Cancer Occurrence in Offsite Neighborhoods Near the Santa Susana Field Laboratory

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Reasons for Concern

- Intensive testing of rocket fuels
- Usage of solvents, chemicals, metals, radionuclides
- Presumed carcinogen contamination
- Lymphomas and lung cancers among workers

- History of accidents, spills and releases
- Possible dispersion offsite by air and water

- Safety conditions relaxed, inadequate monitoring
- History of secrecy and non-responsiveness

Reasons for Scientific skepticism

- Lack of any clear risk found by previous searches

Previous searches were Inconclusive

Study	Periods	Locations	Cancers	Conclusions
Perkins-Wright	1978-82 1983-87	5 LA Tracts	11 Sites	Single Tract Bladder 1.5 83-7 Overall: Inconclusive
Coye-Goldman	1973-82 1983-88 1988-89	Aggregated Tracts by County	14 Sites aggregated	Bladder 1.3 83-88 LA tracts Lung 1.1 88-89 VEN Tracts Suspect Confounding
Nasseri	1988-95	Aggregated VEN Co Tracts	12 Sites aggregated	No positive findings
Morgenstern	1988-95 1996-02	Aggregated LA, VEN Blocks in 3 belts by Distance	9 Sites aggregated	Lung 1.1 Middle Belt 88-95 Melanoma 1.2 Middle Belt 96-02 Thyroid ? Proximity effect Aerodigestive? Proximity effect

Problems with Previous searches

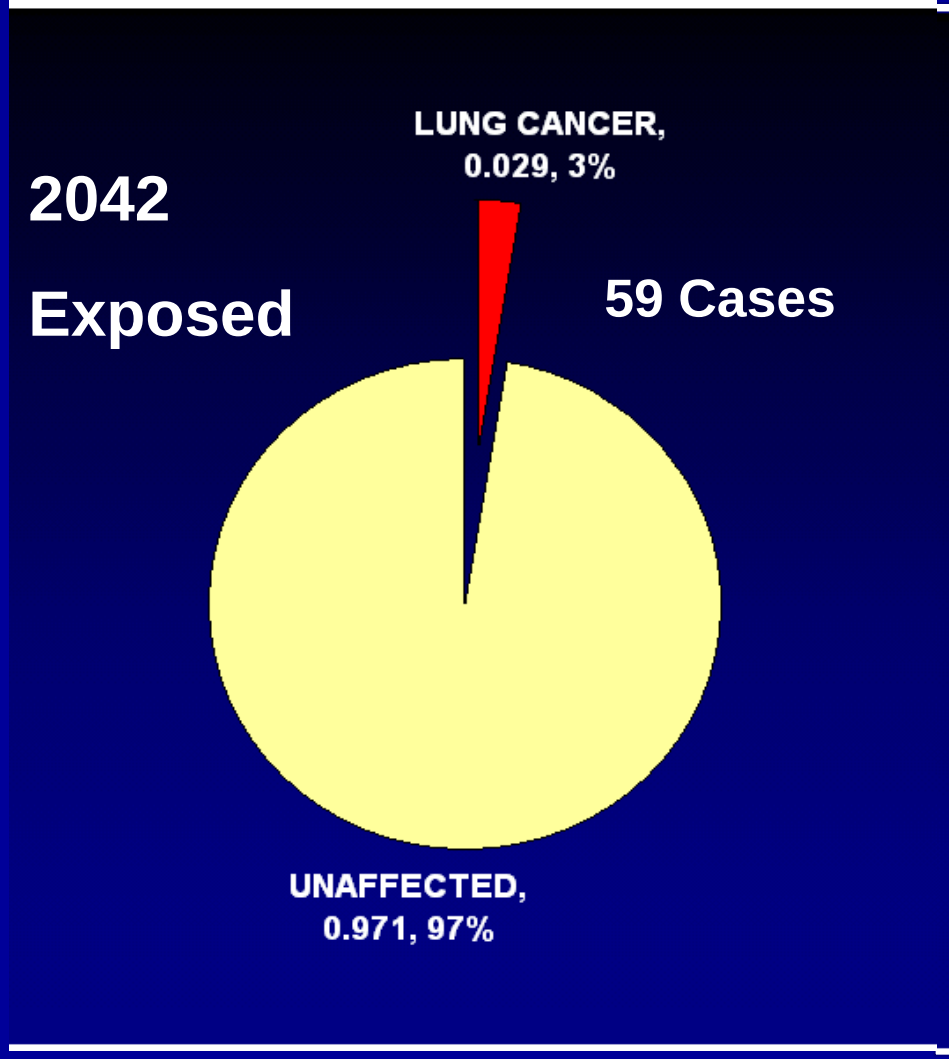
Study	Problems
Perkins-Wright	Multiple comparisons without adjustment Weak associations Bias: response to cluster report Confounded by Race and Social Class
Coye-Goldman	Multiple comparisons without adjustment Weak associations Aggregation obfuscates location Confounded by Social Class
Nasseri	Multiple comparisons without adjustment Aggregation obfuscates location Low statistical power Confounded by Social Class
Morgenstern	Multiple comparisons without adjustment Weak associations Aggregation obfuscates location; Distance is not dose Confounding by Social Class

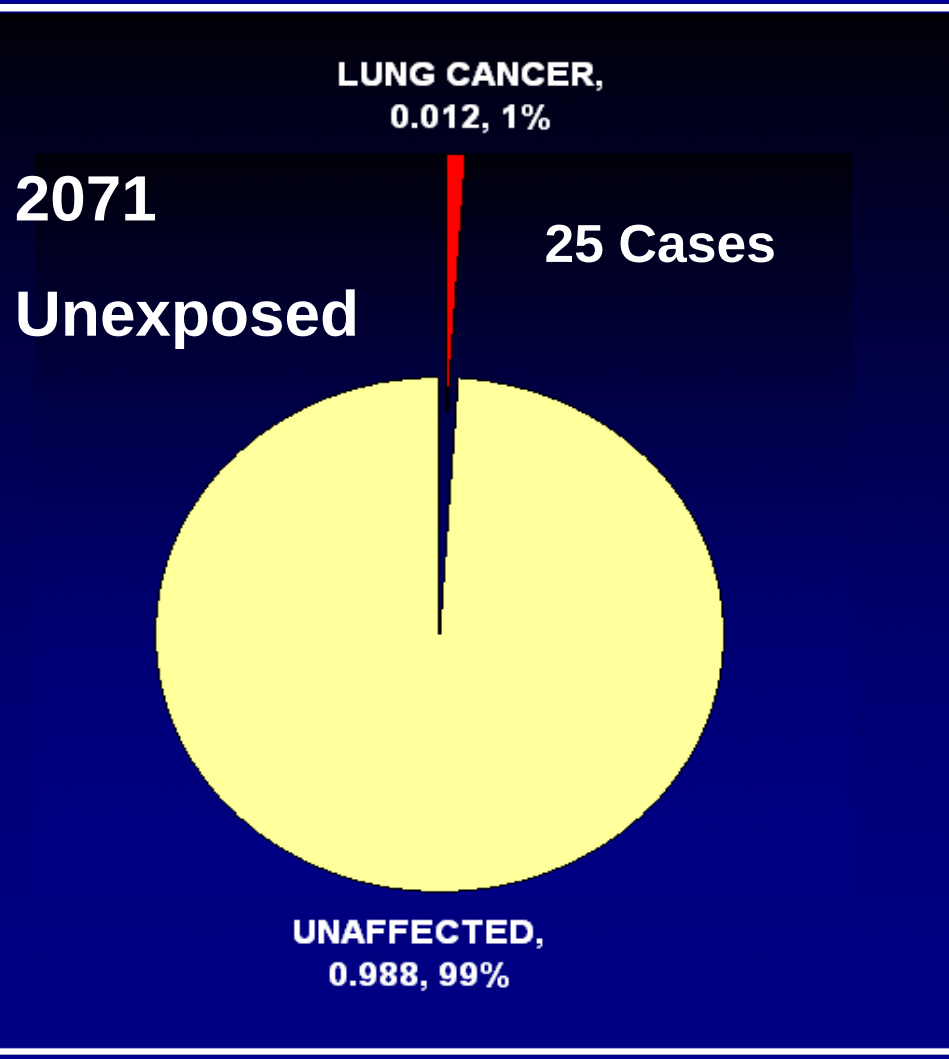
Reasons for Scientific skepticism

- Ambiguous and controversial exposure estimates
- The presence of a carcinogen, especially when technology permits detection of very low levels, does not necessarily constitute a major hazard
- High dose levels are needed to produce a measurable cancer excess

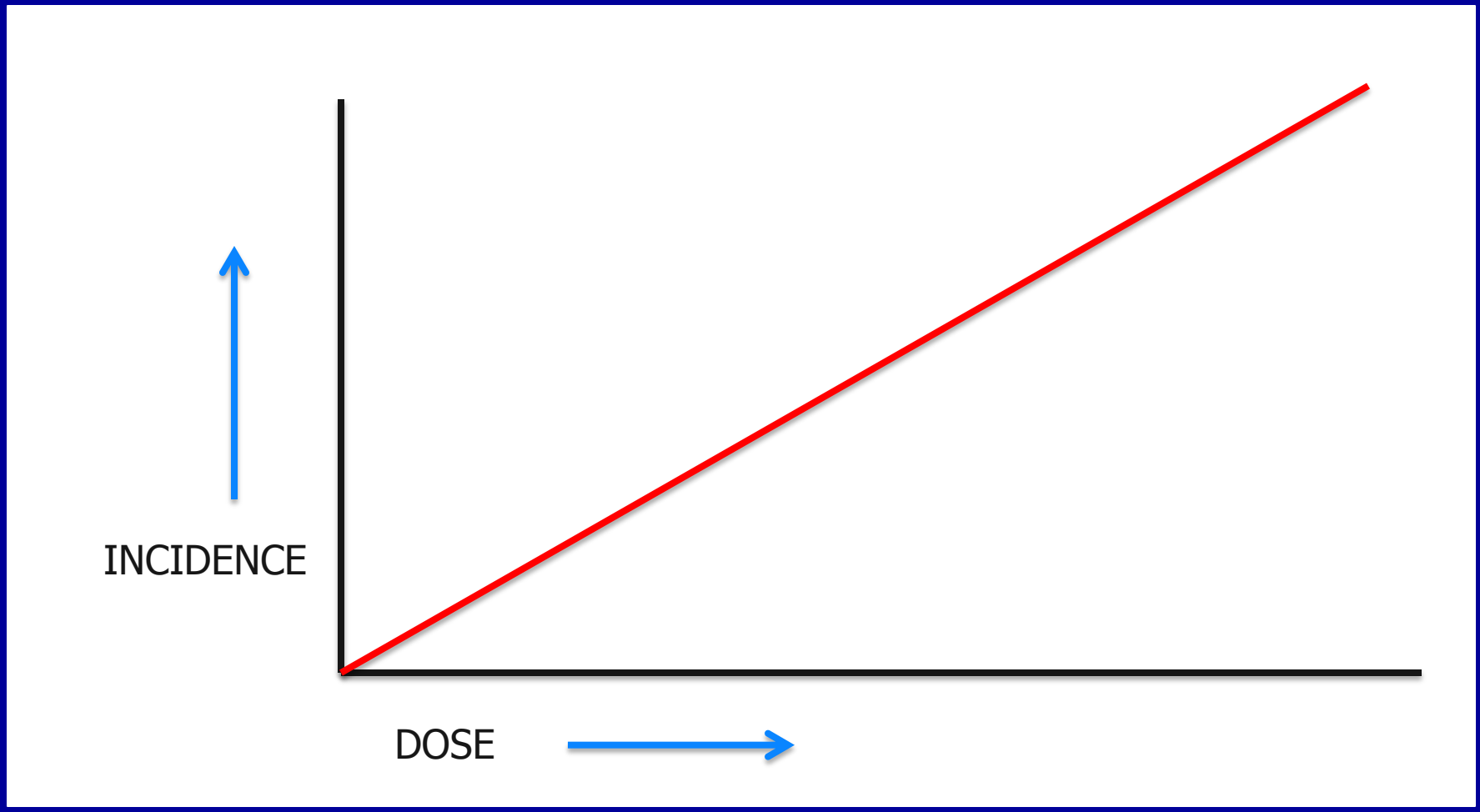
Effect of Industrial exposure to hexavalent chromium:

Mean level 790 micrograms/cubic meter of air





Carcinogenesis increases linearly with dose

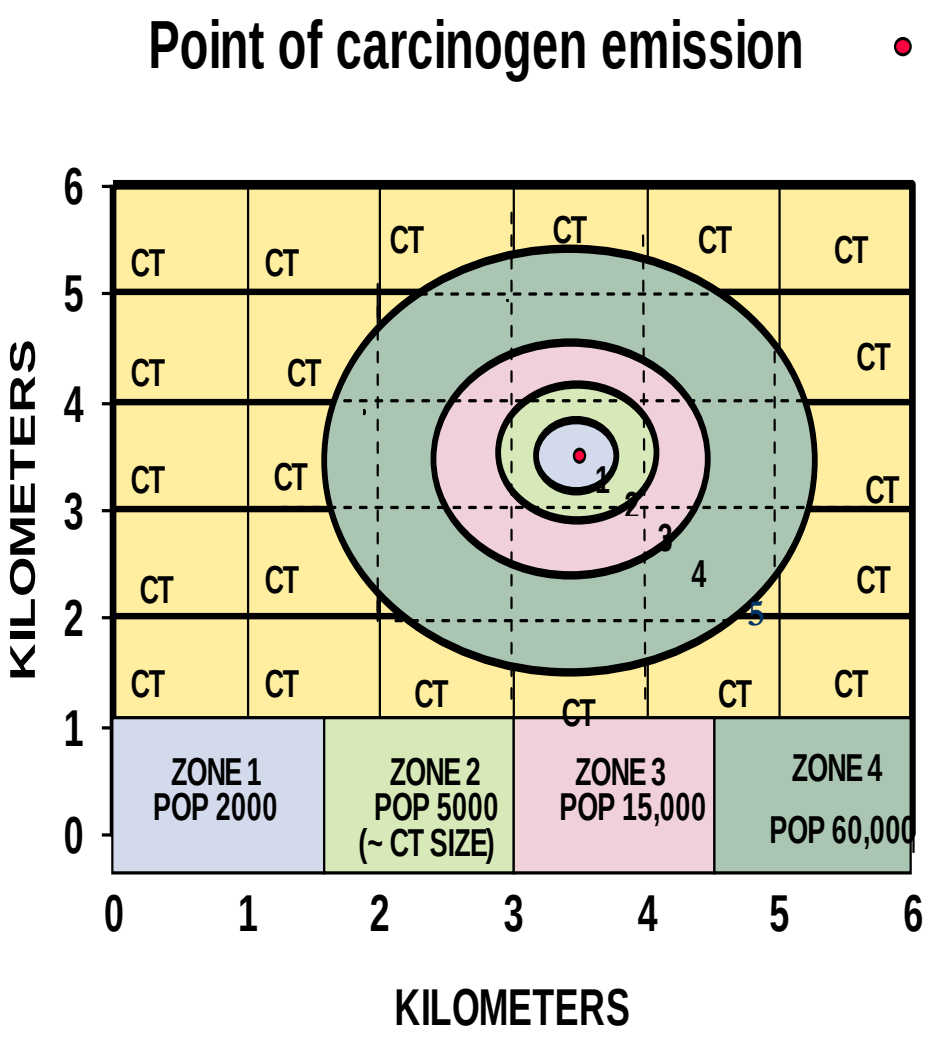


Projected effect of Strongest Community Exposure to Hexavalent Chromium

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

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

Dispersion of carcinogen emissions



Emission dose level to individuals is variable

- Chemicals rapidly disperse into air/water
- As the distance from the site increases:
  - More people are exposed
  - Exposure dose is lower
  - Dispersion results in dilution: dose is inversely proportional to distance

Impact of point emission if dose is thought to double the 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

No more than a single additional case would be expected

Reasons for Scientific skepticism

- Absence of historical precedents

Precedents: Environmental cancer clusters do occur (other than occupational risks)

Fallon, NV: 2000-2001, 16 ALL cases occurred, 0.3 expected

Host to thousands of diverse visitors

Libby, MT: Multiple cases of mesothelioma in a small town

Tailings of asbestos-containing vermiculite

Cappadocia, Turkey: Cluster of cases of mesothelioma

Greece, Italy, New Caledonia: Clusters of mesothelioma

From building materials or whitewash with asbestos

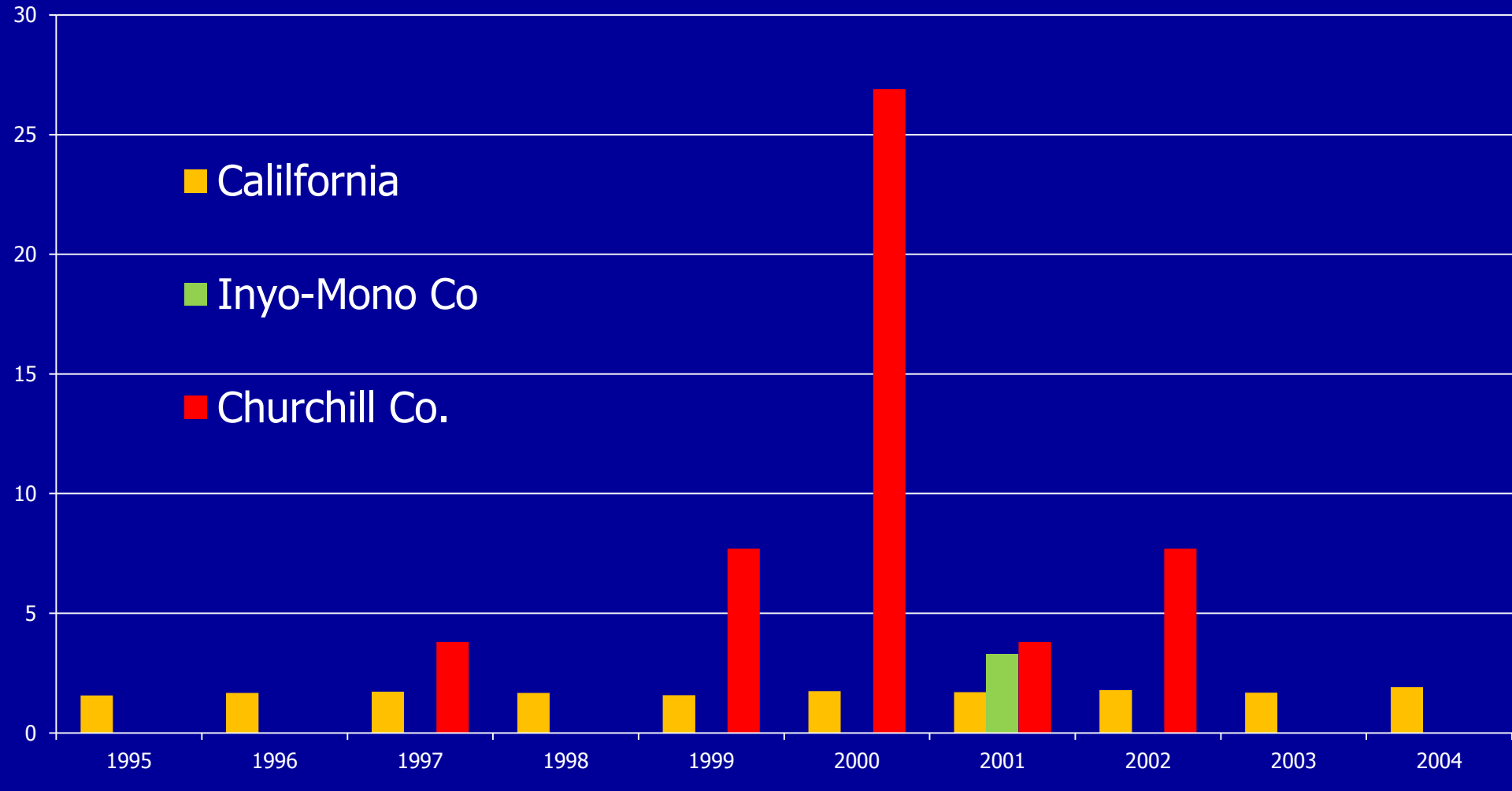
Ukraine/Belorus: Localized thyroid cancer in young persons

From nuclear fallout

Taiwan, Chile, Argentina, Bangladesh: Localized bladder cancer

Groundwater contaminated with natural arsenic deposits

Churchill County (Fallon) ALL Cluster Rate compared to California Rates



If dose is usually weak, why are “clusters” found?
Two different circumstances

Strong direct exposure, highly targeted at close quarters

Household asbestos, person to person virus

Sufficient dose by *short-term but intense* exposure

Sufficient dose to ***single families or compounds***

Strong indirect or distant exposure, disseminated by air/water/soil

Chernobyl, waterborne arsenic, asbestos tailings

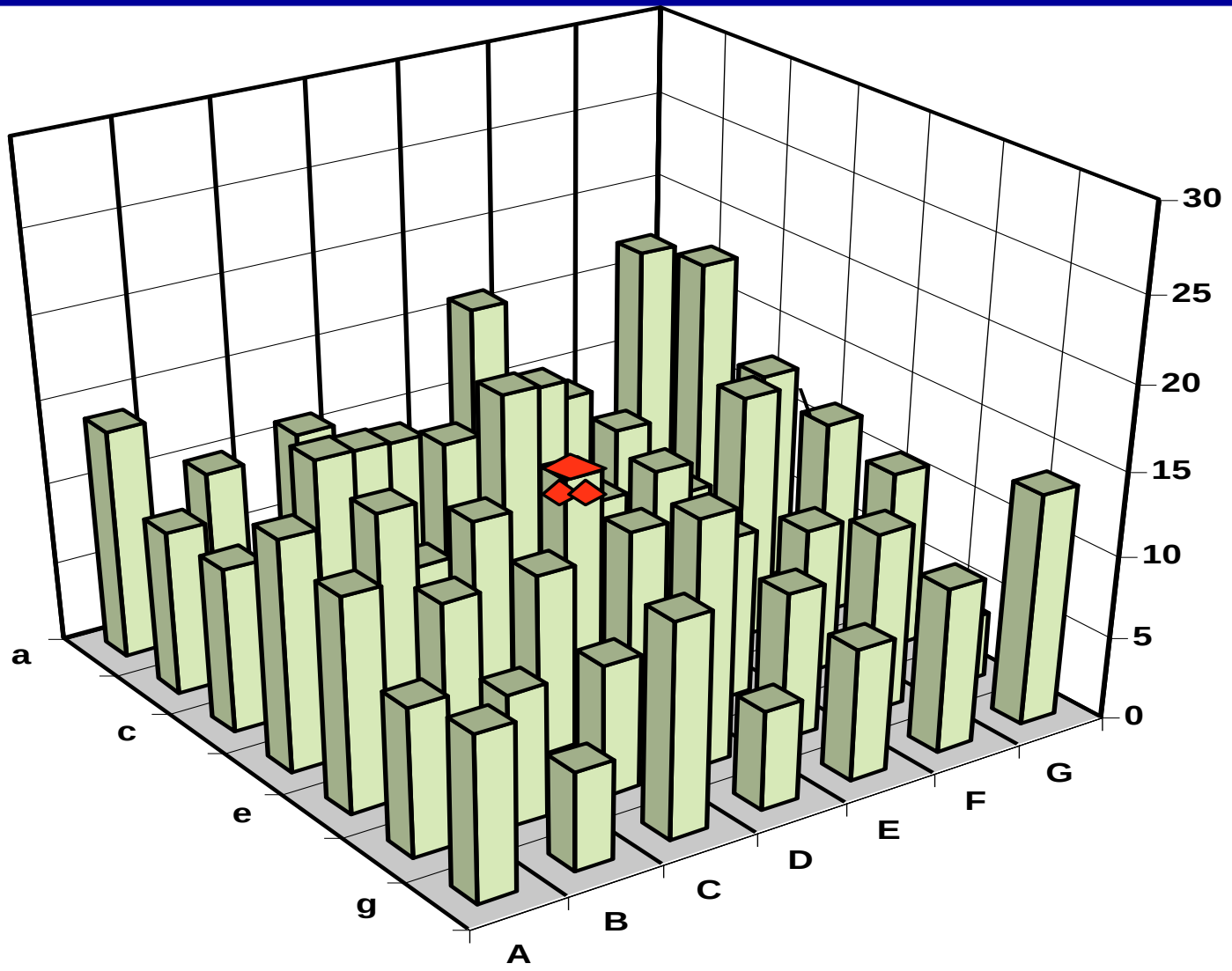
Sufficient dose by ***continuous cumulative*** exposure over the long-term

Sufficient dose disseminated to ***multiple adjacent localities***

Weak exposure

Rare cancers undetectable, common ones lost within random variation

If the cancer is not rare, the usual cases outnumber the added ones (and vary in number by chance)



