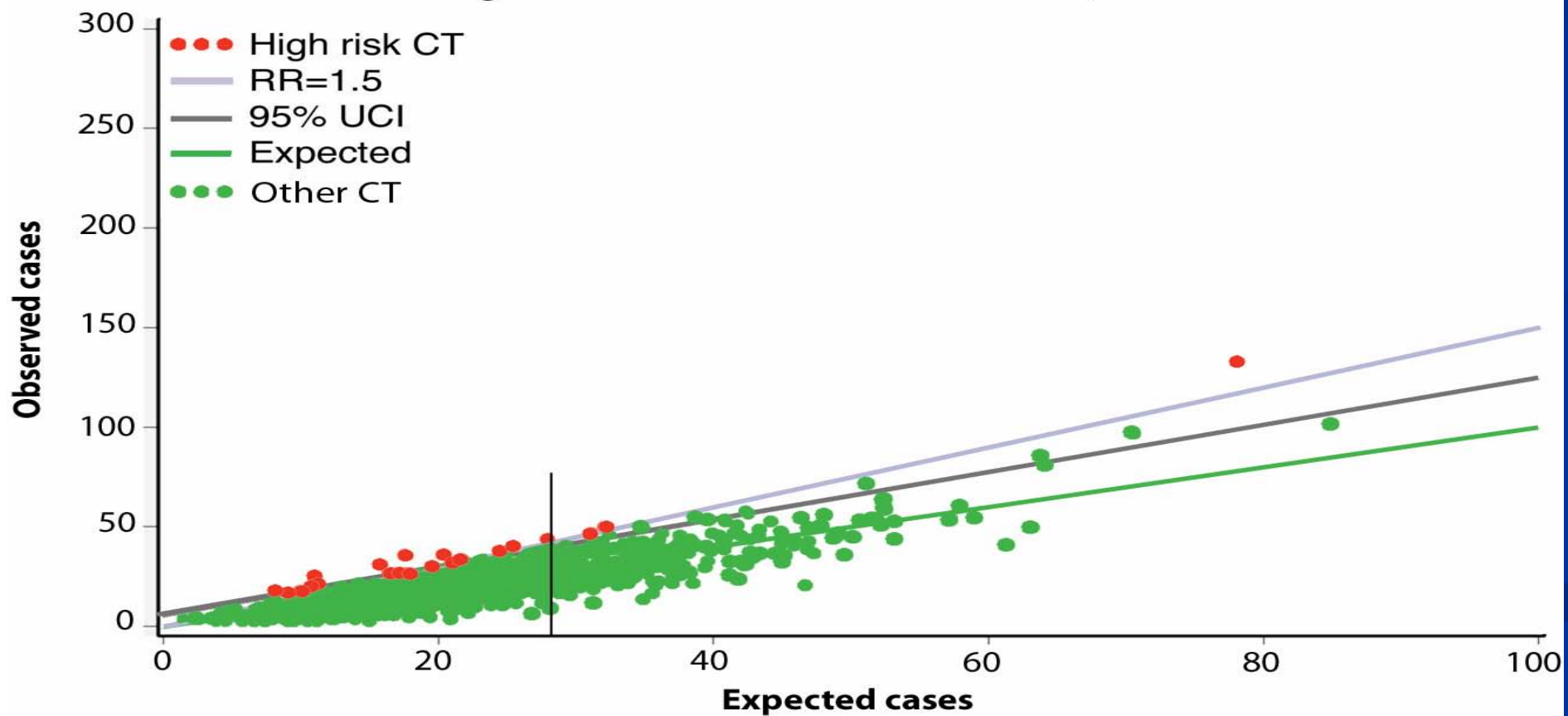
- Say something happens 1% of the time by chance
 - If it happens in your neighborhood, not chance
 - If there are 100 neighborhoods, one is usual
 - If there are 1000 neighborhoods, there should be 10
 - If there are 5000 neighborhoods, there should be 50
 - There are a lot more than 5000 neighborhoods

Relatively small number of cases attributable to emissions



Census Tracts at high risk of COL

according to the number of observed and expected cases



Is a cluster real or by chance?

A judgment call

If this many cases are expected,	At least 5% of tracts will have as many as:	At least 1% of tracts will have as many as:	Given 5,000 tracts at risk, concern gets serious at:
0.5 cases	2 cases	3 cases	6 cases
1 case	3 cases	4 cases	7 cases
2 cases	5 cases	6 cases	9 cases
5 cases	9 cases	11 cases	15 cases
10 cases	16 cases	18 cases	23 cases

Two cases of NHL in the same house: Should we be concerned?

- Incidence of NHL = Incidence of cancer < 25 yrs = 10/100K/yr
- Assuming 4 persons/house, incidence = 40/100K/yr
- = 4/10,000/yr = 1 affected house/2500/yr
- California has 32 million people, 8 million houses
- Therefore California has 3200 houses affected by NHL per year, or 32,000 affected over 10 years
- Assume 3 other persons per house are at risk, or 96,000/yr
- Each year in California, 9.6 houses having one person affected at some point in the previous 10 years will have a second case

- In San Diego County, with 1/10 the California population, one such house would be expected annually.

Deaths from Malignancy in Young People, San Diego County, 2004-2006

	Under 5	5-14	15-24	Total
Leukemia	6	11	18	35
Brain/Spinal cord	4	9	5	18
Sarcomas	2	4	8	14
Lymphomas	0	0	5	5
Other malignancies	7	5	21	33
Total	19	29	57	105

Could any of these deaths been prevented by the application of current knowledge?

- Probably not
- The single breast cancer, if heritable and if heritability had been recognized, might have been prevented by mammography or prophylactic mastectomy
- Even the single person dying with lung cancer had probably not had enough smoking time.

Deaths in Young People, San Diego County, 2004-2006

Cause of Death	>5	5-14	15-24
Malignant neoplasms	19	29	57 (53)
Infectious Disease	8	5	13
Other chronic diseases	71	104	214
Congenital anomalies	185	11	207
Auto accidents	3	226	246
Motorcycle accidents	0	34	34
Other accidents	35	85	132
Overdoses	0	29	29
Suicides	0	100	204
Murders	6	150	161
Total	318	796	1232

How is cancer to be prevented?

Stop smoking and drinking	Personal choice
Adopt and active lifestyle, control weight	Personal choice
Avoid sunburns and excess sun	Personal choice
Support surveillance of toxins, cancers	State
Support regulation of carcinogens	Federal/State
Support research on causation	Federal
Take part when asked to participate	Personal choice
Screen: breast, colon, cervix, skin	Personal choice