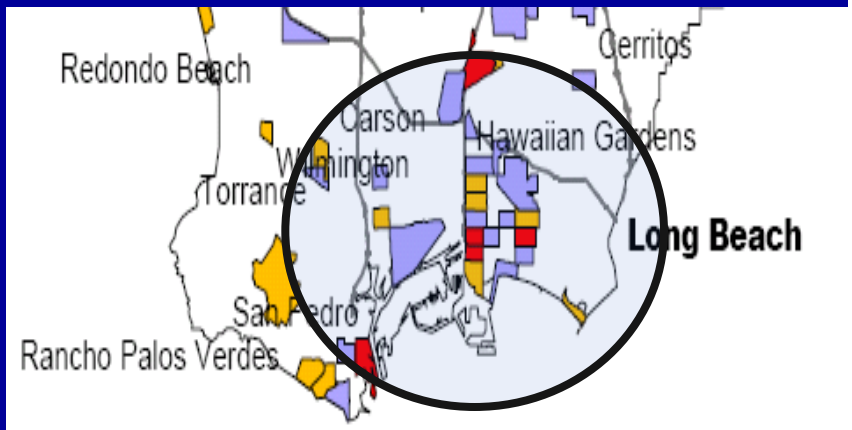
The Challenge

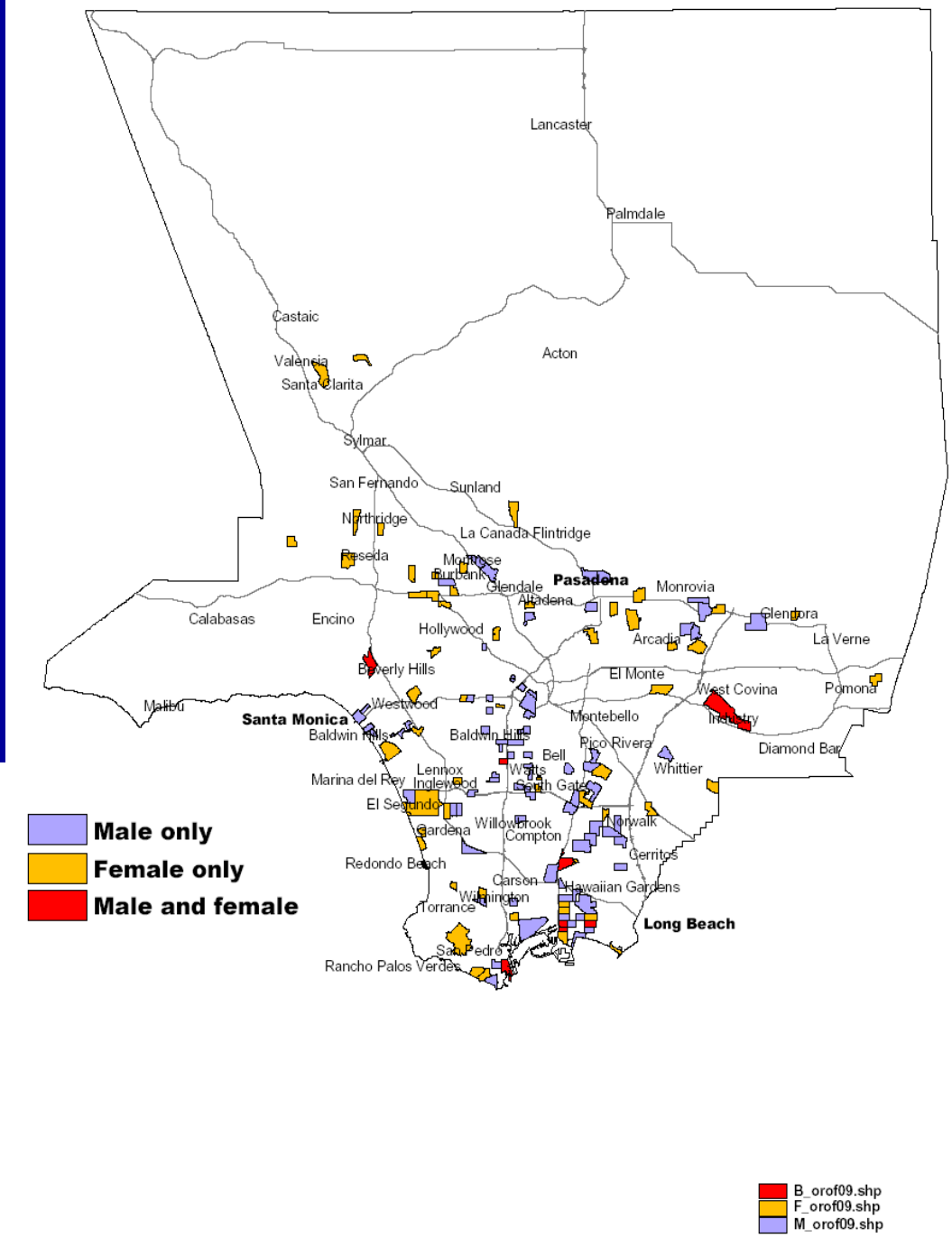
- Some offside residents may have been exposed to carcinogens at ***some*** dose
- They may well have ***some*** added cancer risk.
- The challenge is to see if a ***measureable and unambiguous*** increase in risk has been produced.
- Must examine ***individual*** neoplasms and ***individual*** tracts

To demonstrate an unambiguous association:

- Increase must be at least 50%, a relative risk of 1.5 (there are too many alternative explanations for a weaker link)
- Chance must be excluded
- Adjacent tracts (localities) offsite should have high exposure in common
- Here is a local example

Carcinoma of the Oropharynx





Steps in Linking Environmental Carcinogenicity to a Particular Locality

1. Assess the likelihood that any association between cancer incidence and a residential locality could be explained ***by chance***

2. Ensure that any such association cannot be explained by ***a bias***

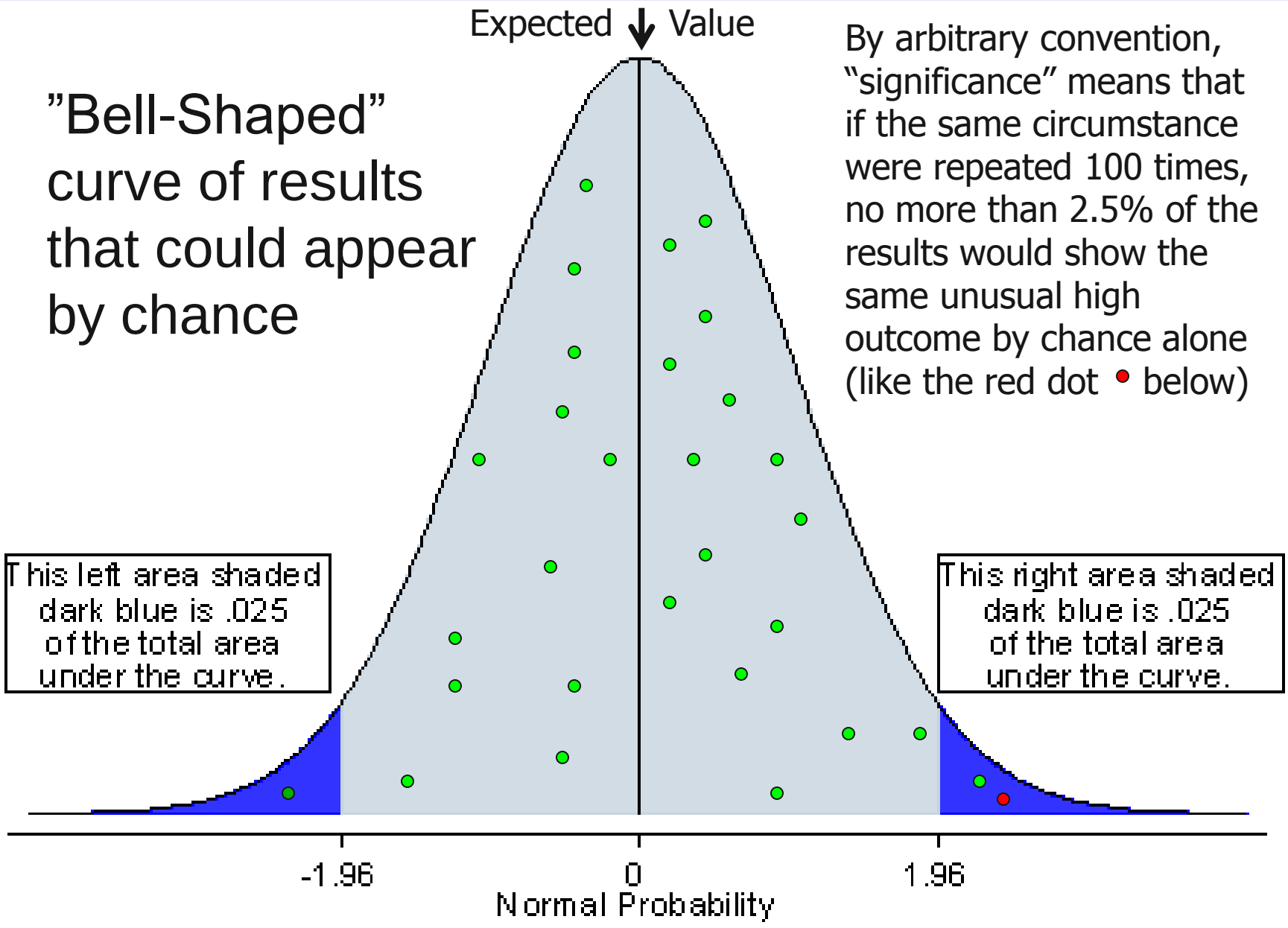
3. Ensure that any such association cannot be explained by the ***characteristics of local residents?***.

1. Assessing chance

- The conventional method is to identify by computation any excess difference which is statistically significant at the level of 95% confidence

- Method is based on the appropriate distribution of random possible results—chance can never be ruled out, just quantified at an arbitrary level.

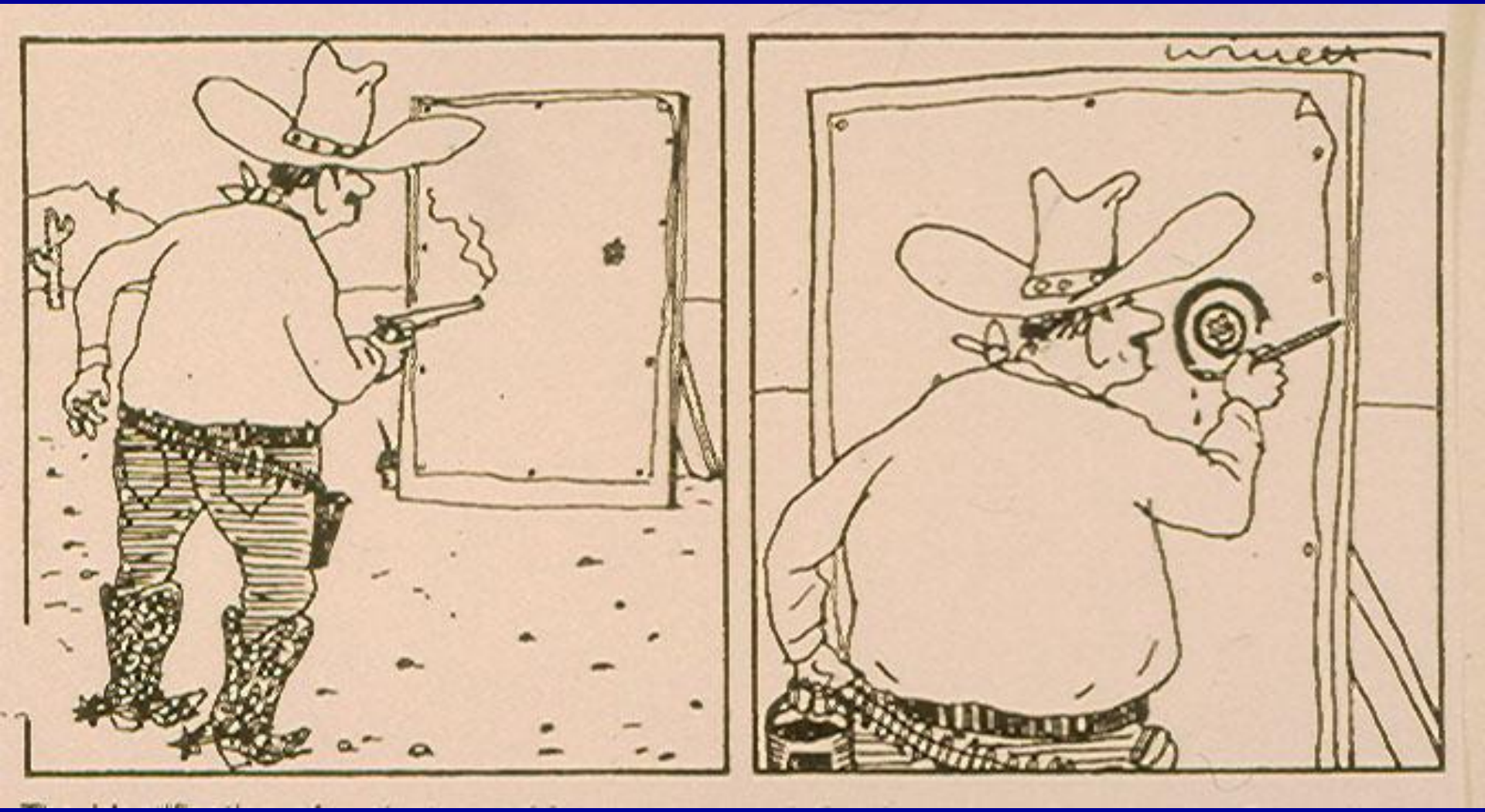
- We perform this exercise to screen tract/cancers


Expected Value
"Bell-Shaped" curve of results that could appear by chance
By arbitrary convention, "significance" means that if the same circumstance were repeated 100 times, no more than 2.5% of the results would show the same unusual high outcome by chance alone (like the red dot • below)
This left area shaded dark blue is .025 of the total area under the curve.
This right area shaded dark blue is .025 of the total area under the curve.
-1.96
0
1.96
Normal Probability

2. Bias comes in several forms

- Registry errors: unlikely, because ascertainment is very complete and in effect done blindly to place, age, race, etc.
- Census errors: underestimation of the number of persons, especially high risk persons, makes the excess look too large. This is a common problem in rapidly changing neighborhoods
- Texas sharpshooting: If investigation is initiated by a reported “cluster”, we already know the rate is not going to be low, and the statistical test is meaningless

“TEXAS SHARPSHOOTING”



AIM, SHOOT, AND ONLY THEN--
DRAW THE TARGET

Multiple Comparisons

- .
- The more cancers, periods, and tracts tried, the more likely are extreme findings

- Solution: instead of relying upon “significance” for each tract/cancer, we screen all tract-cancer combinations by significance, then calculate how often each extreme result could occur by chance among all CA tracts

- The following Poisson table gives this percentage for selected observed numbers given the number expected.

Percent of searches expected to find N or more cases observed according to the mean expected

Mean expected	1 Obs	2 Obs	3 Obs	4 Obs	5 Obs	6 Obs	7 Obs	8 Obs	9 Obs	10 Obs	11 Obs	12 Obs
1	63.2%	26.4%	8.0%	1.9%	0.4%	0.1%	0.01%					
2		59.3%	32.2%	14.2%	5.2%	1.6%	0.4%	0.1%	0.02%	0.01%		
3			58.4%	36.0%	19.2%	9.1%	3.4%	1.2%	0.4%	0.1%	0.03%	
4				56.7%	37.1%	21.5%	11.1%	5.1%	2.1%	0.8%	0.3%	0.1%
5					55.8%	38.3%	23.7%	13.3%	6.8%	3.2%	1.3%	0.5%
6						55.4%	39.3%	25.5%	15.2%	8.3%	4.2%	1.9%
7							54.9%	40.0%	27.0%	16.9%	9.8%	5.3%
8								54.8%	40.8%	28.4%	18.4%	11.3%
9									54.3%	41.1%	29.2%	19.5%
10										45.3%	32.8%	21.4%

For example:

- When 2 cases are expected and 6 are observed, 1.6% of localities of that size would find as many or more than 6 by chance.

- That means in160 California localities

3. Explore alternative explanations for any cluster: ***They are important considerations***

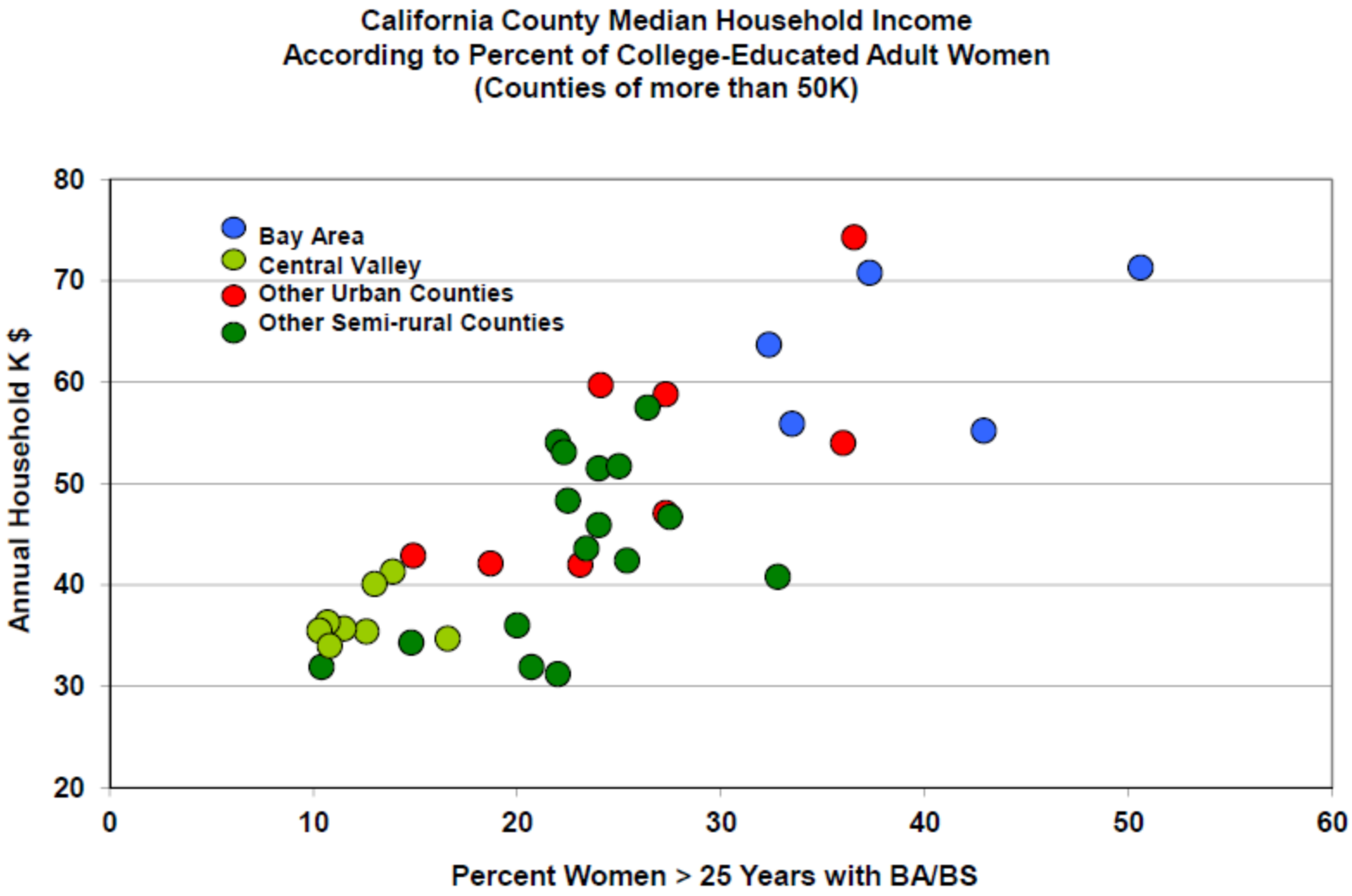
- Other known causes of that particular cancer
  - Rarely measureable by locality: example--smoking
- Race/Ethnicity, (approximate by tract)
  - Measureable surrogate causes like—skin color
- Education and Income (approximate by tract)
  - Measureable surrogate for causes like—sexual and reproductive history

A rough commonality of lifestyle characterizes the residents of any neighborhood

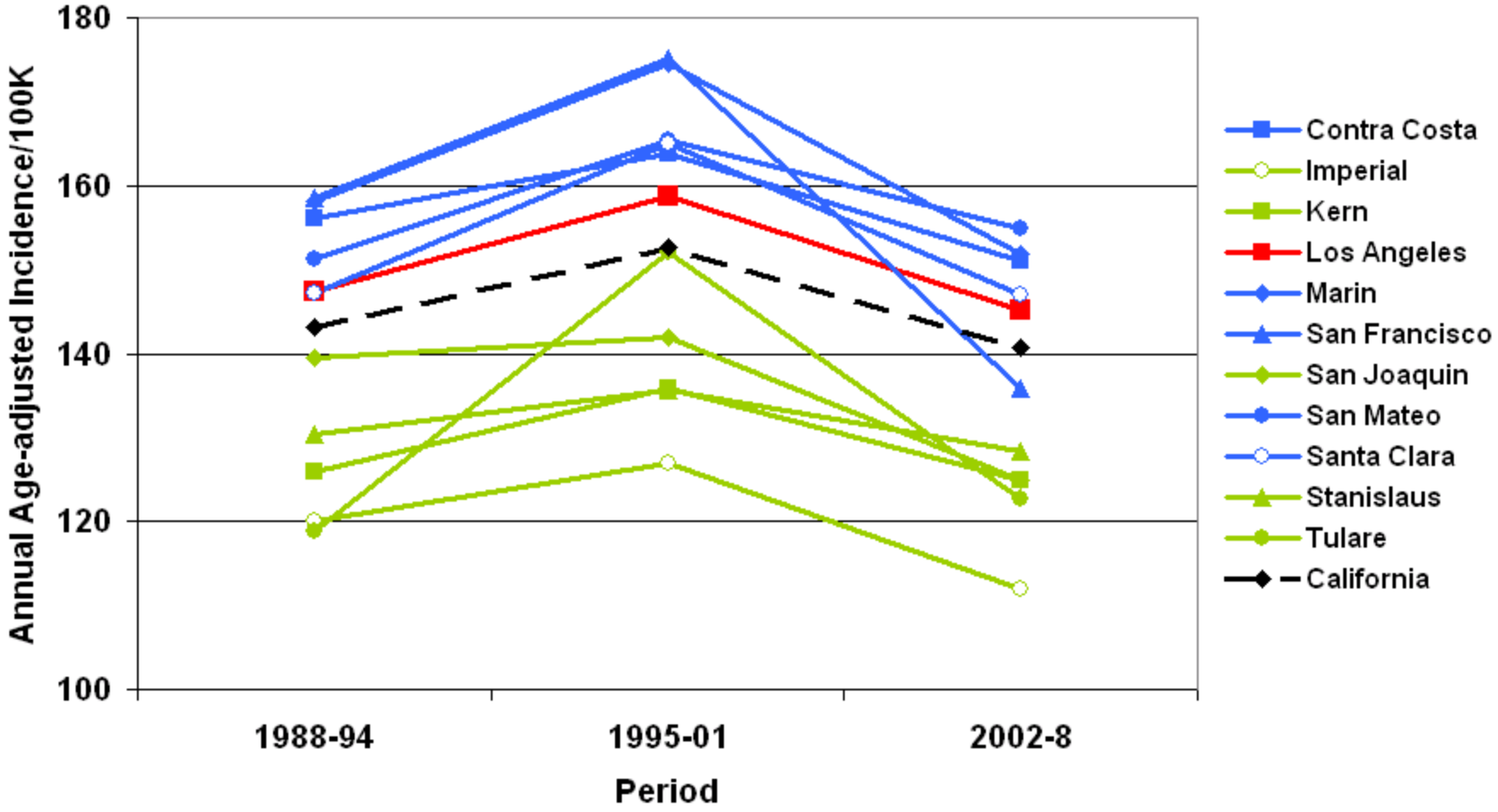
- Neighborhood choice is personal and particular
  - Preferred location, location, location
- Thus birds of a feather tend to flock together

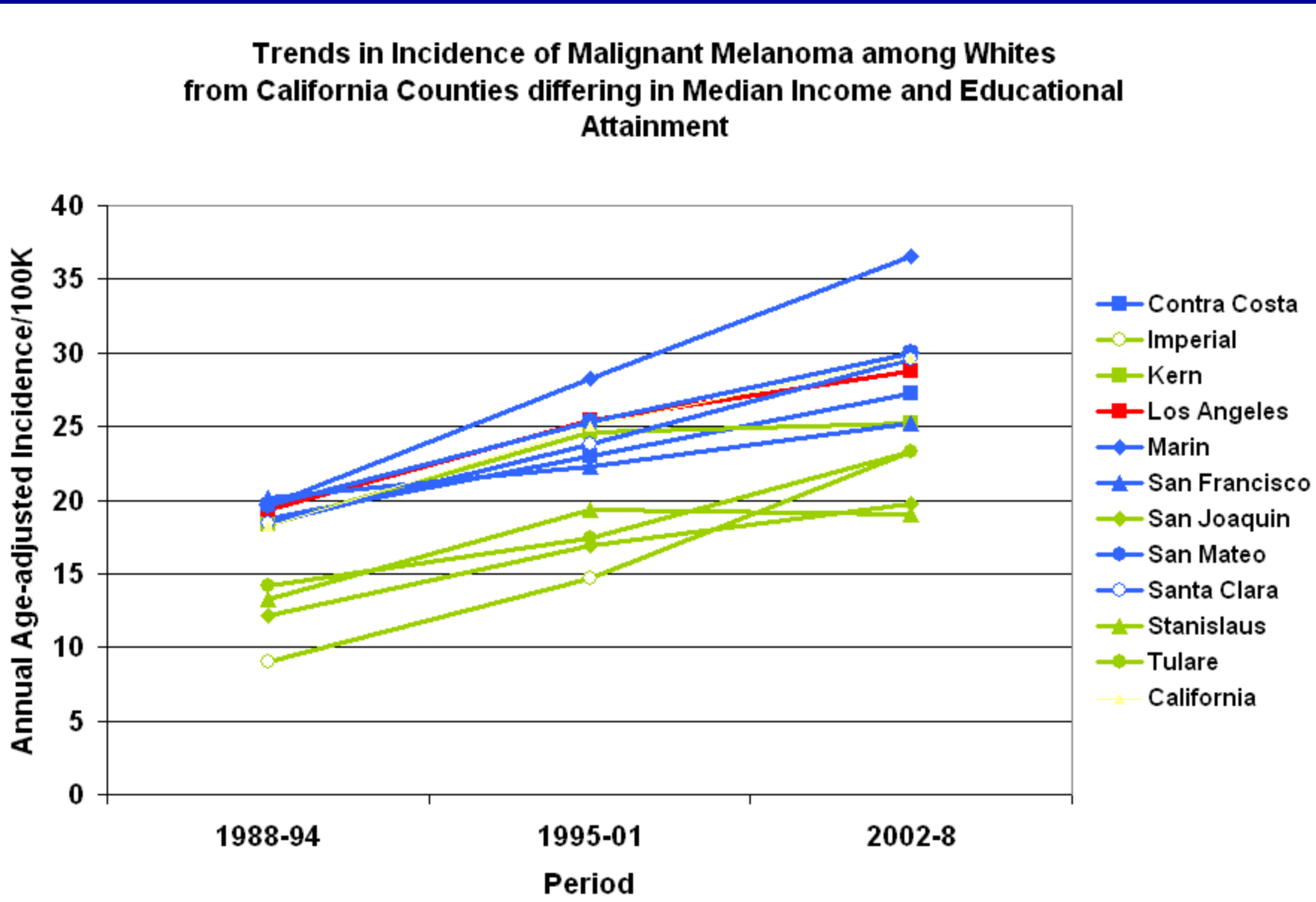
- Obvious on both County and Census tract levels
  - Ethnicity, education, friends, habits, occupation

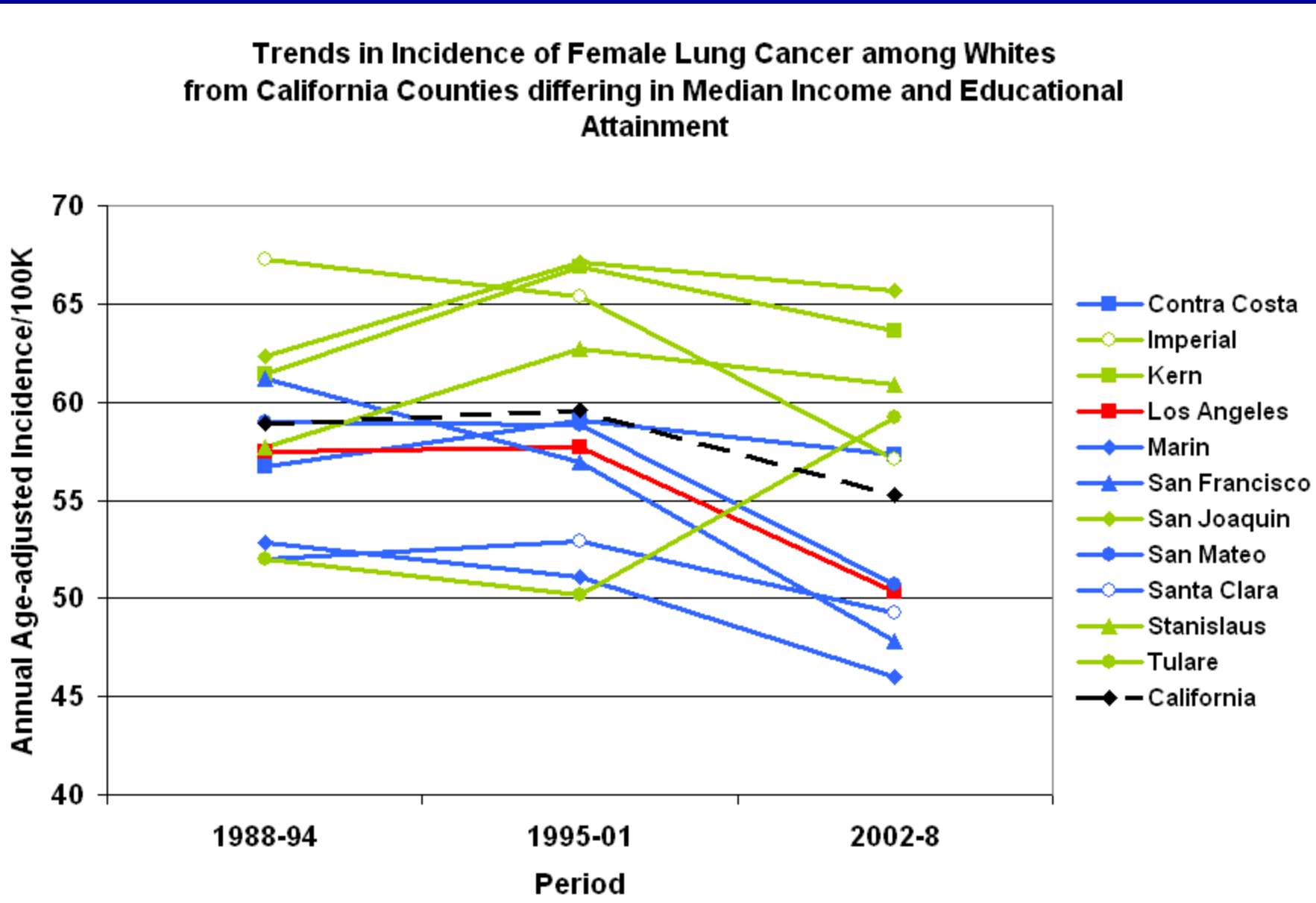
- Shows up in cancer patterns


California County Median Household Income
According to Percent of College-Educated Adult Women
(Counties of more than 50K)
Bay Area
Central Valley
Other Urban Counties
Other Semi-rural Counties
Annual Household K $
80
70
60
50
40
30
20
0
10
20
30
40
50
60
Percent Women > 25 Years with BA/BS

Trends in Incidence of Breast Cancer among White Females from California Counties differing in Median Income and Educational Attainment



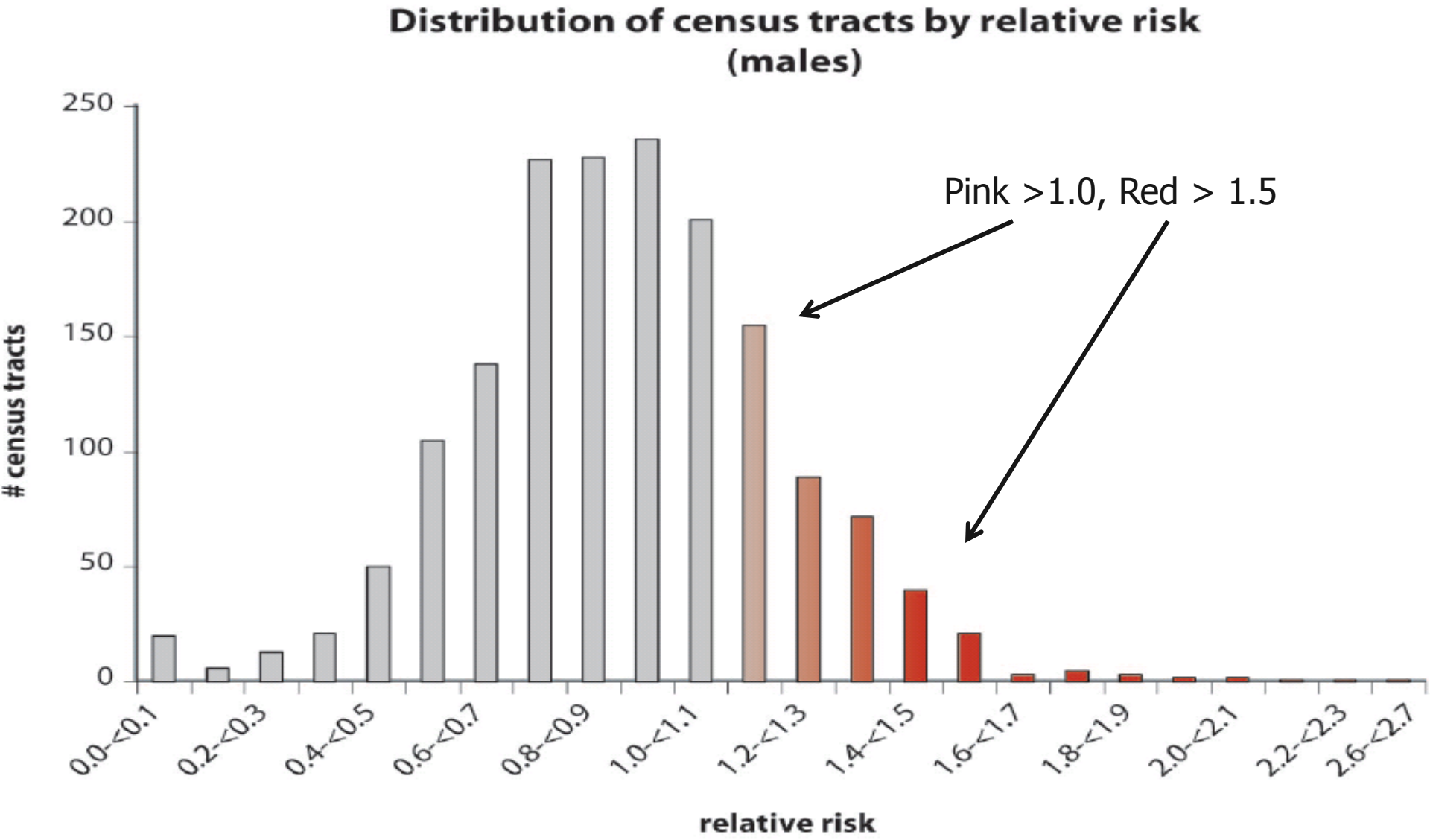

Trends in Incidence of Malignant Melanoma among Whites from California Counties differing in Median Income and Educational Attainment
Annual Age-adjusted Incidence/100K
40
35
30
25
20
15
10
5
0
1988-94
1995-01
2002-8
Period
Contra Costa
Imperial
Kern
Los Angeles
Marin
San Francisco
San Joaquin
San Mateo
Santa Clara
Stanislaus
Tulare
California


Trends in Incidence of Female Lung Cancer among Whites from California Counties differing in Median Income and Educational Attainment
Annual Age-adjusted Incidence/100K
70
65
60
55
50
45
40
1988-94
1995-01
2002-8
Period
Contra Costa
Imperial
Kern
Los Angeles
Marin
San Francisco
San Joaquin
San Mateo
Santa Clara
Stanislaus
Tulare
California

From Counties to Census tracts

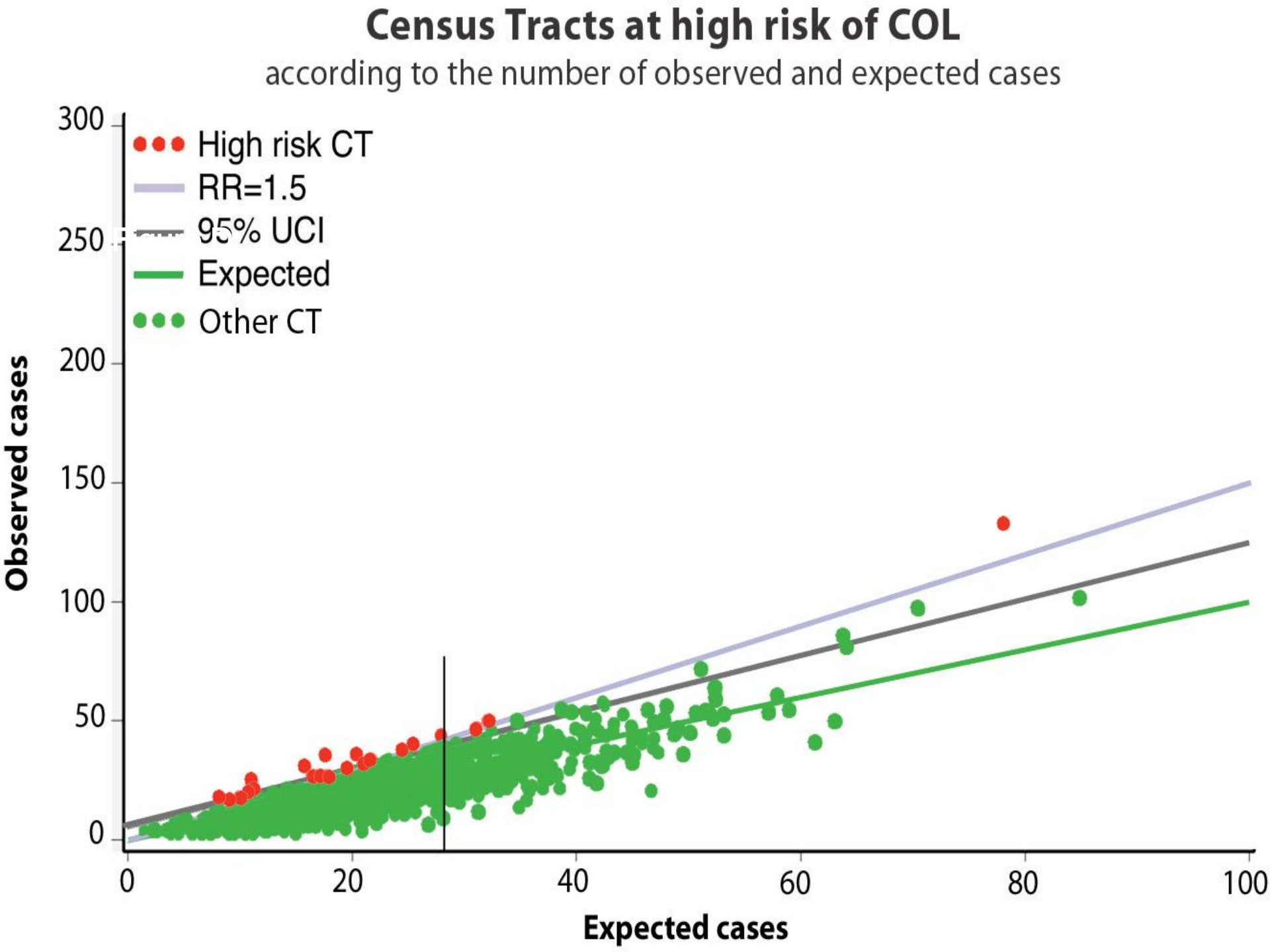
- We define localities as census tracts because the census gives us accurate populations by age and sex
- Census tracts are smaller than counties, averaging about 5000 persons but varying in size from hundreds to tens of thousands
- Thus variation in cancer occurrence comes from three factors, usually in this order:
  - Size of the tract population
  - Chance
  - Prevalence of causal factors

Colon Carcinoma in LA

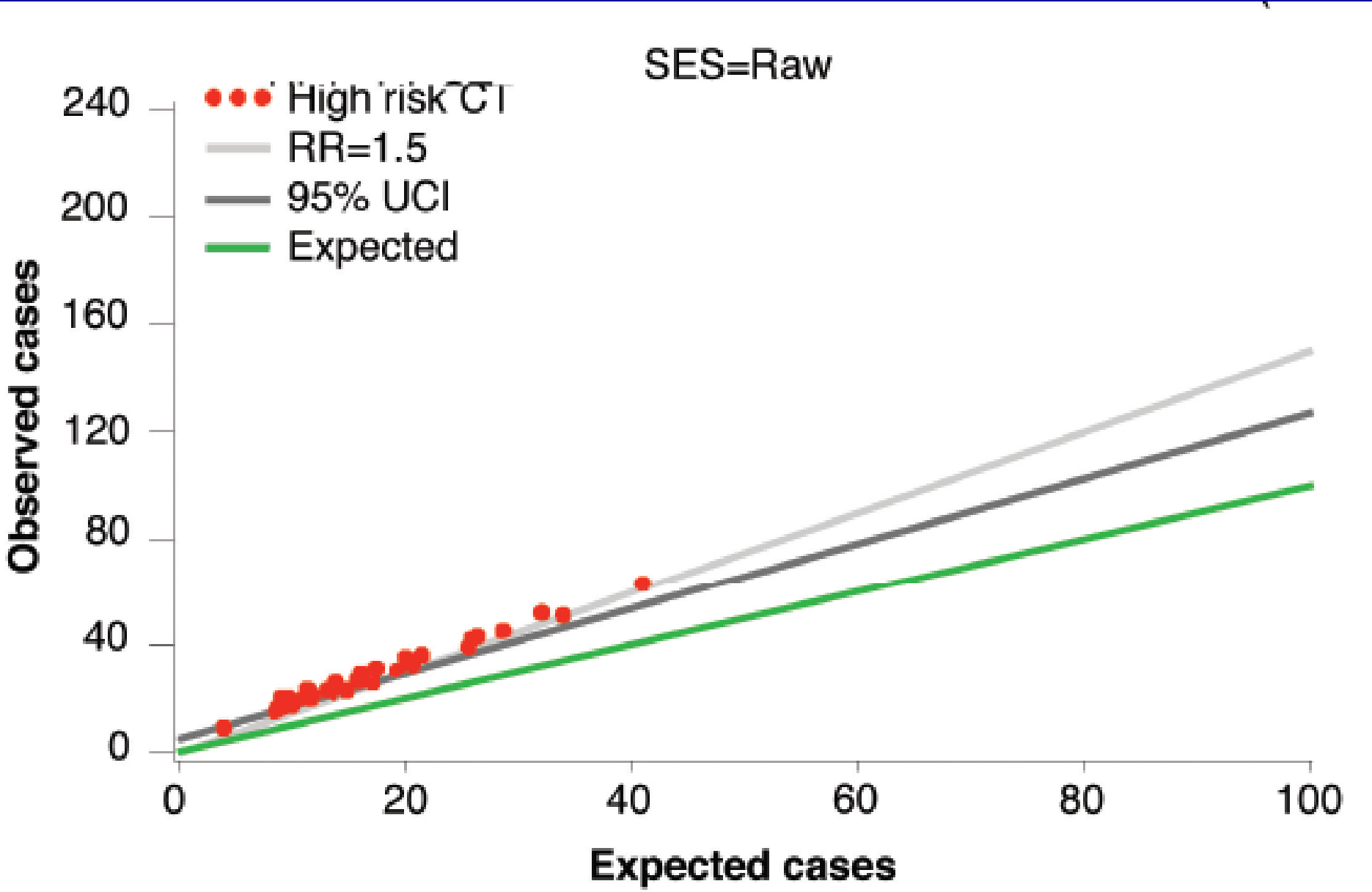


Because the tract size varies, we can describe the tracts by the number of cases expected and observed rather than by rate

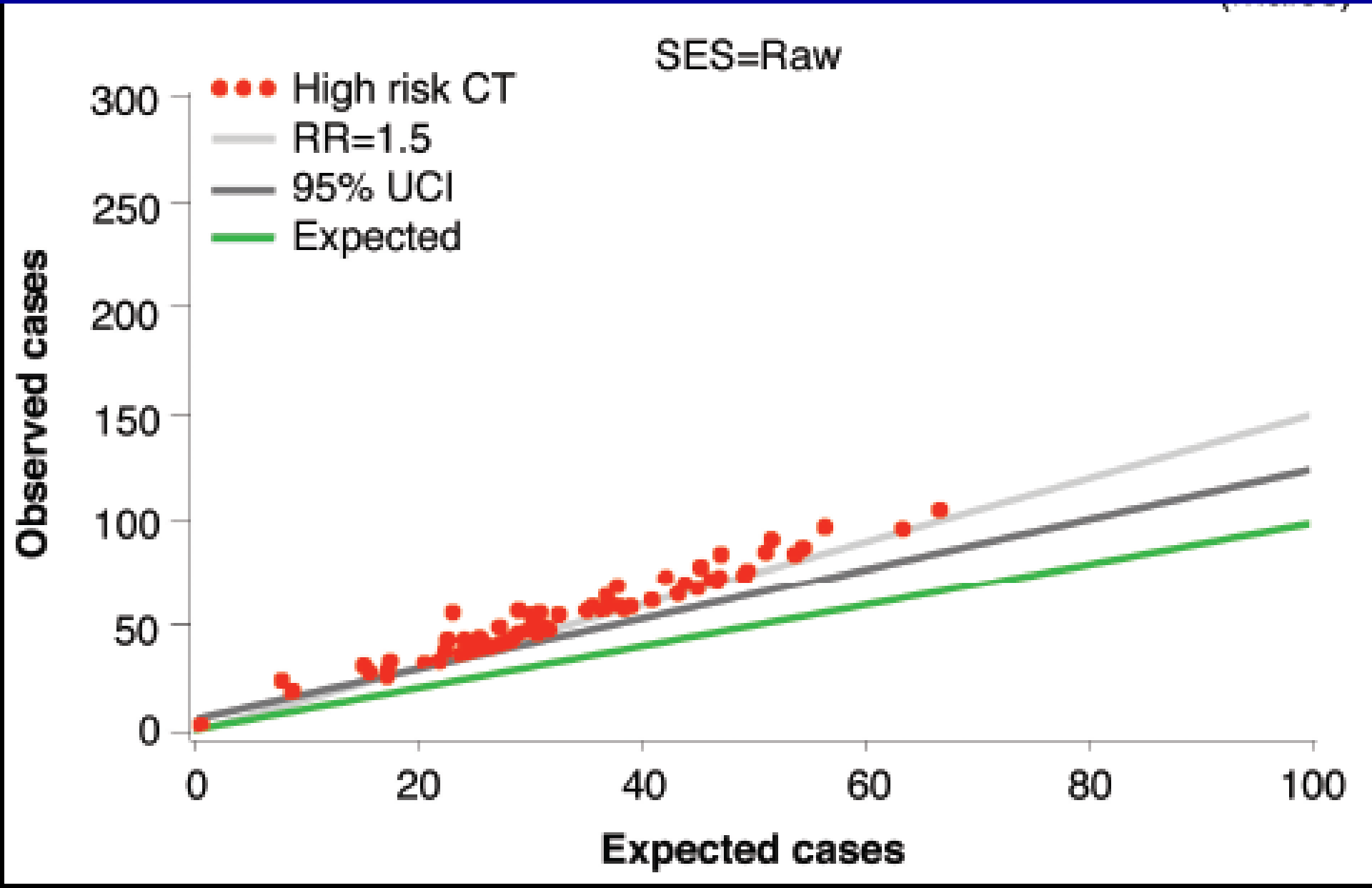
- For a given expected case number horizontally, we represent each tract vertically by a dot for the observed case number
- Lines showing both a standard risk (50% increase) and a measure of “significance” are shown.
- A dot above the lines in red represents a “significant” increase.
- Those occurring by chance will usually touch a line. The higher the red dot, the higher the incidence.
- Different cancers show different patterns depending on how localized high risk is found


Census Tracts at high risk of COL
according to the number of observed and expected cases
High risk CT
RR=1.5
95% UCI
Expected
Other CT
Observed cases
Expected cases
300
250
200
150
100
50
0
0
20
40
60
80
100

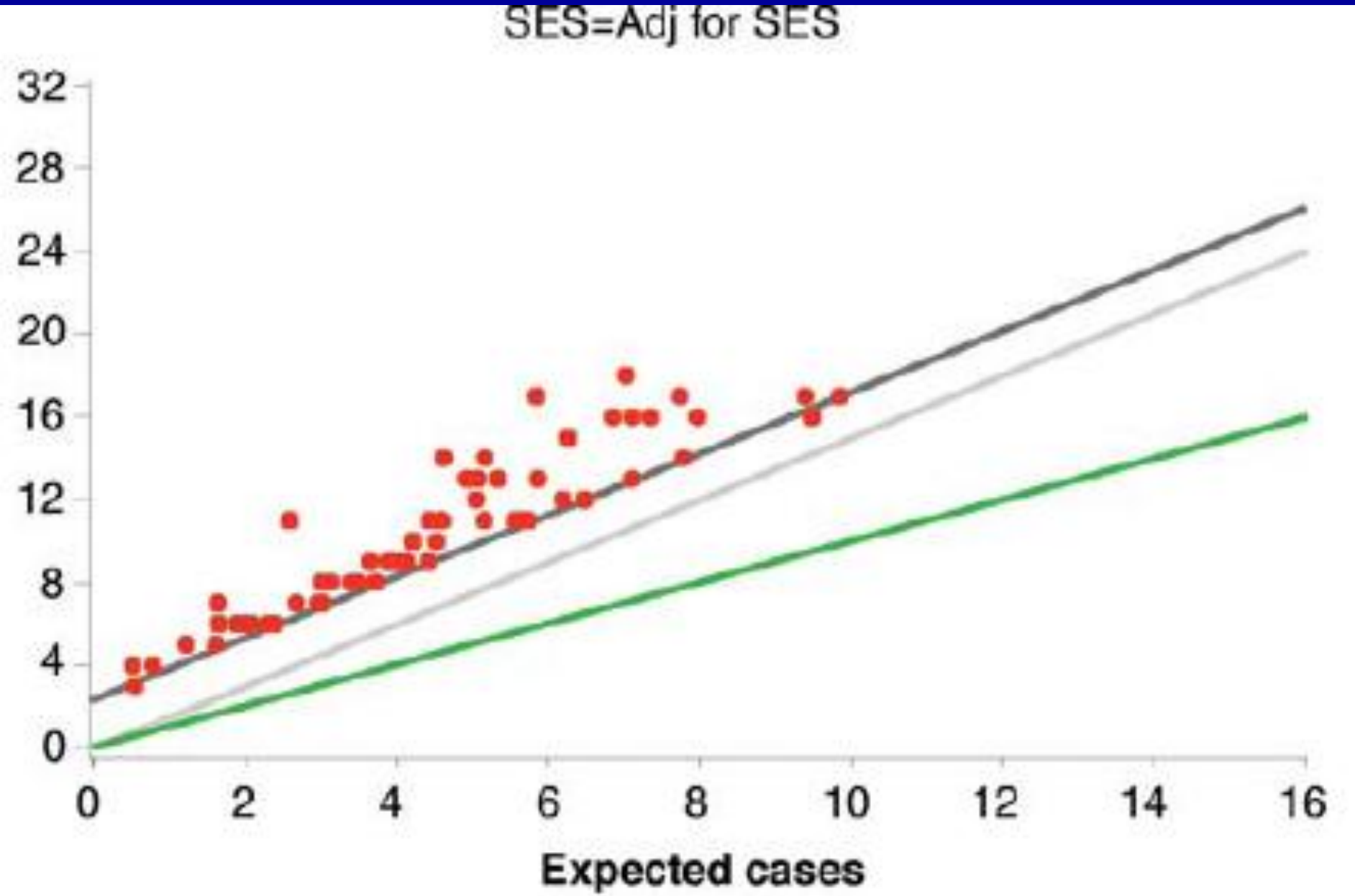
Female Colon Cancer



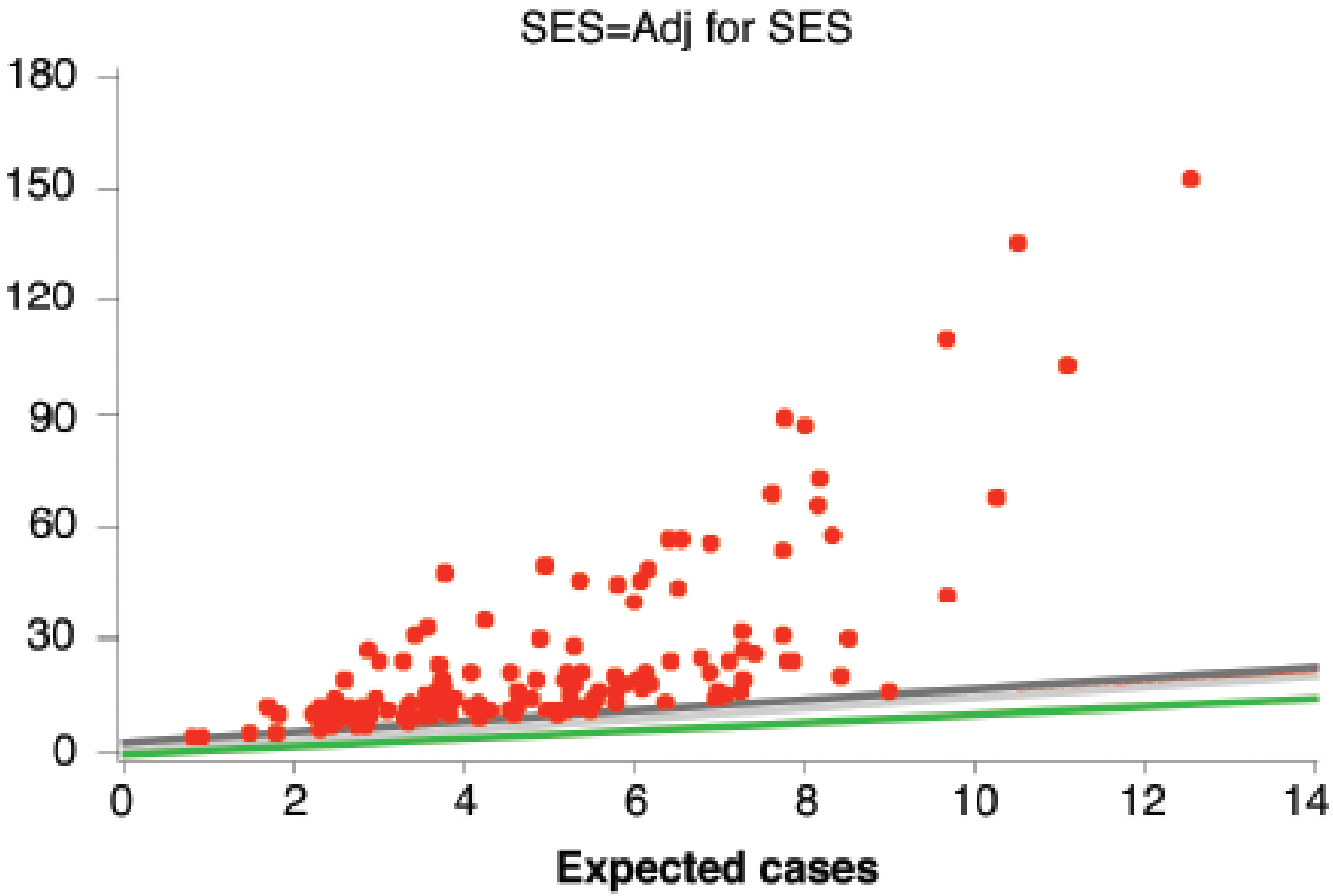
Male Lung Cancer



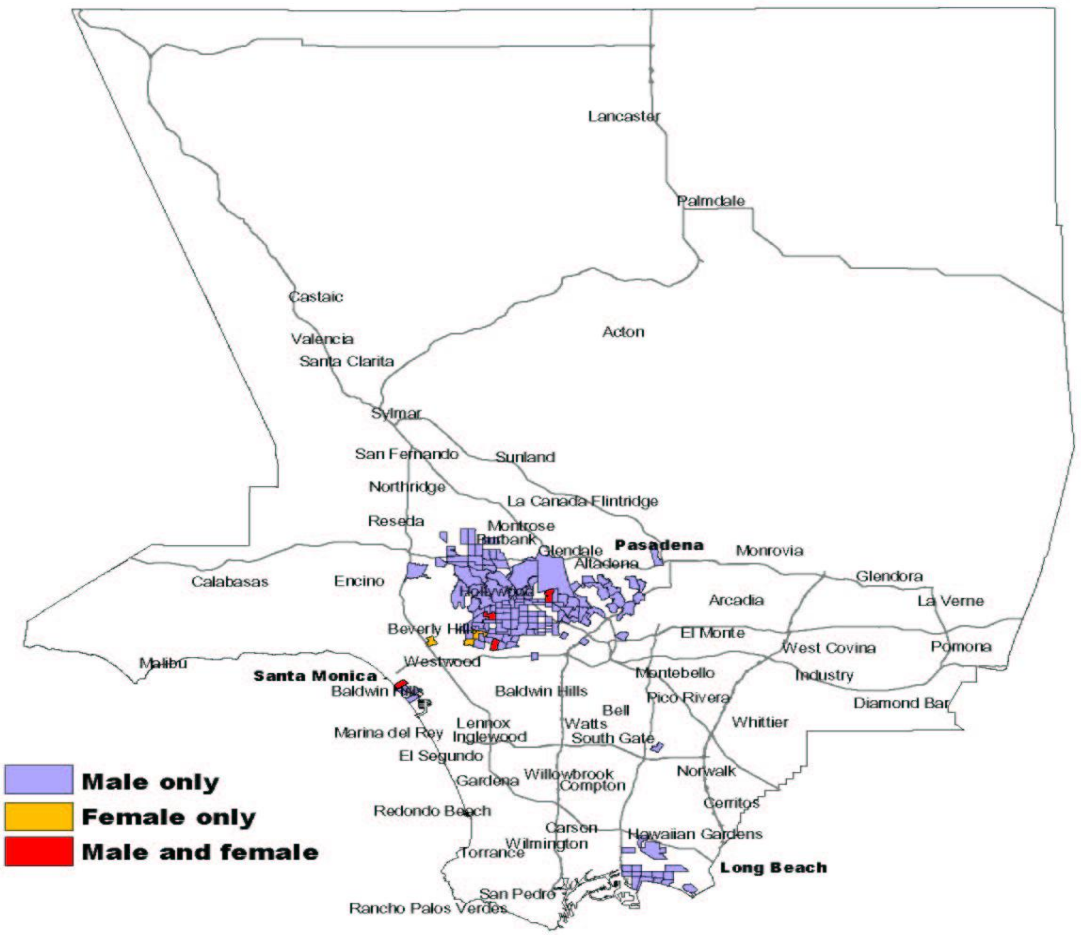
Female Oropharyngeal Cancer



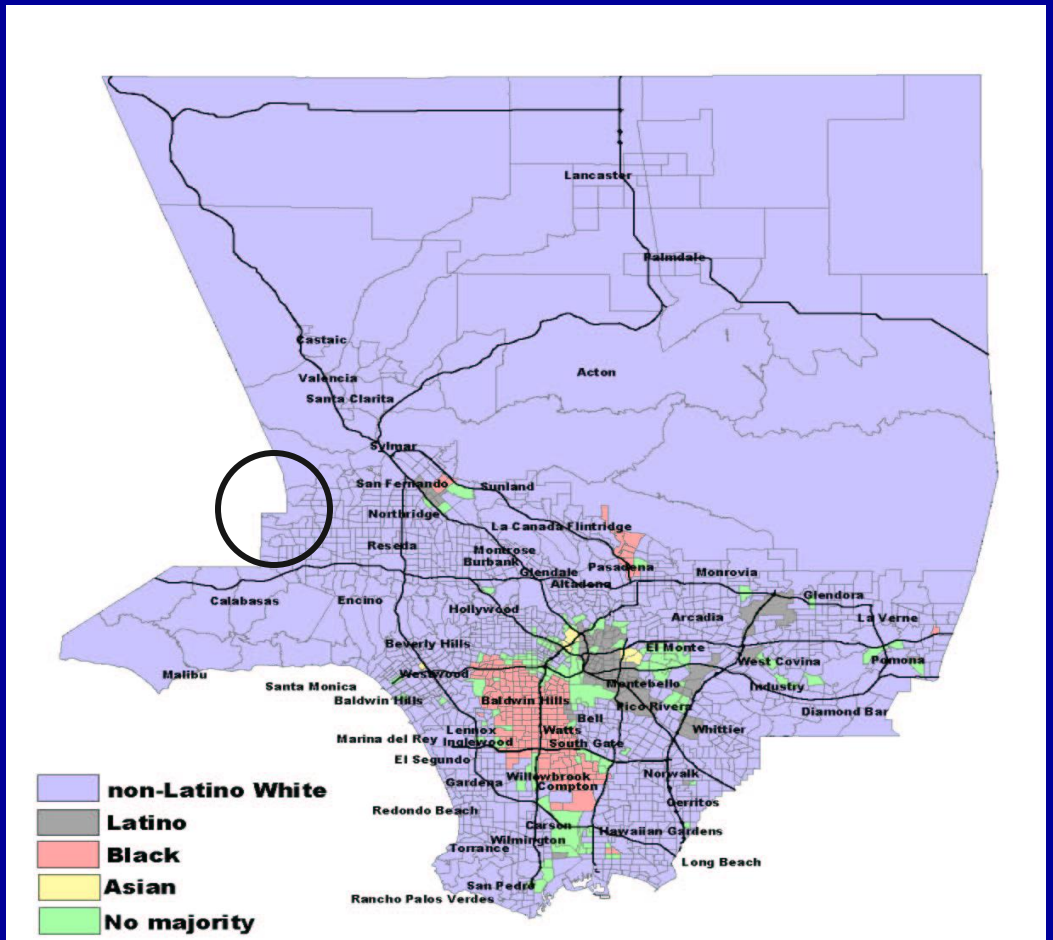
Male Kaposi Sarcoma



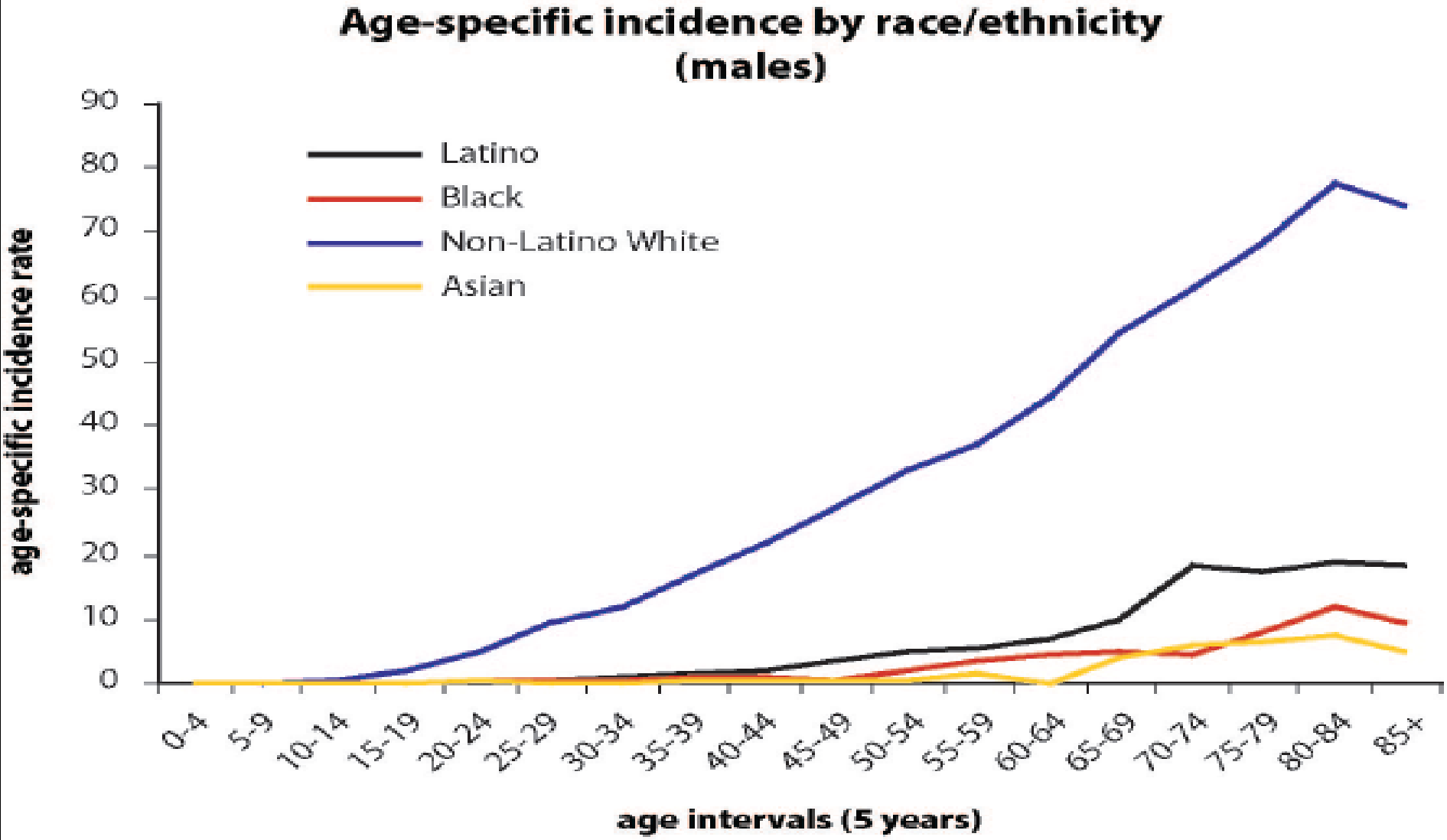
KAPOSI SARCOMA



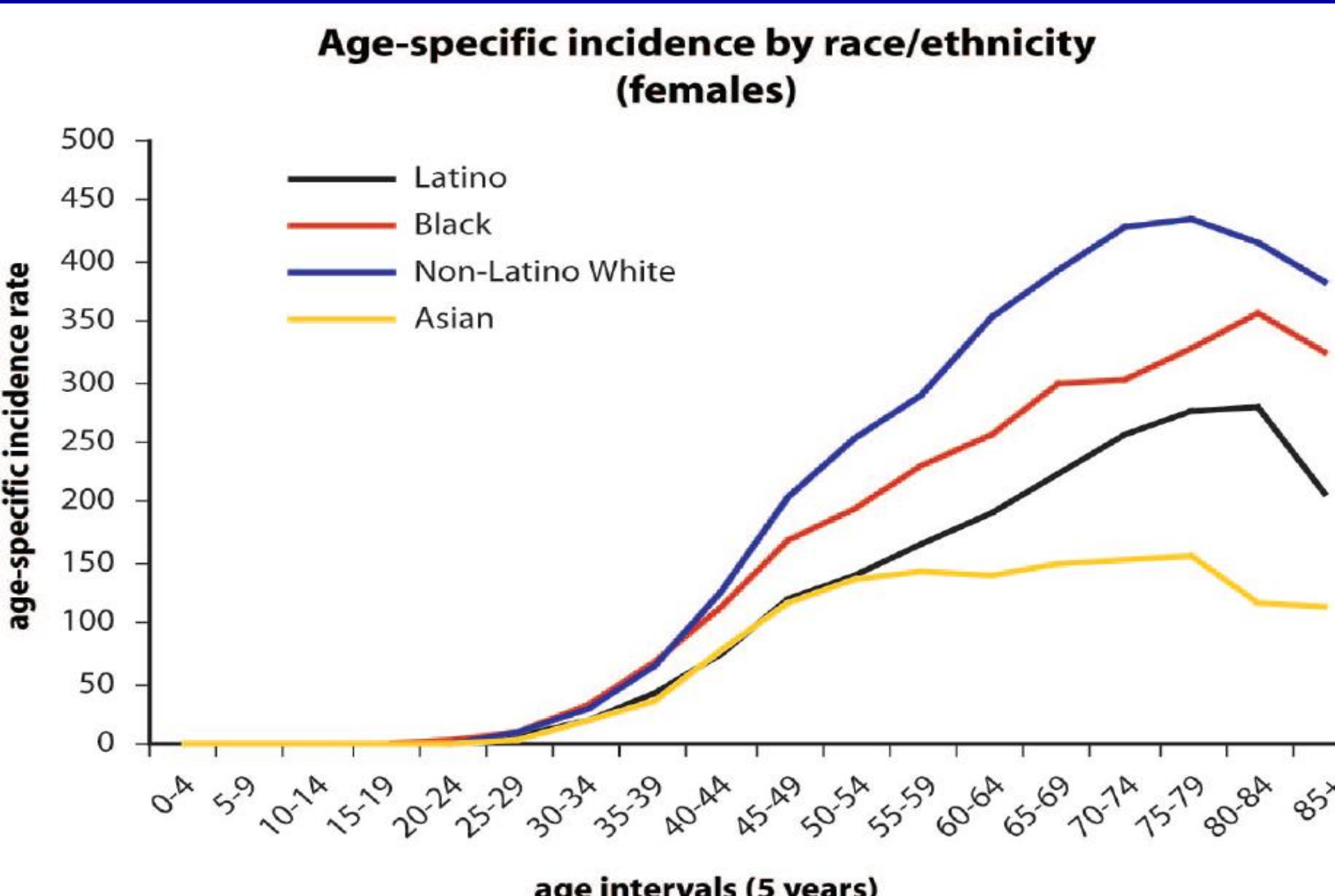
CENSUS TRACTS BY MAJORITY CASE RACE/ETHICITY



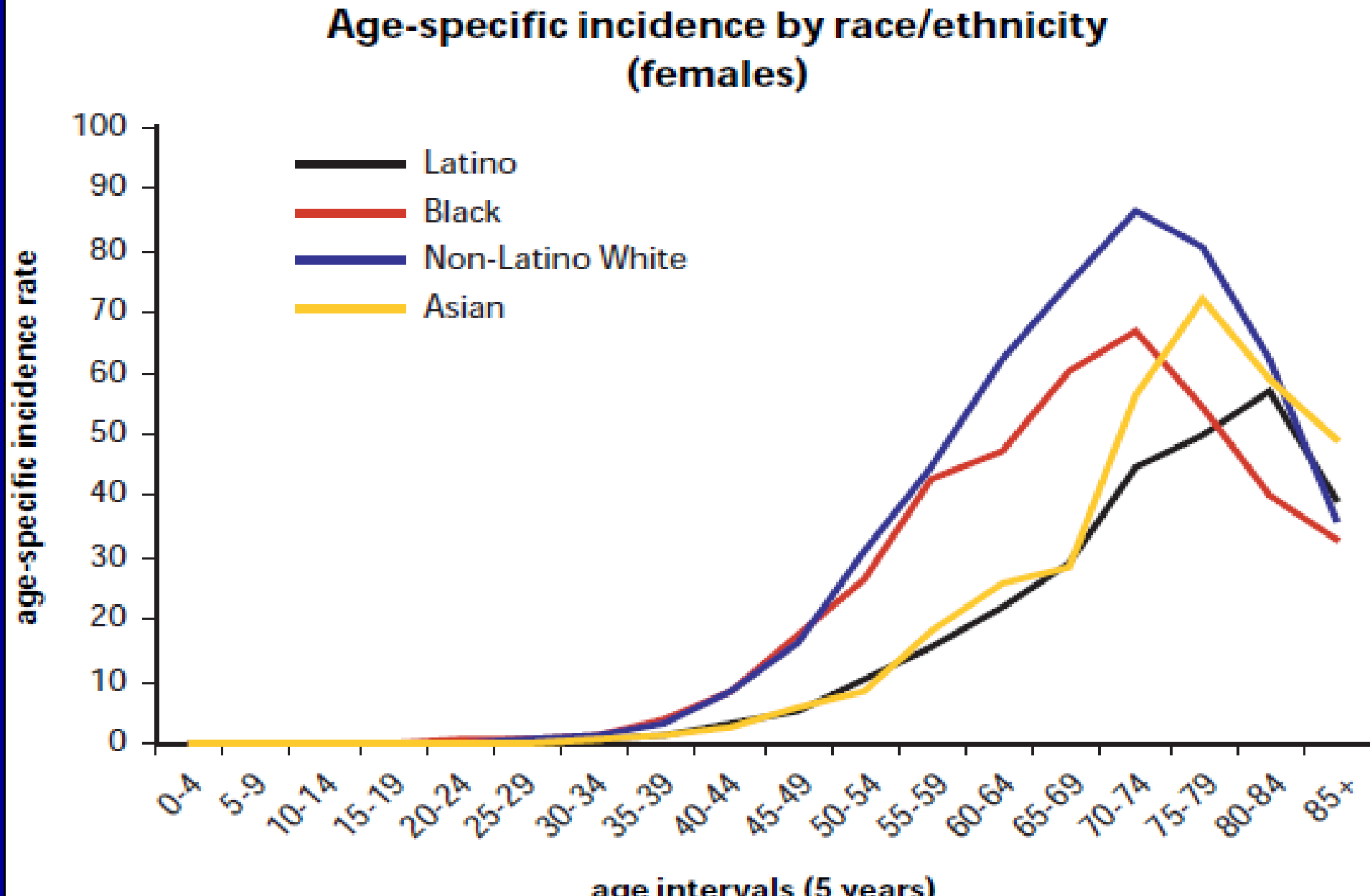
Malignant Melanoma



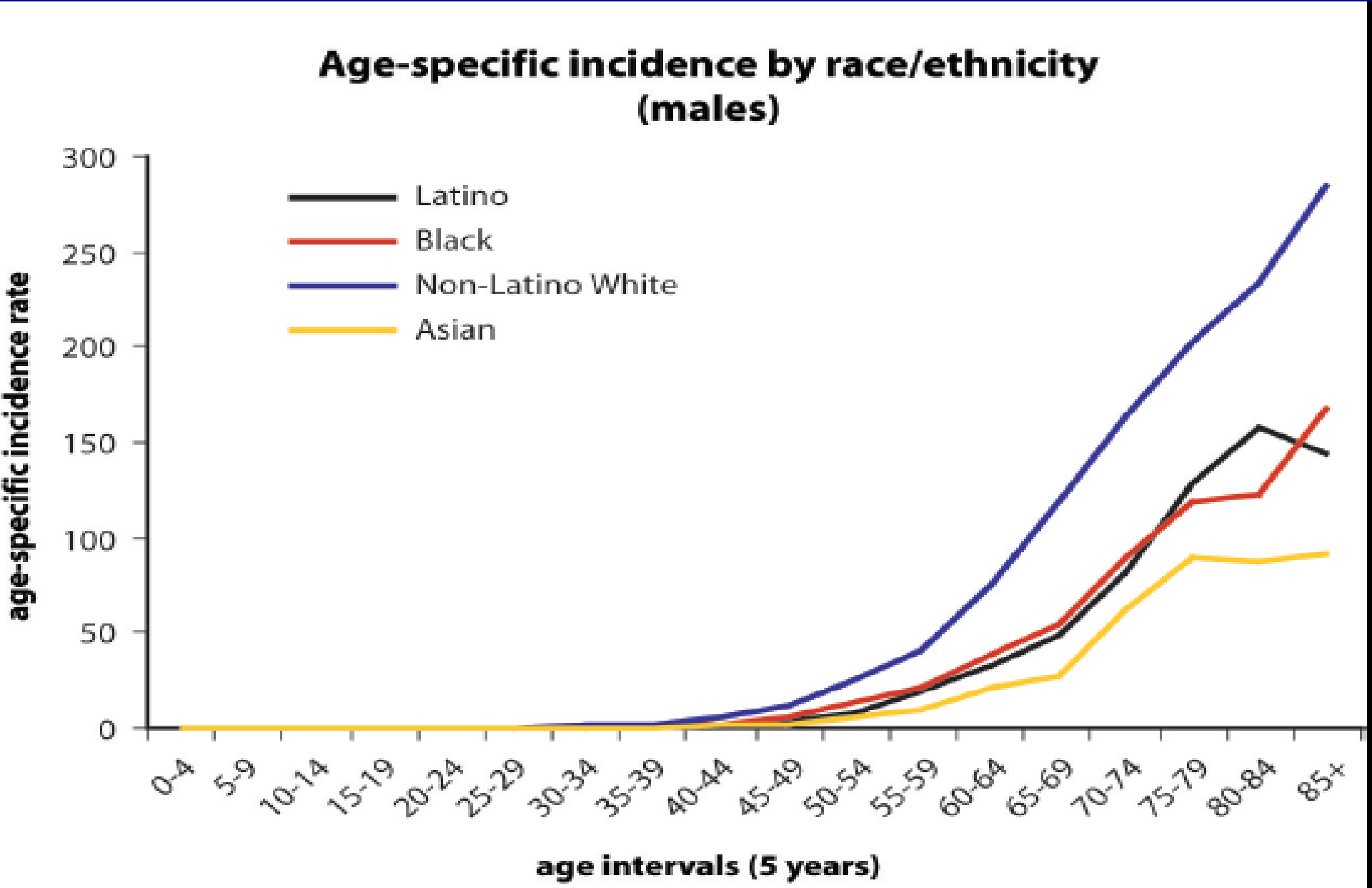
Female Breast Cancer



Female Lung Adenocarcinoma



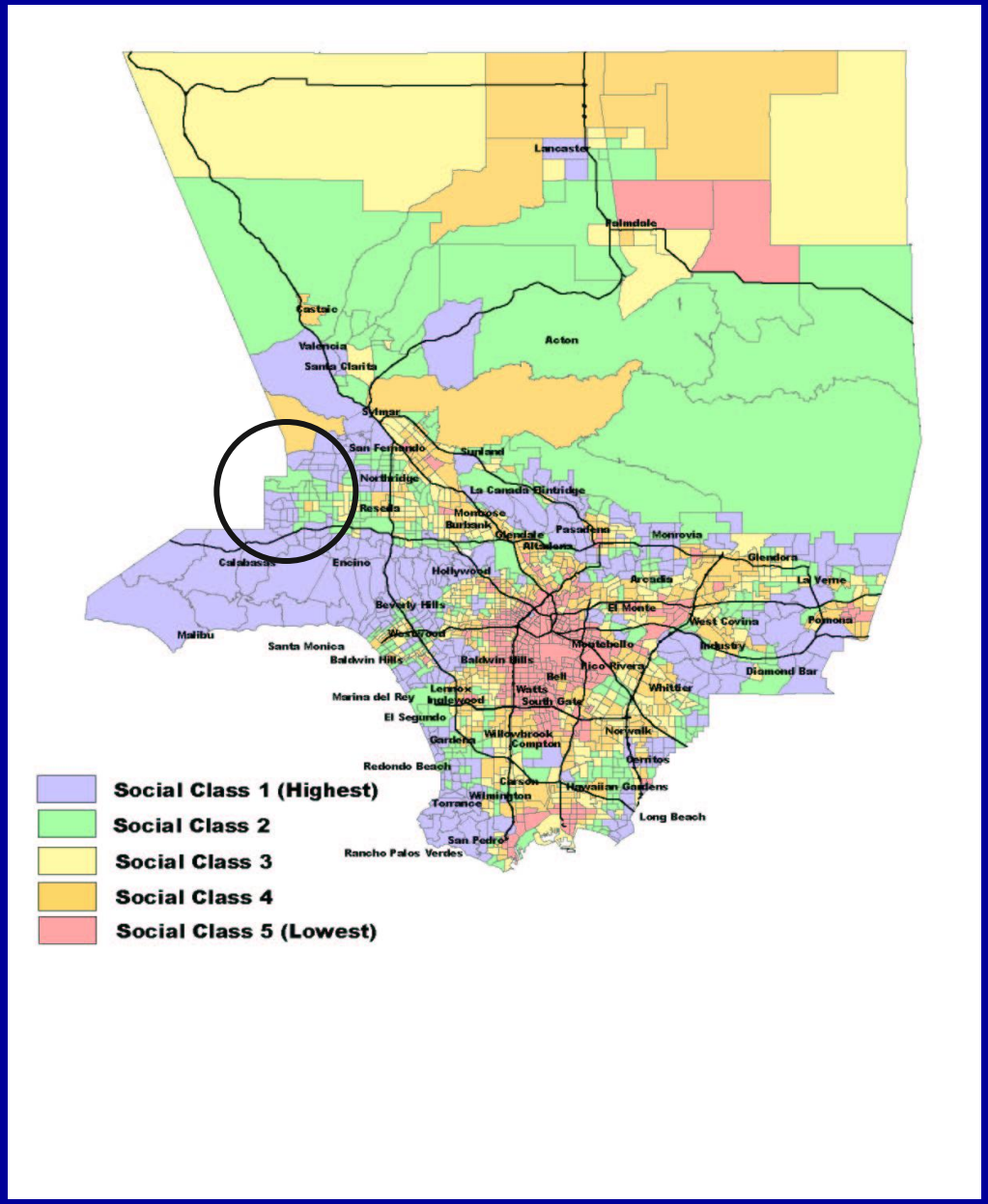
Bladder Cancer



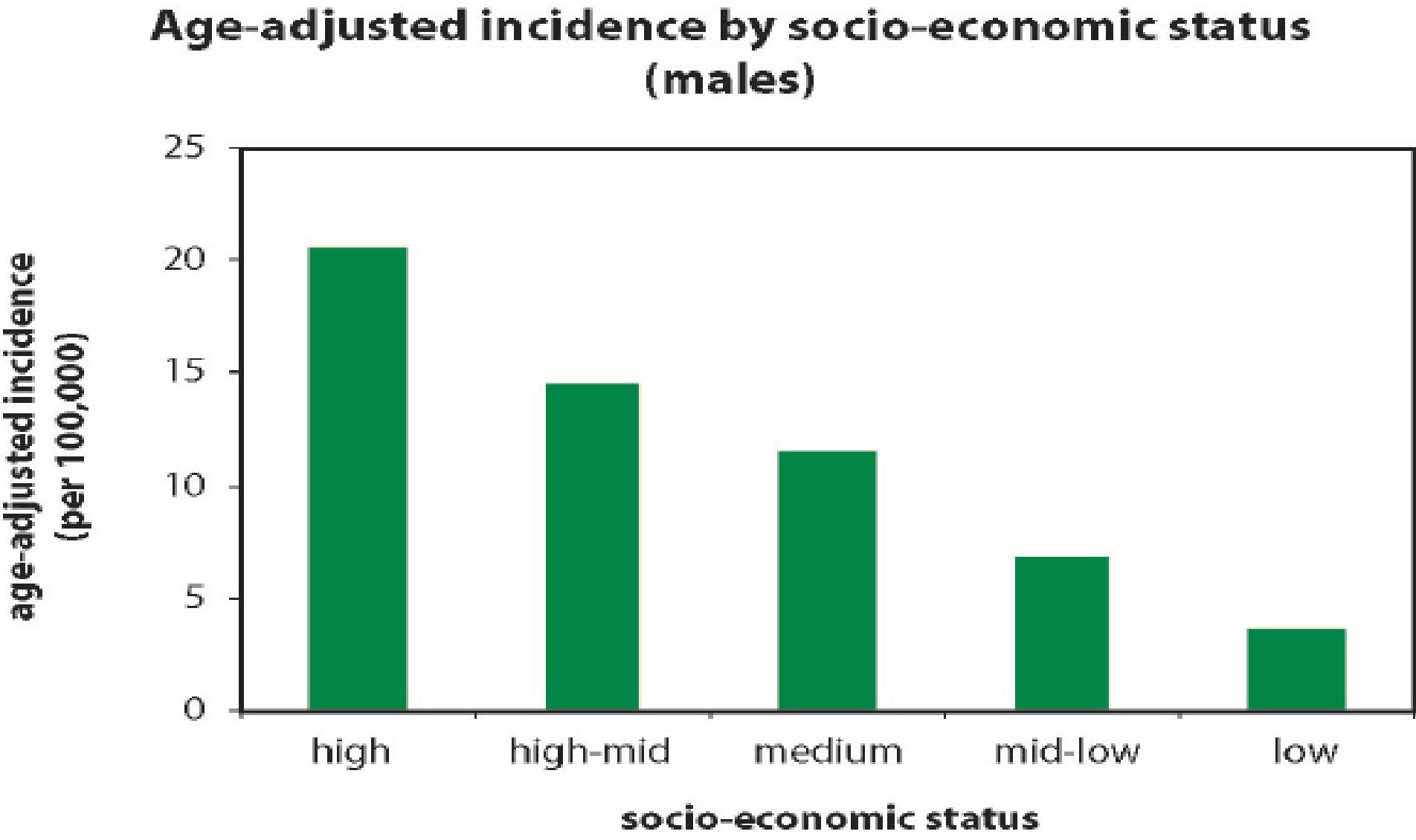
Other cancers higher in other Race/Ethnicity groups

- Prostate cancer higher in African-Americans
- Liver cancer higher in East Asian-Americans
- Gall Bladder and stomach cancer higher in Latino-Americans

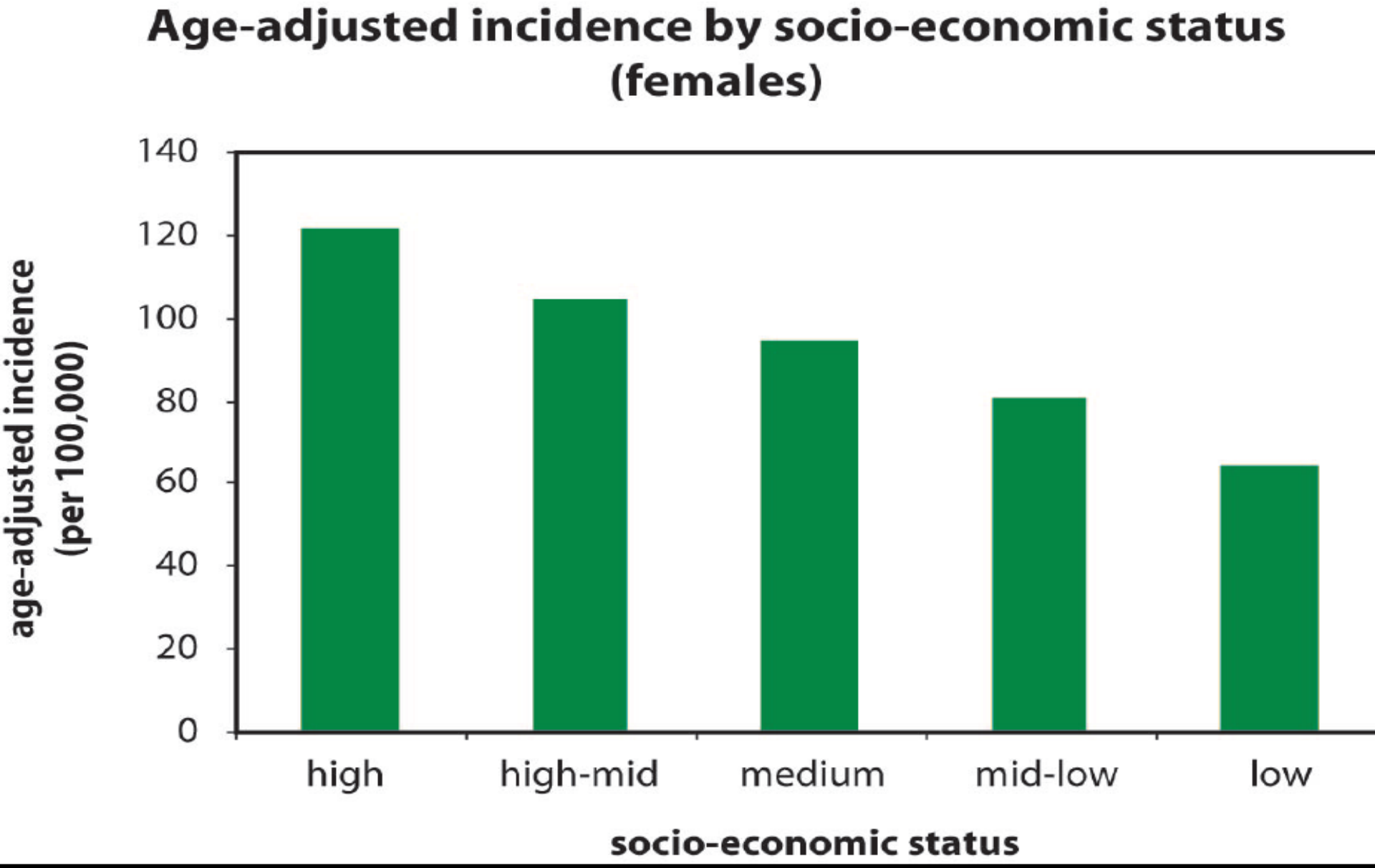
CENSUS TRACTS BY SOCIAL CLASS



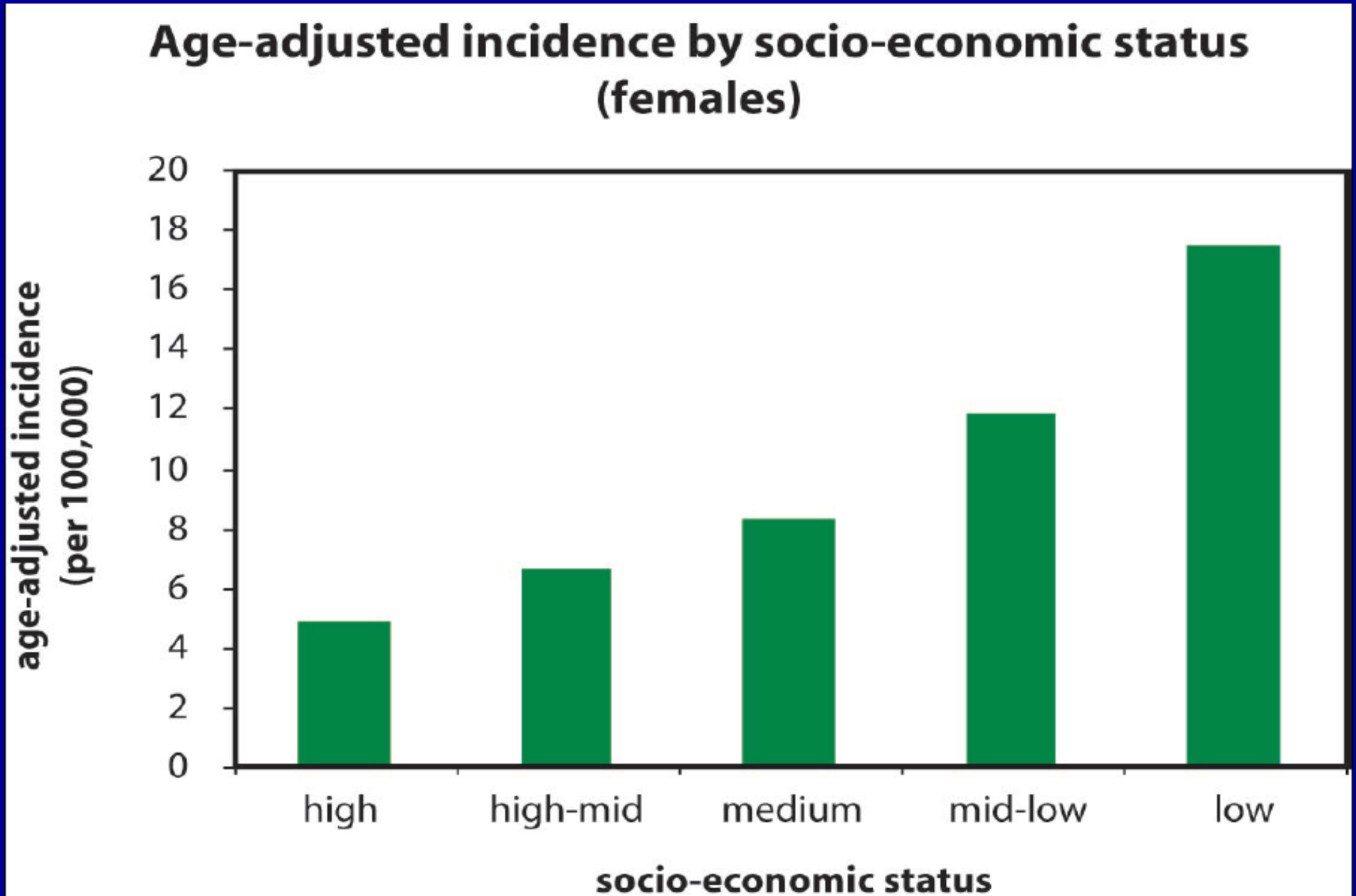
Malignant Melanoma



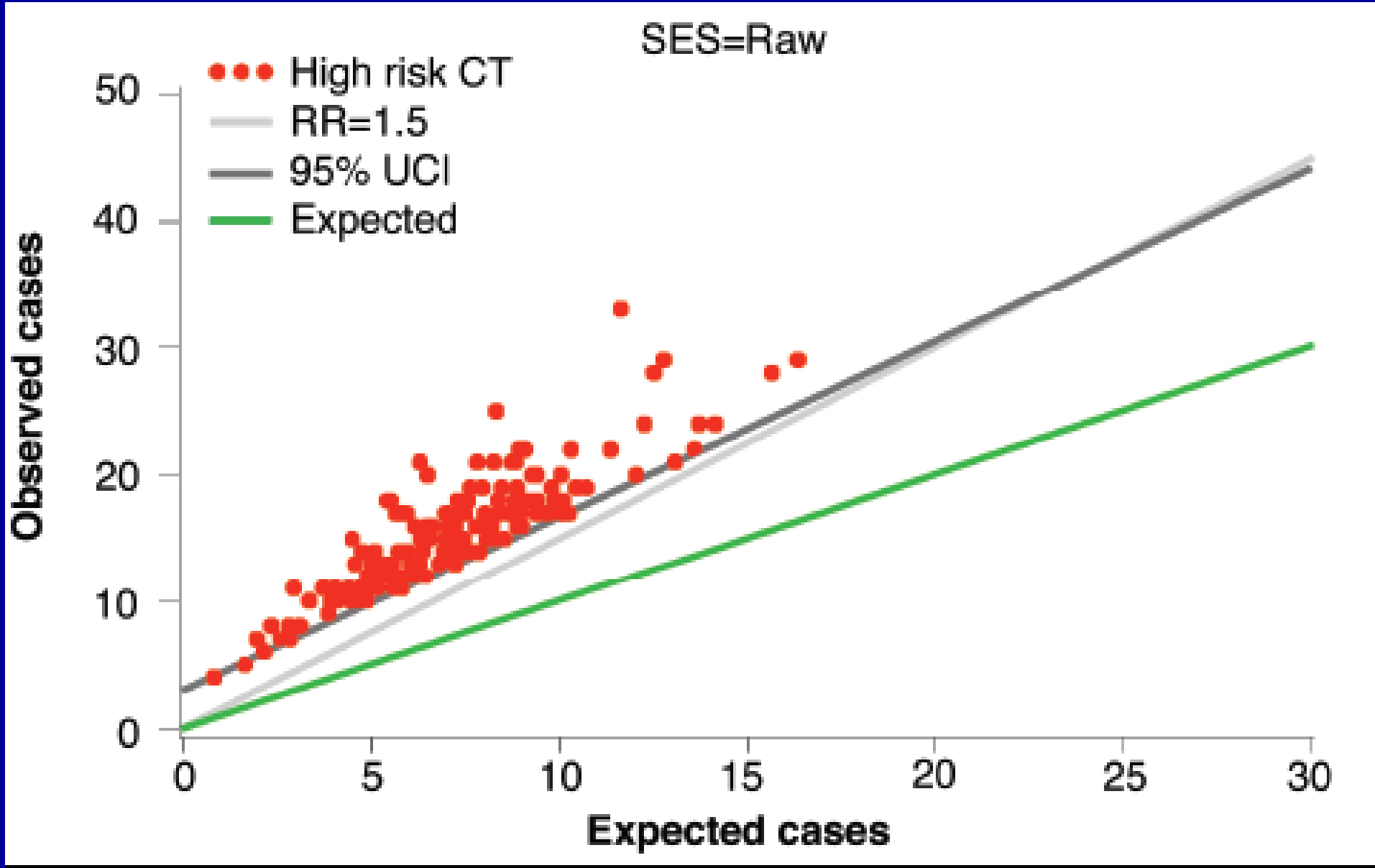
Female Breast Cancer



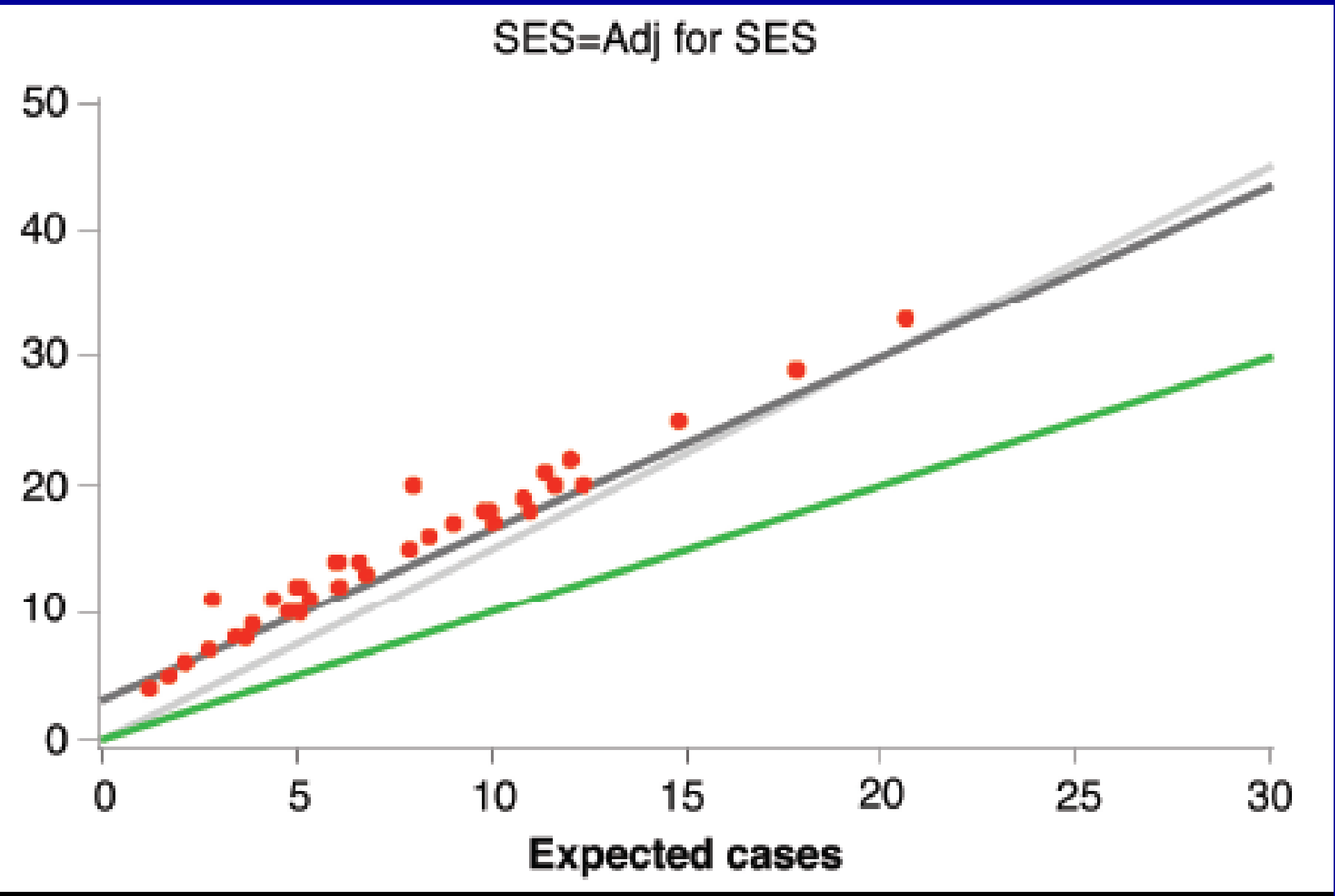
Cancer of the Cervix



Female Cancer of the Cervix



Female Cancer of the Cervix

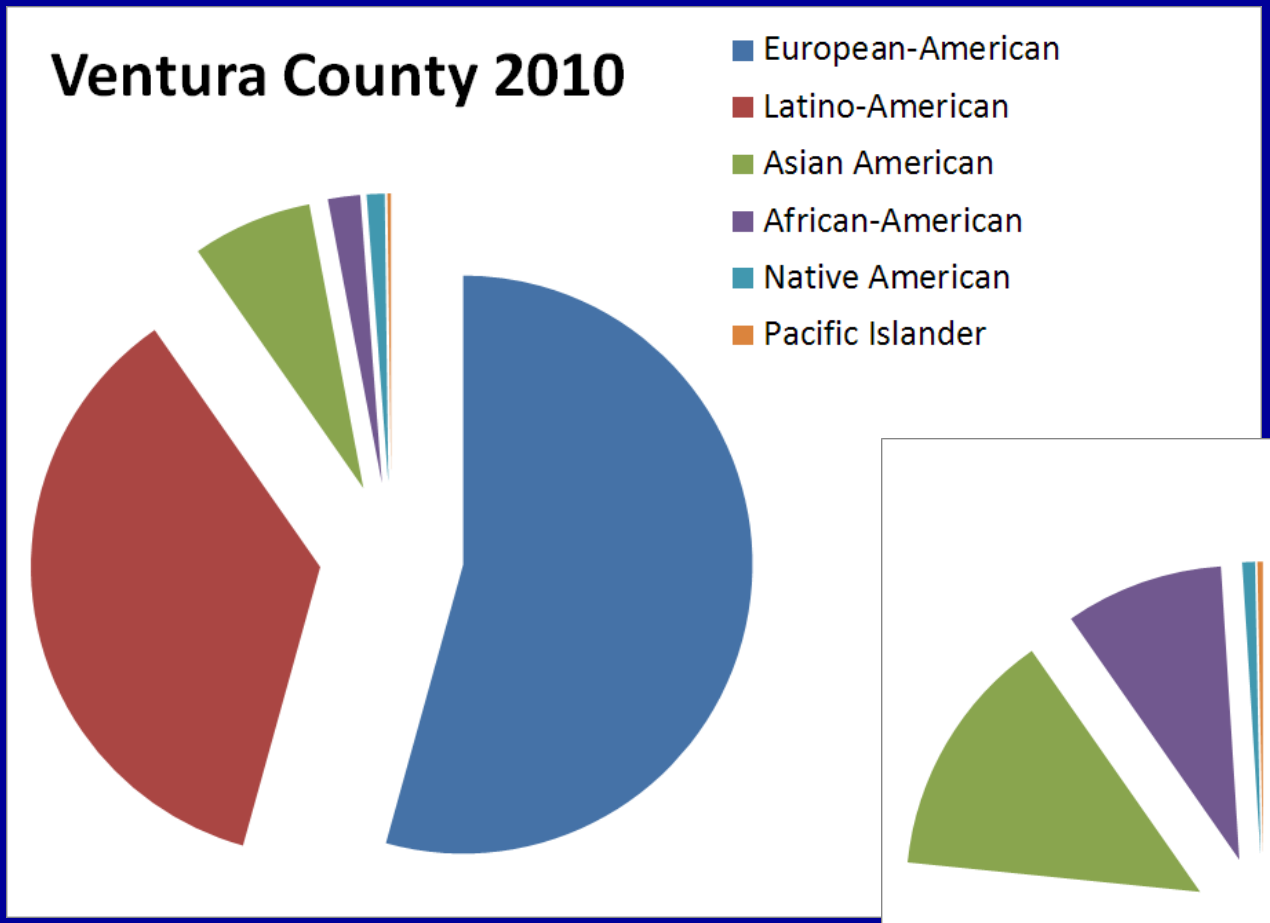


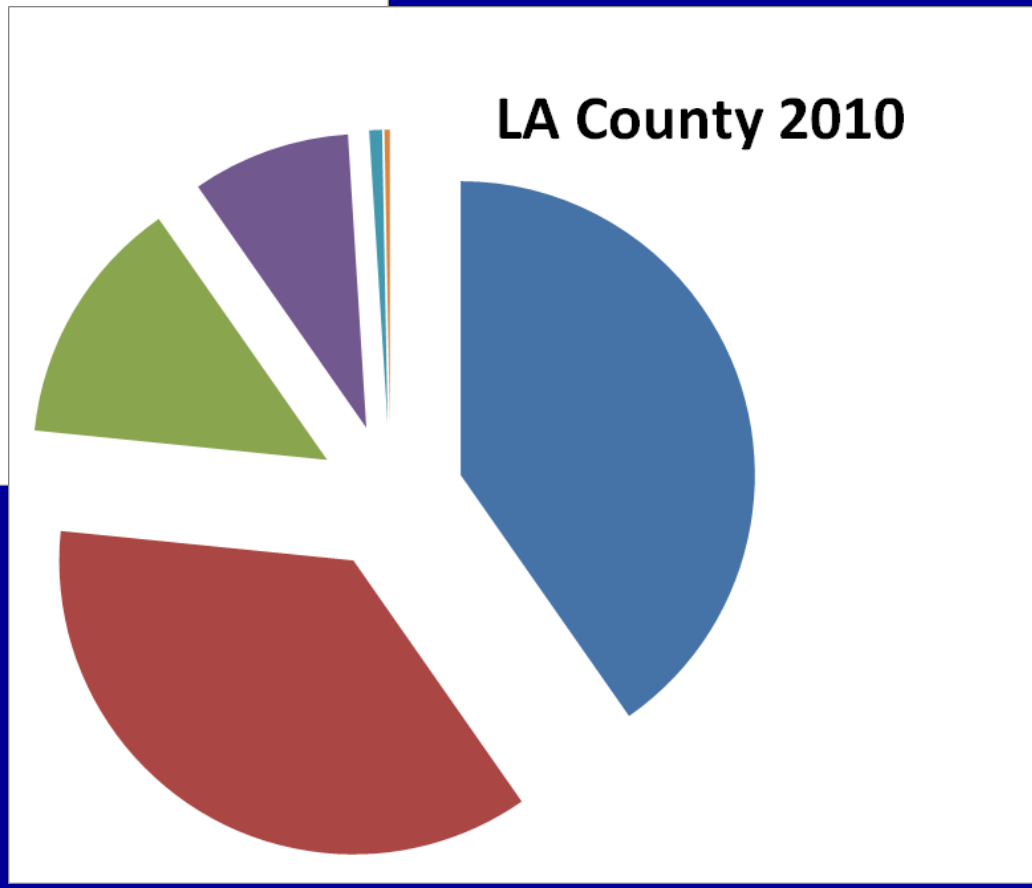
Cancers “cluster” for different reasons

- Lung cancer clusters by smoking, race, education
- Oropharynx cancer by smoking/drinking
- Cervical cancer by self/partner’s sexual activity
- Kaposi sarcoma clustered by sexual preference
- Prostate cancer clusters by race, access to care
- Stomach cancer clusters by history of poverty
- Liver cancer clusters by parental ethnicity
- Thyroid cancer clusters by access to screening
- Mesothelioma clusters by occupation
- Melanoma clusters by race and education
- Breast cancer clusters by education/occupation

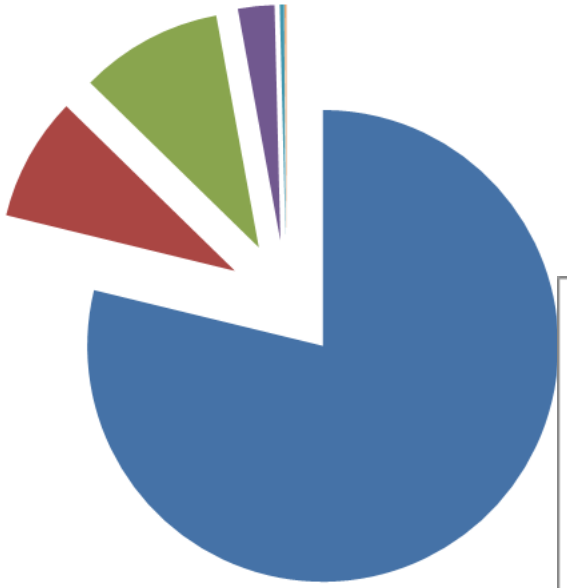
Characteristics of SSRL Offsite Tracts

- They are not characteristic of their respective Counties in terms of:
  - Income and, doubtless, education
  - Race/ethnicity

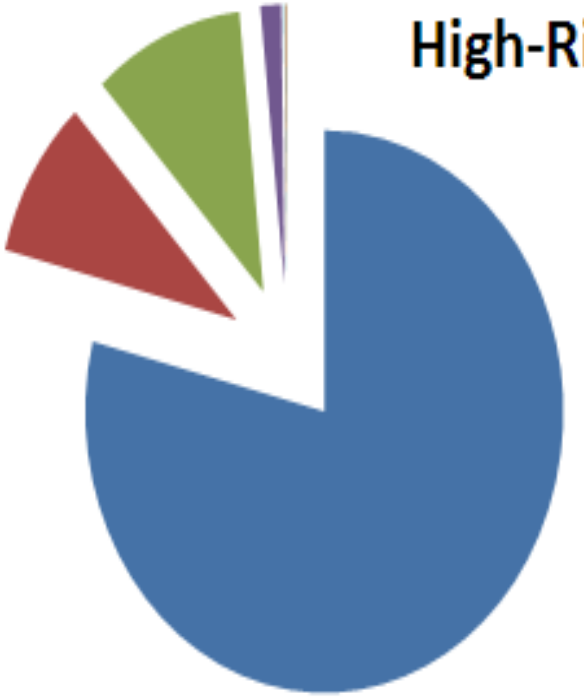

Ventura County 2010
European-American
Latino-American
Asian American
African-American
Native American
Pacific Islander


LA County 2010

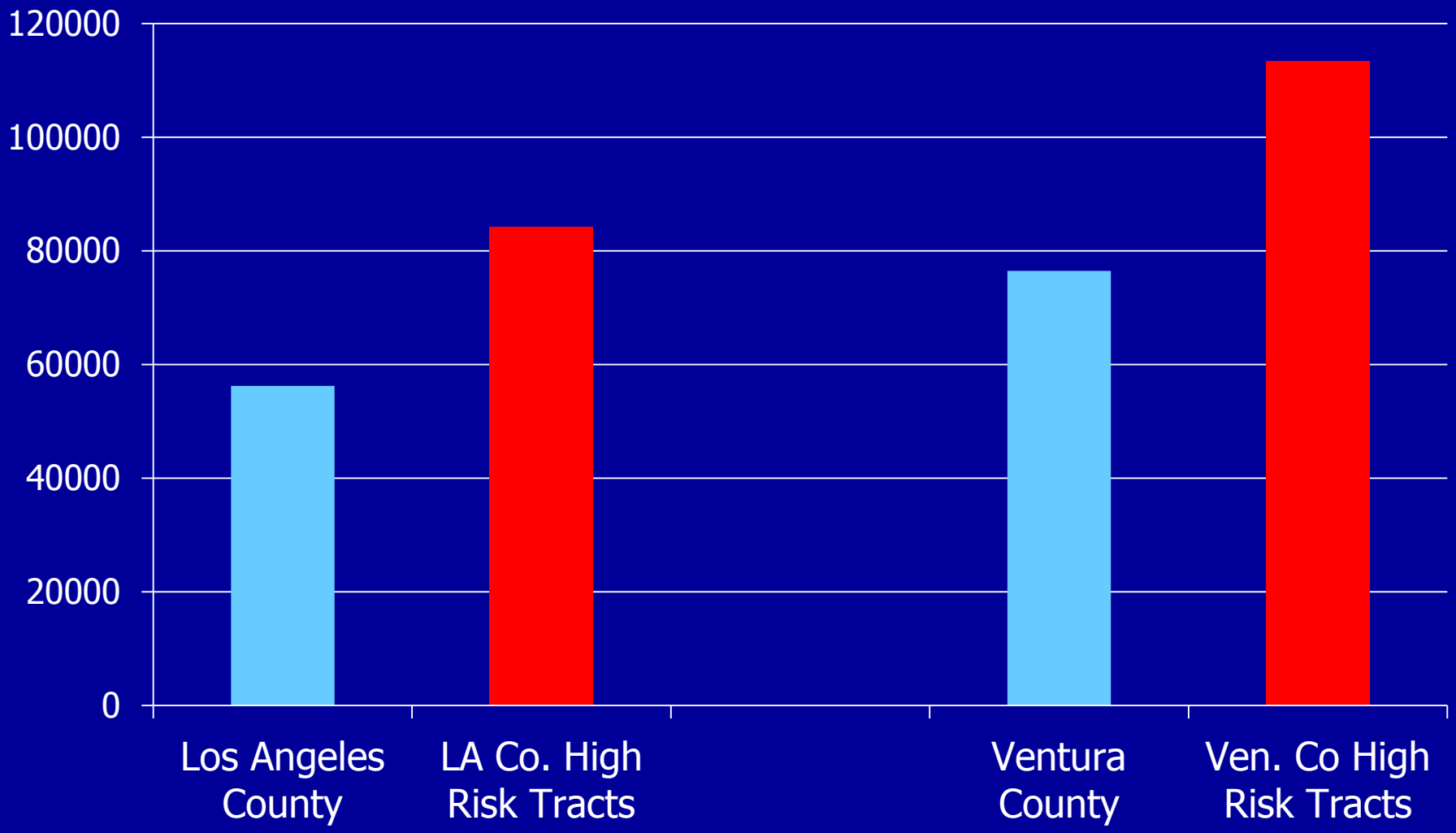
LA County High-Risk Tracts



Ventura County High-Risk Tracts



Median Family Income of Counties and of High Risk Tracts



From where do case reports come?

- Cancer reporting is mandatory since 1988
- California Cancer Registry covers the State
- All invasive malignancies (a few benign tumors)
- All cases found in a CA resident at diagnosis
- Hospitals collect reports to maintain certification
- Non-hospital labs, death certificates covered
- Reports returned to the place of residence
- Around 99% complete by regular audits using sampling and death certificates

Malignancies according to Annual (Age-Adjusted) New Cases /100,000

- **50+: M Prostate, F Breast**
- **30-49: MF Lung, M/F Colorectum**
- **10-29: MF Melanoma, M Oropharynx, M Bladder, F Ovary, F Endometrium, MF Non-Hodgkin Lymphoma, M Leukemia**
- **5-9: M Stomach, M Larynx, M Testes, F Melanoma, F Thyroid**
- **F Cervix, F Oropharynx, F Leukemia, MF Pancreas, MF Kidney, MF Brain**
- **<5: M Thyroid, M Penis, F Stomach, F Larynx, F Bladder, MF Liver, MF Esophagus, MF Gallbladder, MF Hodgkin Lymphoma, MF Eye**

Selection of malignancies

- Every cancer has a unique set of causes
  - (A few exposures, i.e. smoking, cause a portion of several cancers, but the rate of cancer at all sites is not informative)
- Cancers were selected for assessment:
- In all, thirteen different malignancies
  - The four most common cancers
  - Others possibly caused by chemicals/radiation

Cancers selected

Neoplasm	Major Causes	Descriptive Predictors
Lung	Cigarette smoking	Blue collar occupation
Bladder	Cigarettes, aniline dyes (rare)	White Race
Pancreas	Cigarette smoking	None strong
Oropharynx	Tobacco, Alcohol, Pap.Virus	None strong
Leukemia	Genes, benzene, ? virus	None strong
Breast	Genes, Hormones	Higher education
Colorectal	Genes, Diet, Activity	None strong
Prostate	Genes, Diet	Race, Age, Access to screening
Thyroid	Ionizing radiation (rare)	Access to screening
Brain	Ionizing Radiation (rare)	None strong
Liver	Hepatitis B, C viruses	National origin
NHL	Immune depletion	None strong
Melanoma	Sunlight, light skin	Race, Higher education

Screening Methods

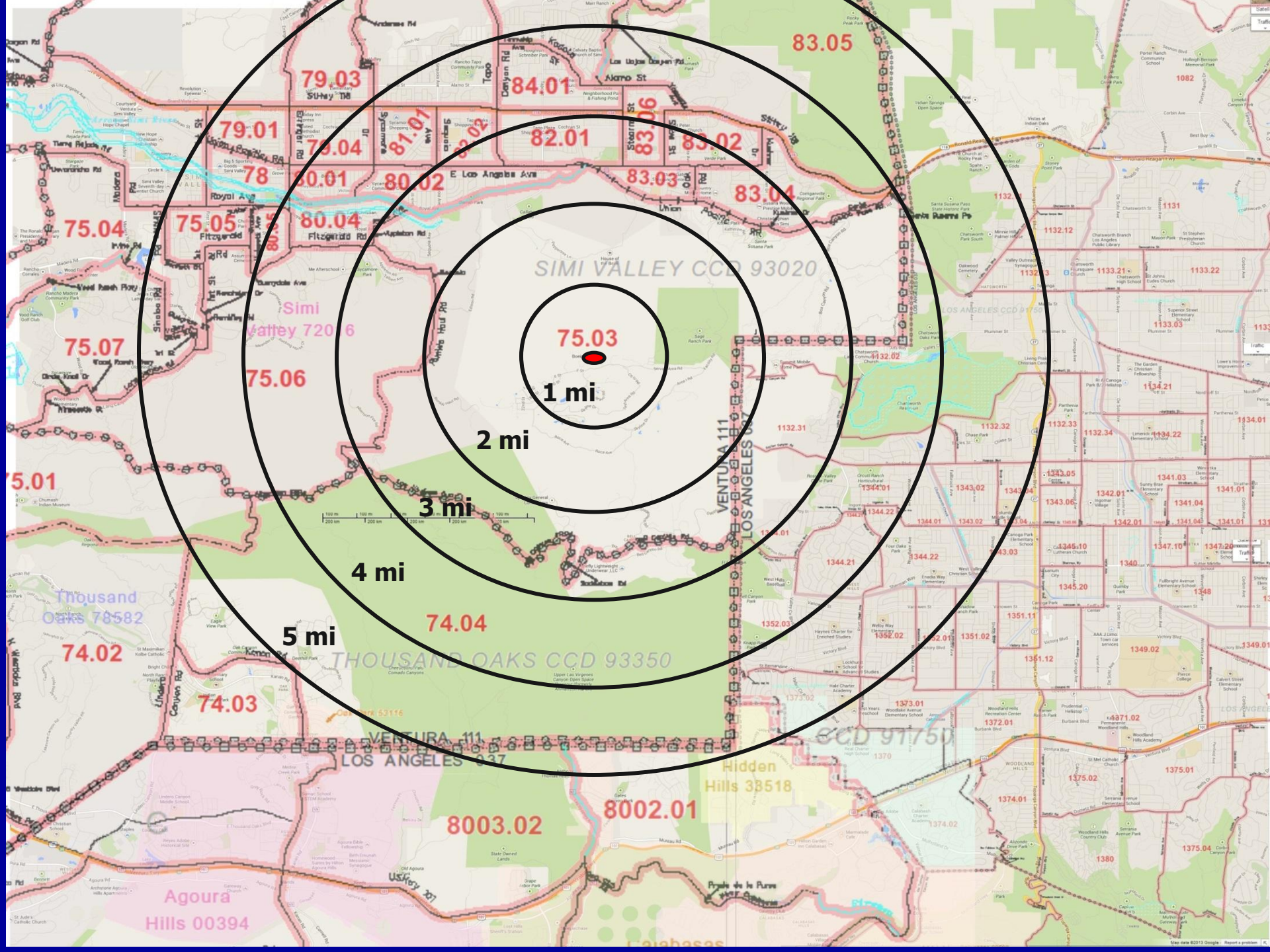
- Genders assessed separately
- Three time periods:
  - 1988-95, 1996-2003, 2004-2010
  - Separate denominators from 3 censuses

- All census tracts within 5 miles of SSFL
  - 1988-95: 22 VEN, 16 LA census tracts
  - 1996-2003 : 29 VEN, 17 LA census tracts
  - 2004-2010: 29 VEN, 17 LA census tracts

- Number of comparisons:
  - 130 period-tracts X 24 gender-cancers= 3120 searches
  - Up to 78 (3 per gender-cancer) “significantly” high-risk tracts by chance

Screening Criteria

- Significantly higher rate than County mean at the 95% confidence level ($p < 0.05$)
- At least a 50% increase in risk ($RR > 1,5$)
- Histological (Causal) homogeneity of excess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To find a result consistent with local cancer causation by disbursed carcinogen

- Consistent risk over calendar time
- High risk for both genders in the same area
- Higher risk proximate to SSRL
- Geographic clustering of high risk areas
- Pattern consistent with dispersion flow
- We screen by a relative risk (RR) of 1.5, but if RR is below 2.0, any observed case would likely have occurred anyway

- No plausible alternative explanation is available

Reasons for Caution in Assessing Impact

- 3 “Significant” excesses each are expected by chance

- No known clear evidence of personal exposure
- Waterborne and airborne dispersion imprecise
- Dosage is unknown

- Exposed workers are likely to reside together
- Census errors: rapid local growth may distort incidence estimates

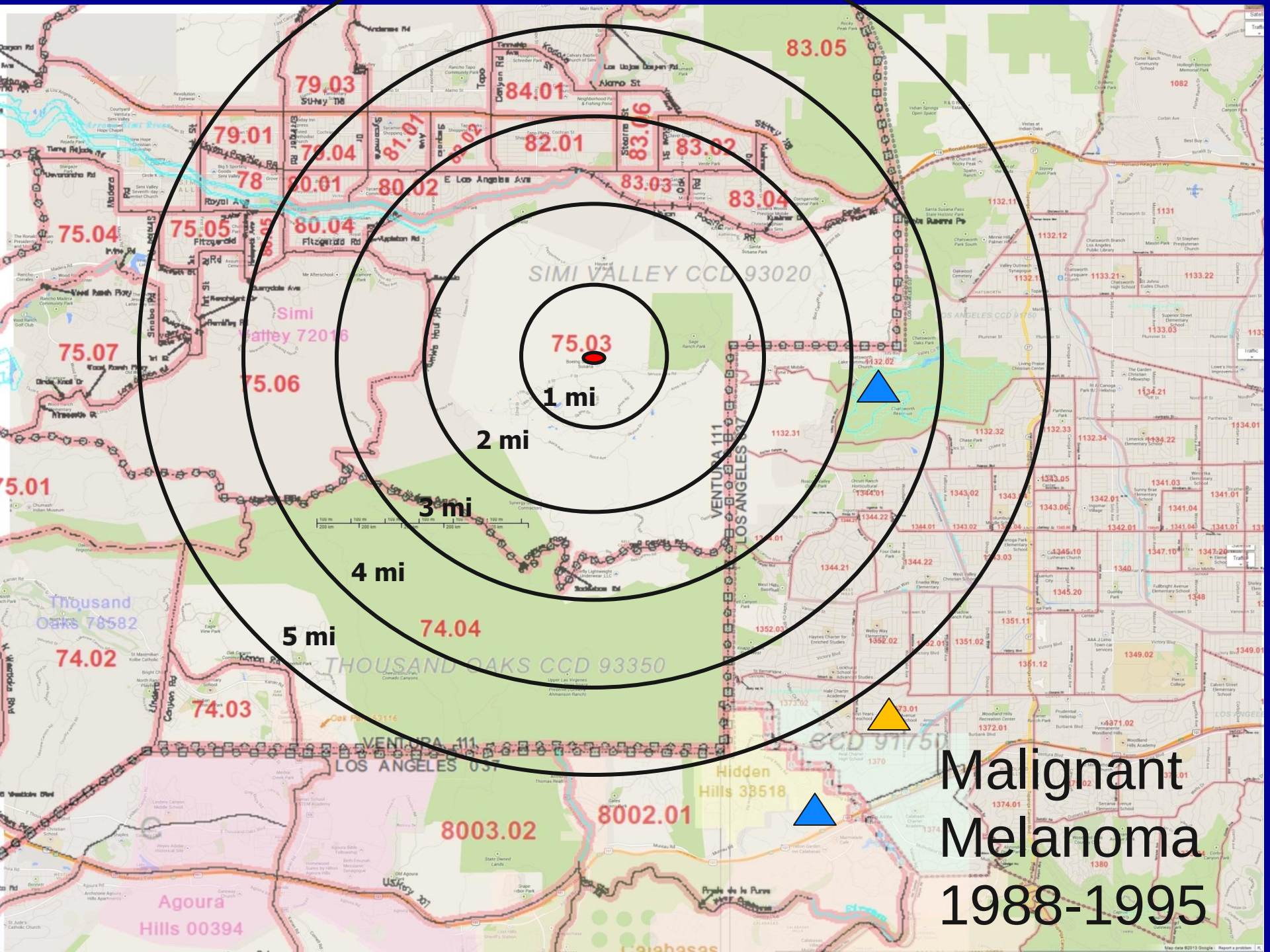
- Evaluation is based on residential address at diagnosis

Summary Screening Findings

Neoplasm	"Significant" tract-periods	In Both genders	In Adjacent tracts	In 2 or more periods
Breast	26 (3 exp)	---	8	6
Melanoma	23 (6 exp)	8	17	7
Colorectal	7 (6 exp)	2	0	0
Lung	4 (6 exp)	0	0	1
Prostate	4 (3 exp)	---	0	0
Thyroid	3 (6 exp)	0	0	0
Brain	3 (6 exp)	0	0	0
NHL	2 (6 exp)	0	0	0
Leukemia	1 (6 exp)	---	---	--
Bladder	1 (6 exp)	---	---	---
Oropharynx	0 (6 exp)	---	---	---
Liver	0 (6 exp)	---	---	---
Pancreas	0 (6 exp)	---	---	---

Legend

Period	Males	Females	Both
1988-1995			
1996-2003			
2004-2010			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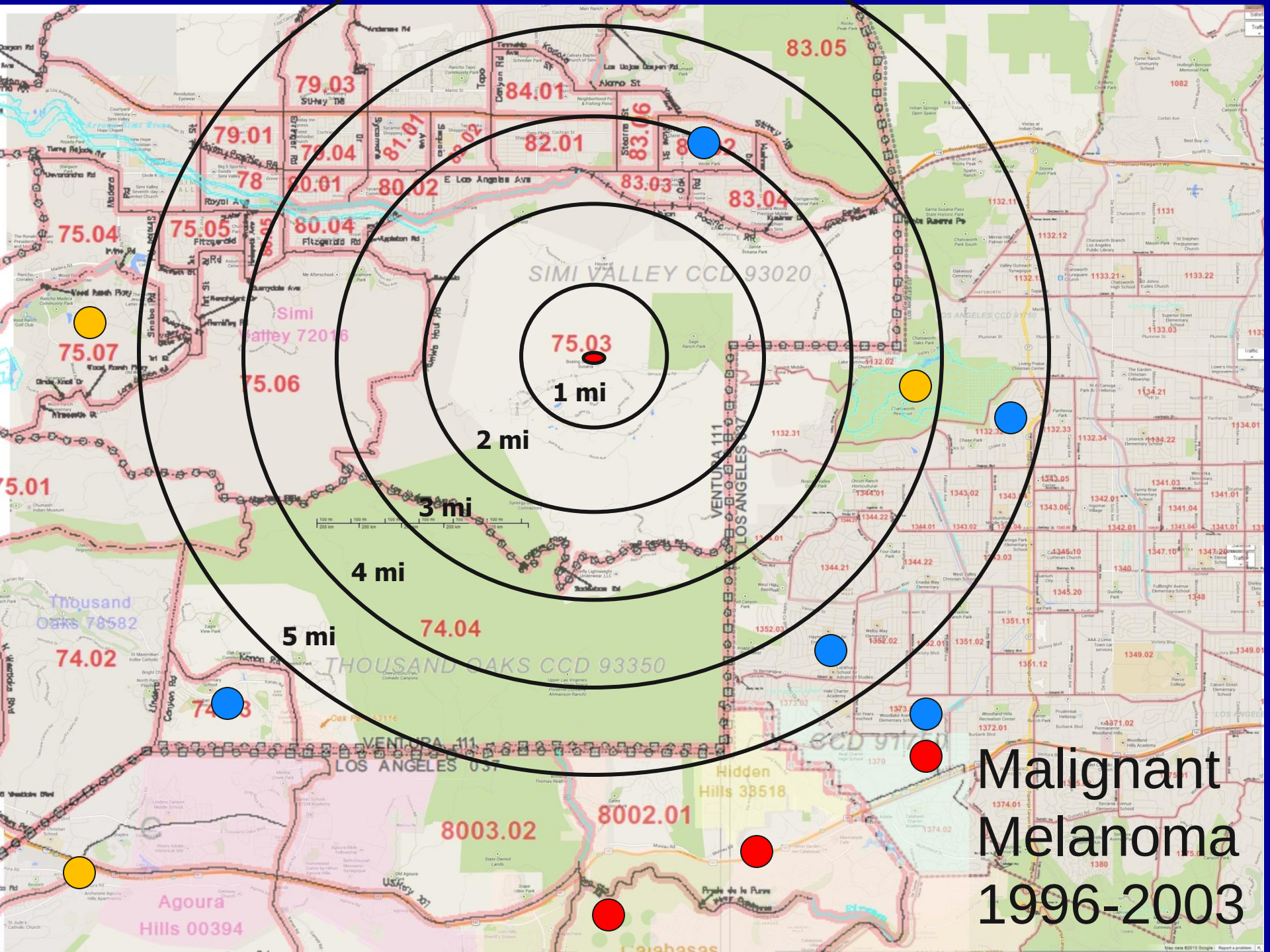
Malignant Melanoma 1988-1995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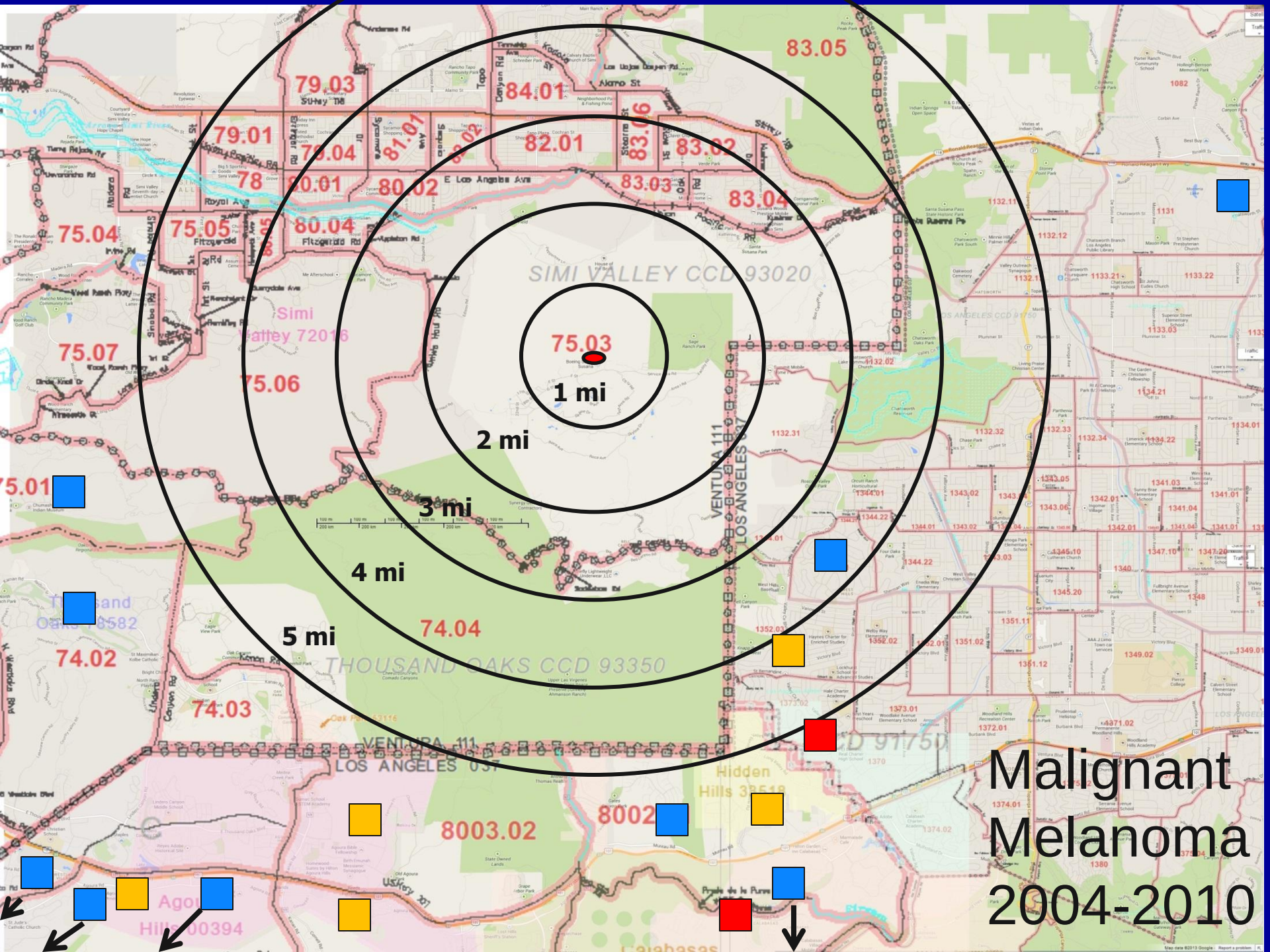
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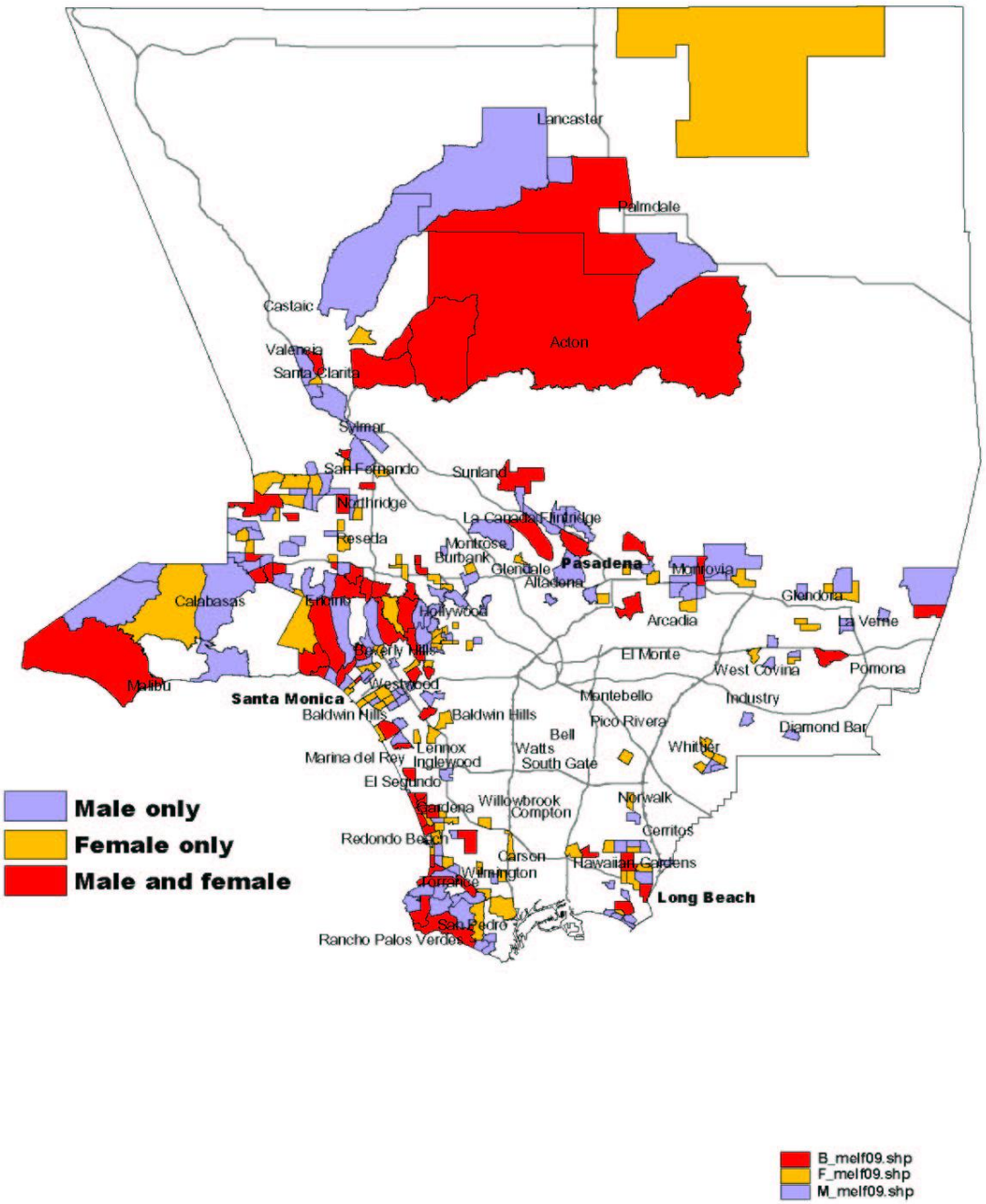
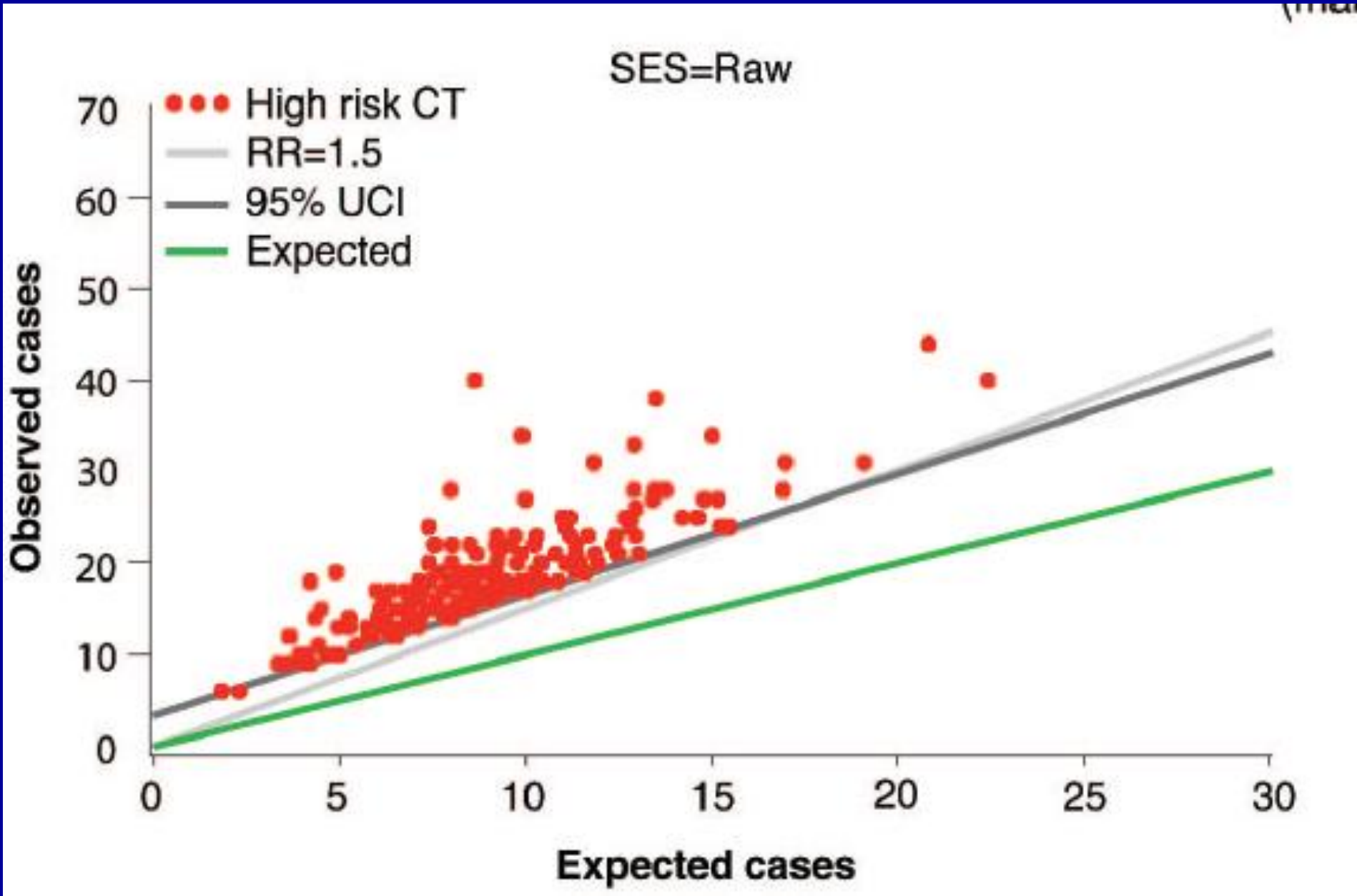
Malignant
Melanoma
2004-2010

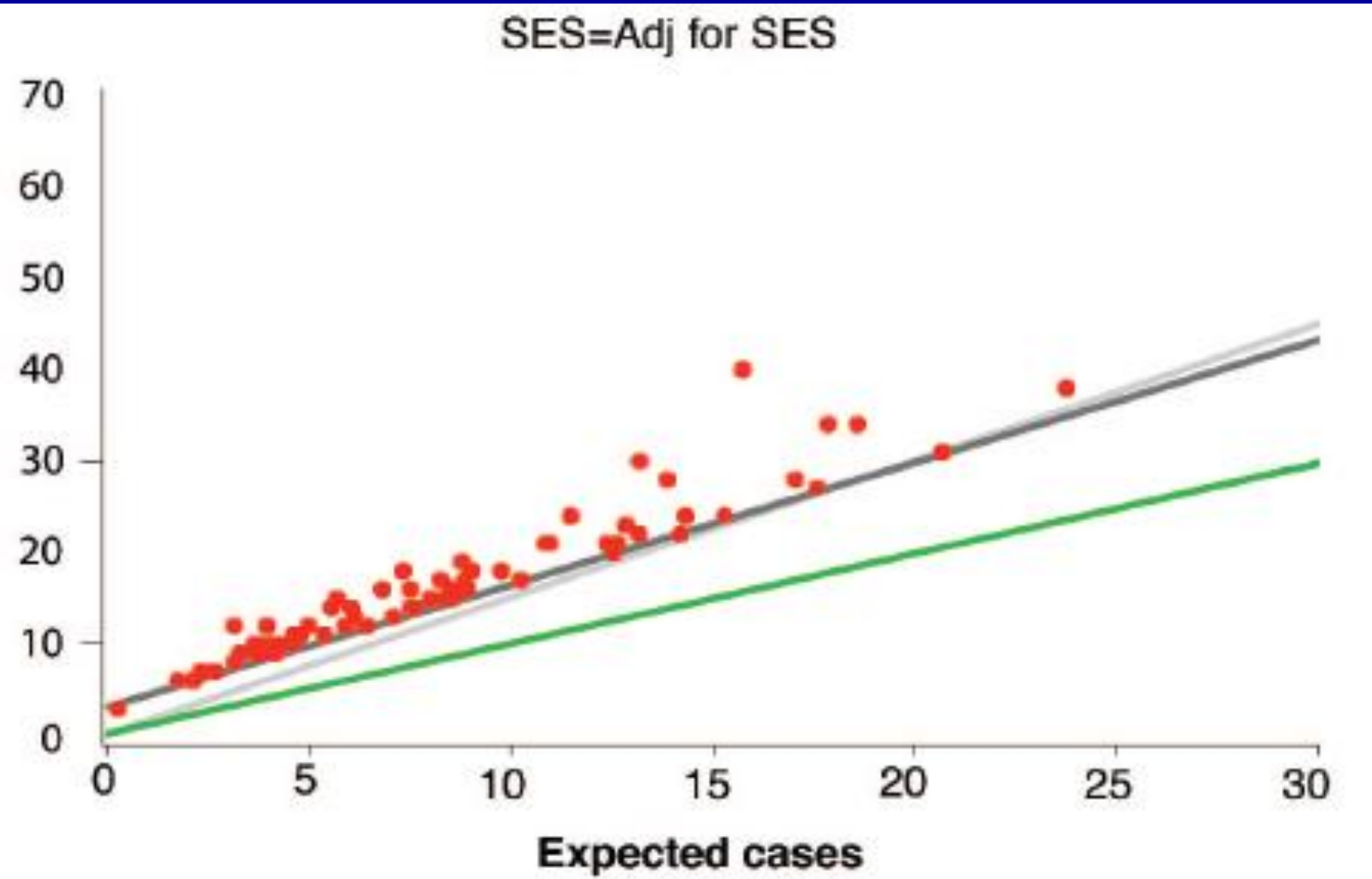
Malignant Melanoma



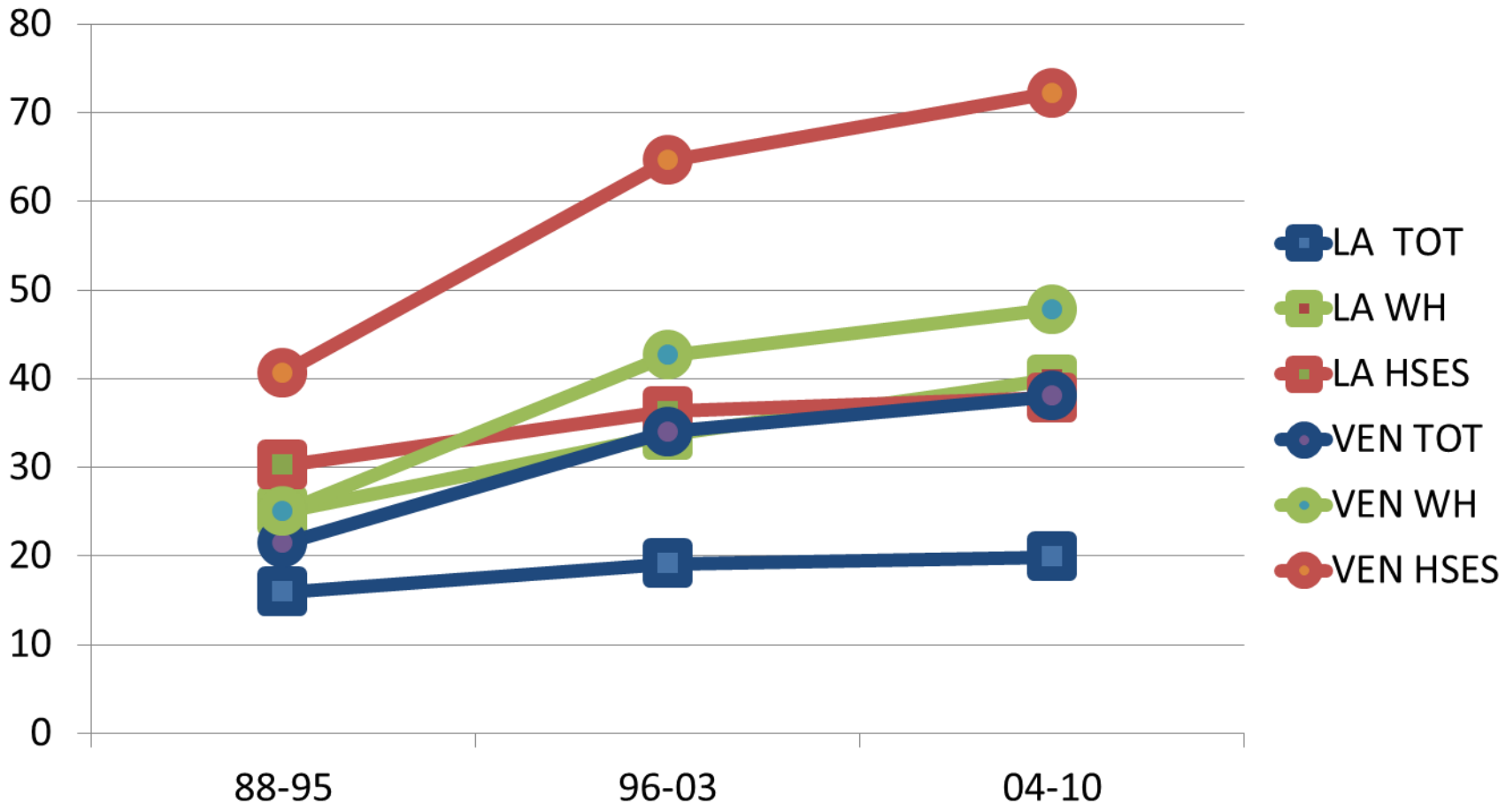
Malignant Melanoma



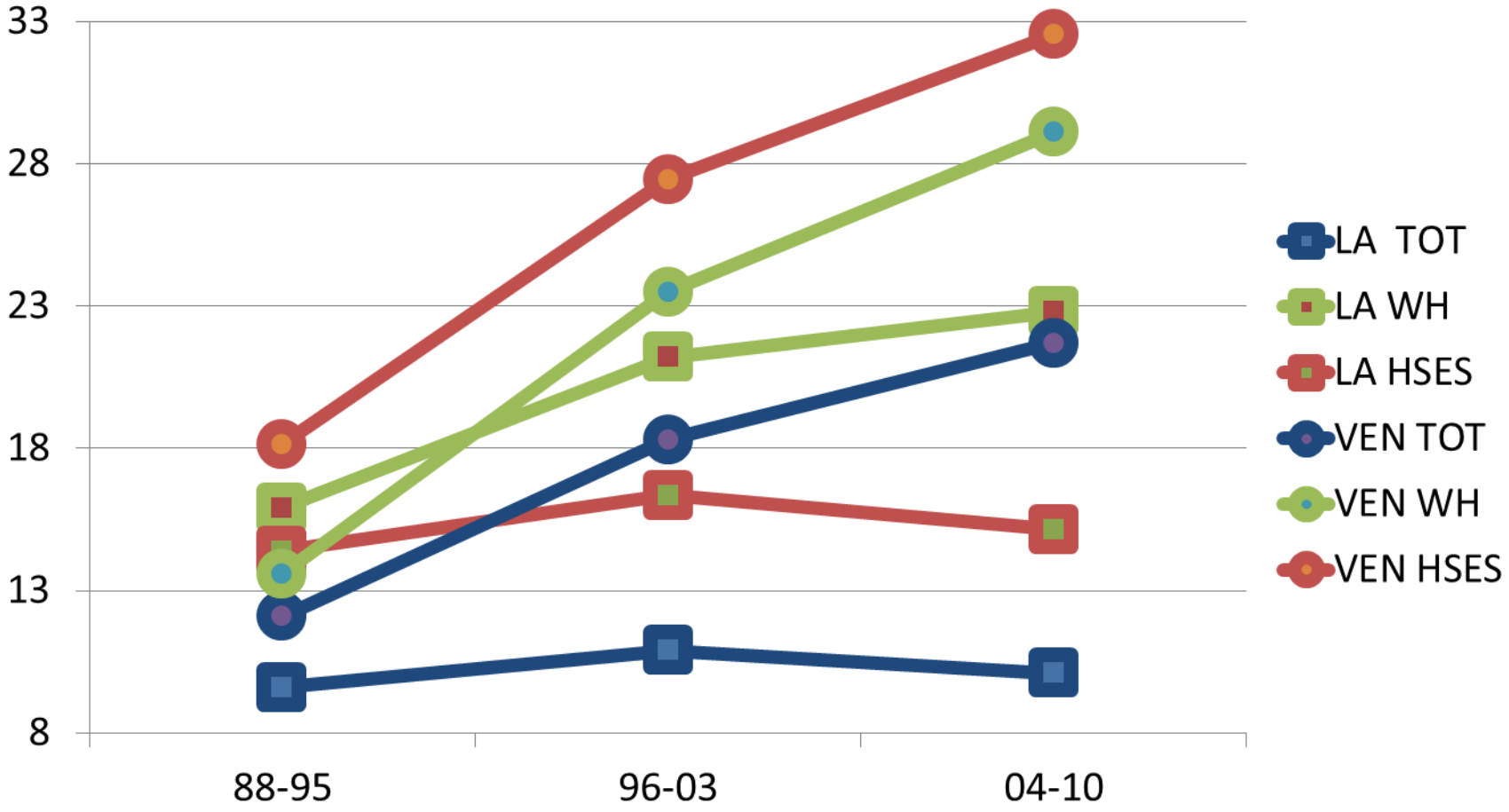
Malignant Melanoma-Adjusted for SES

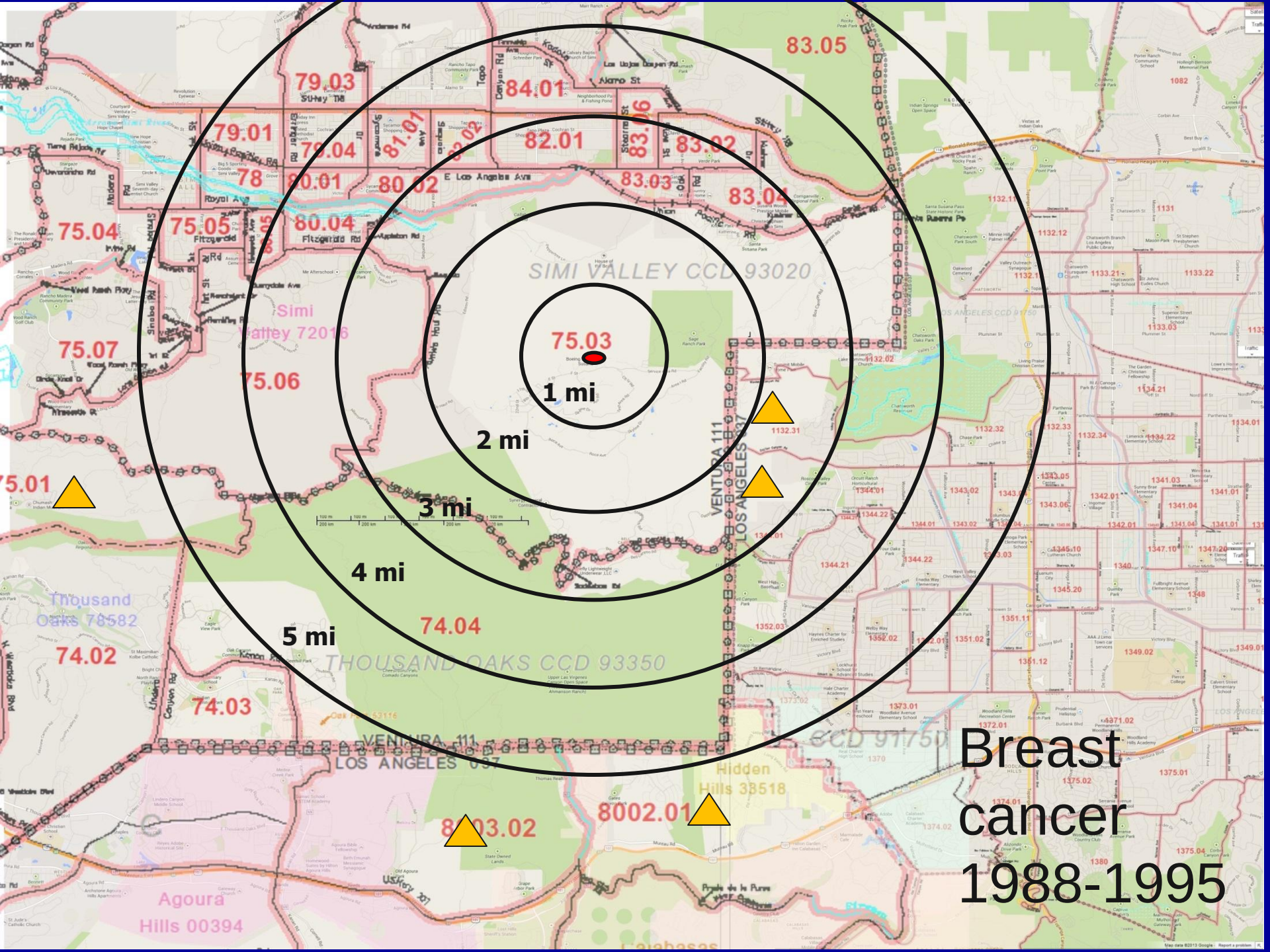


MALE MELANOMA



FEMALE MELANOMA

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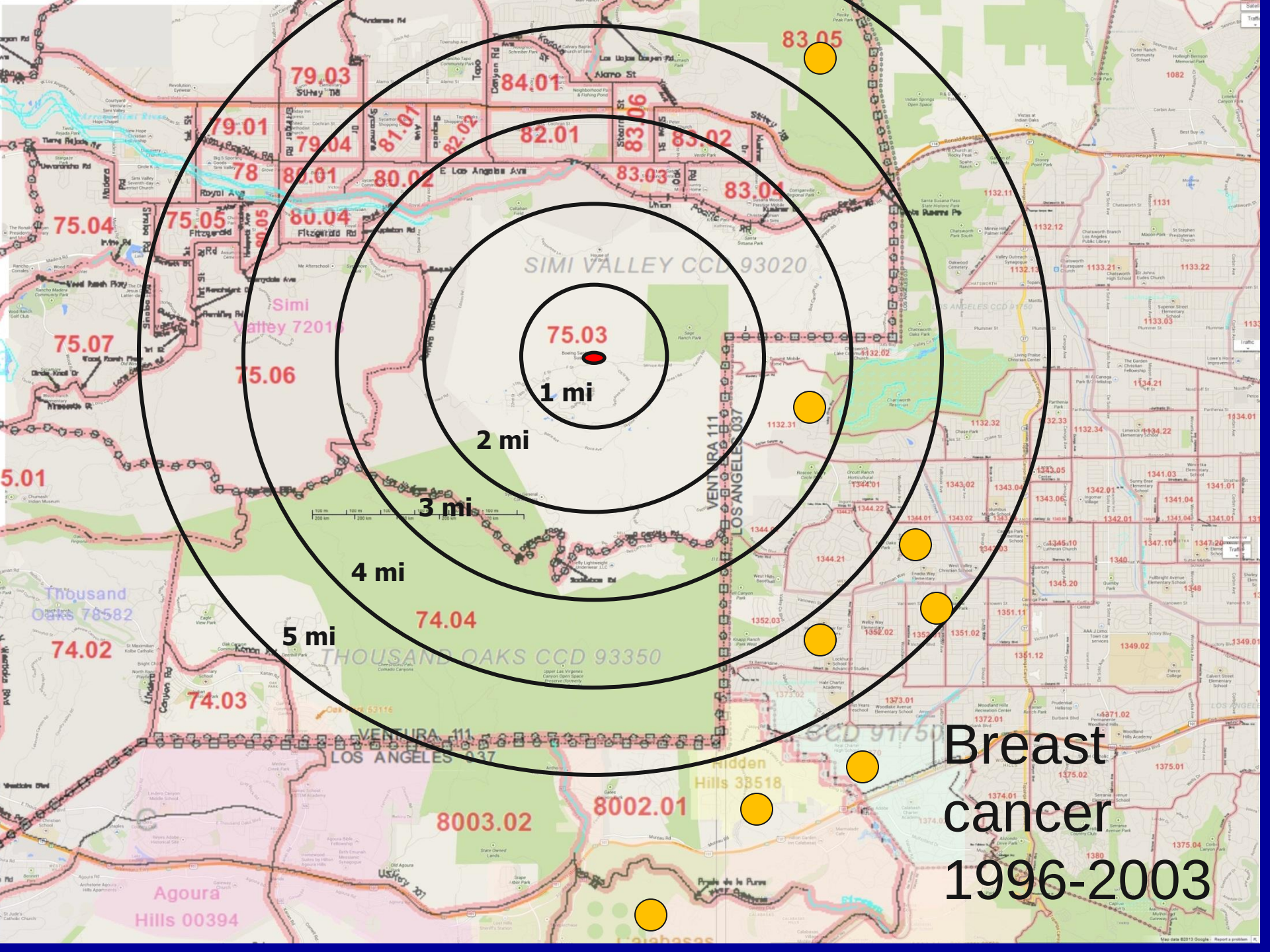
Breast cancer 1988-1995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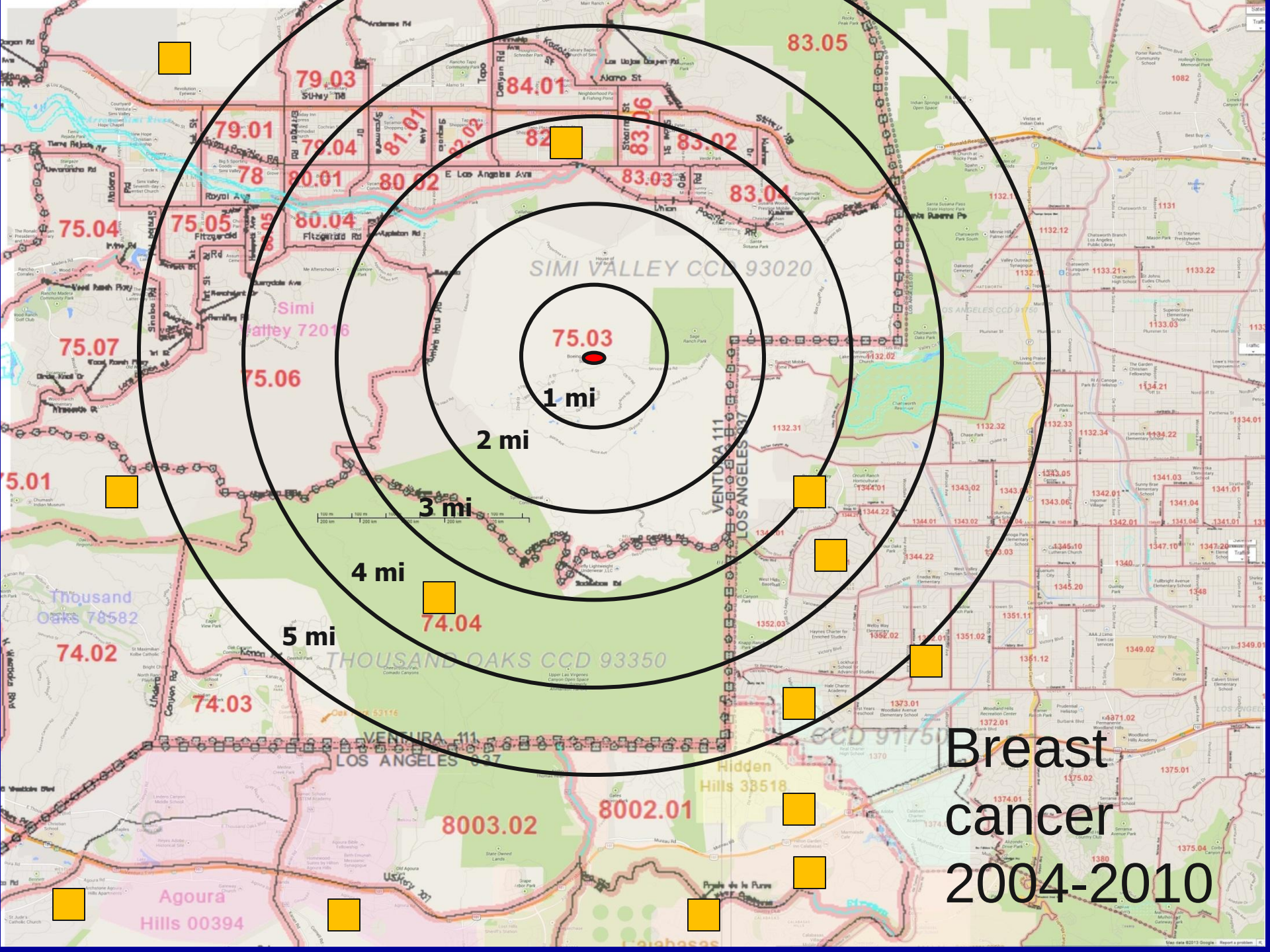
Breast cancer 1996-2003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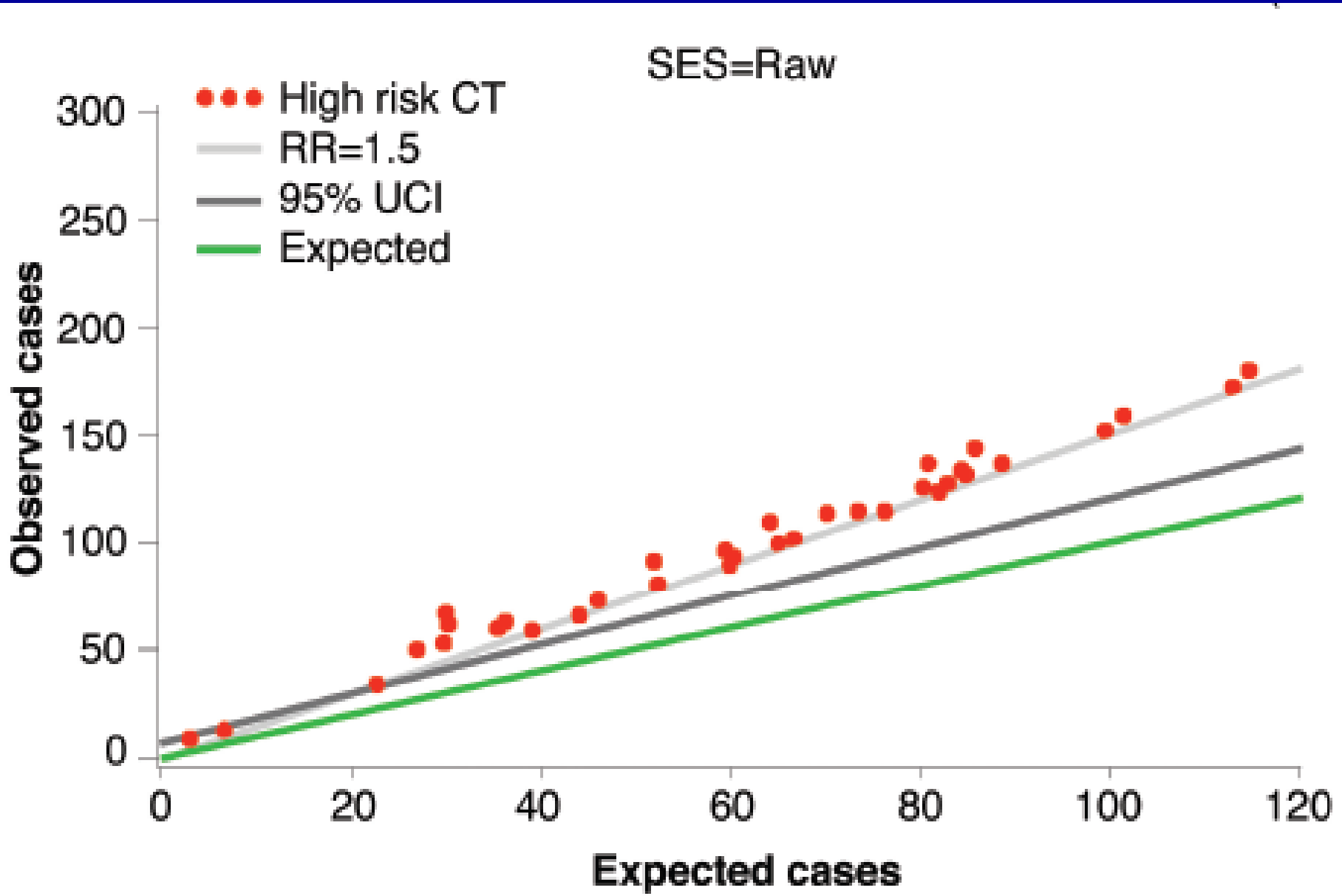
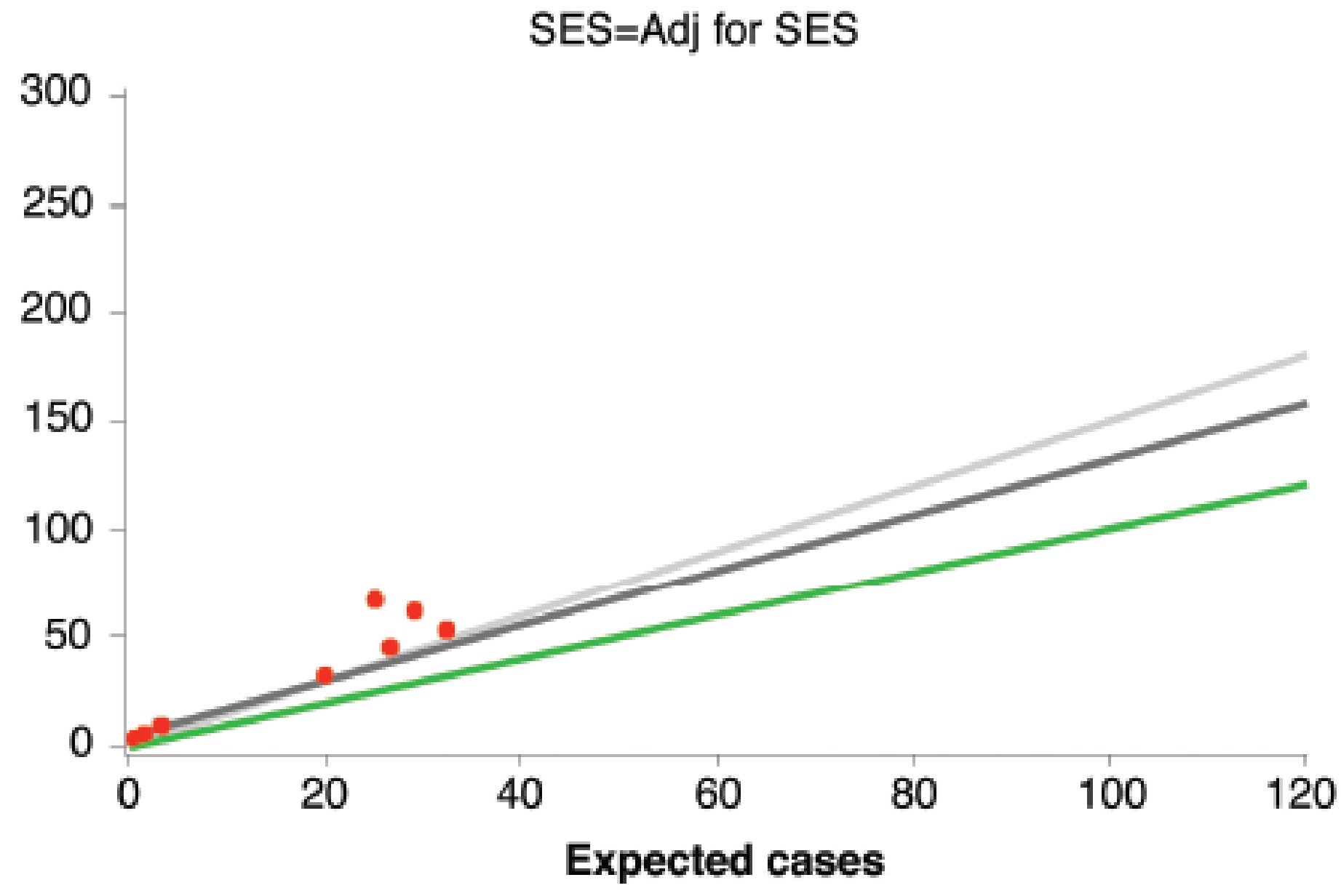
Breast cancer 2004-2010

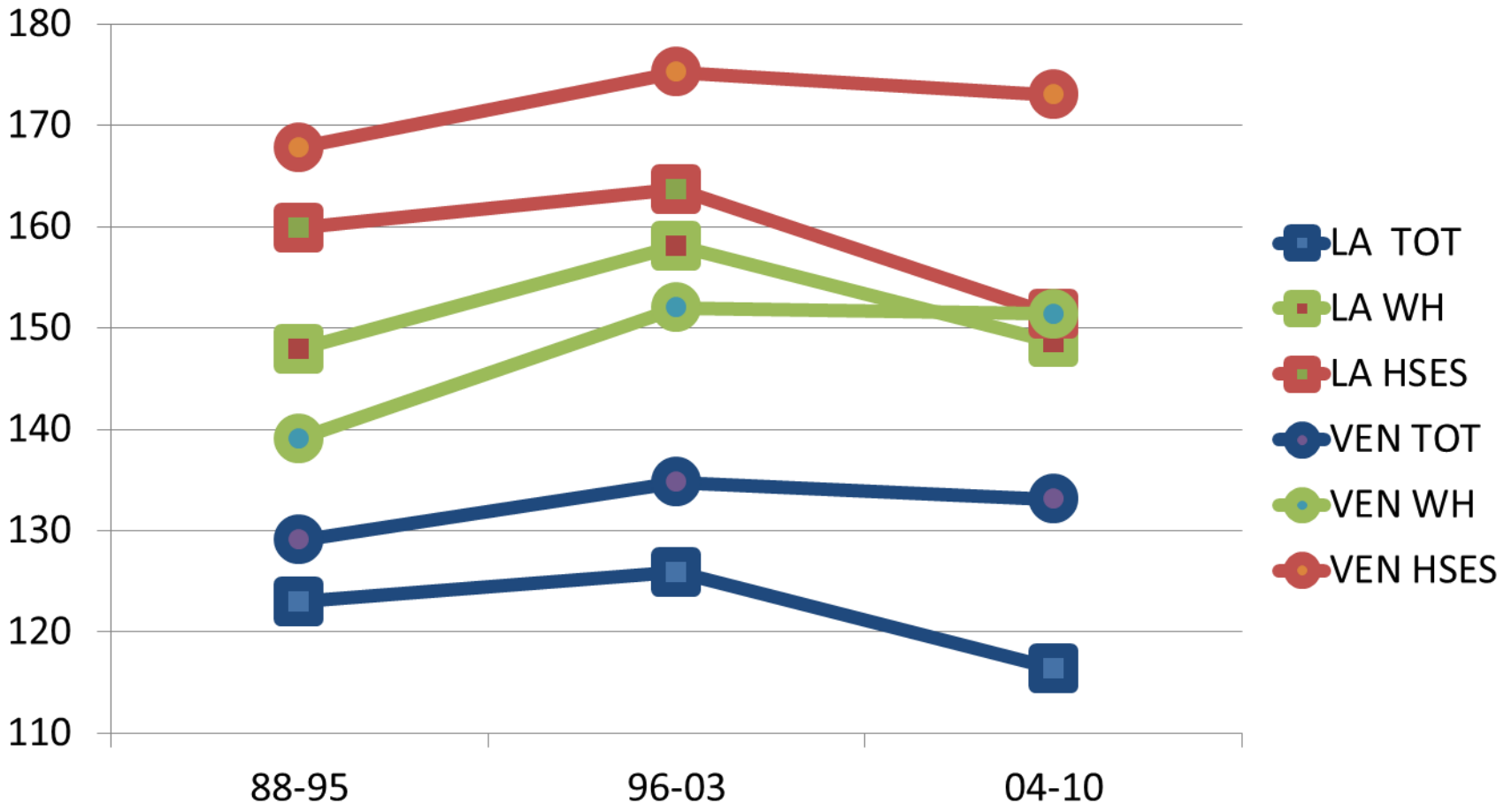
Female Breast Cancer

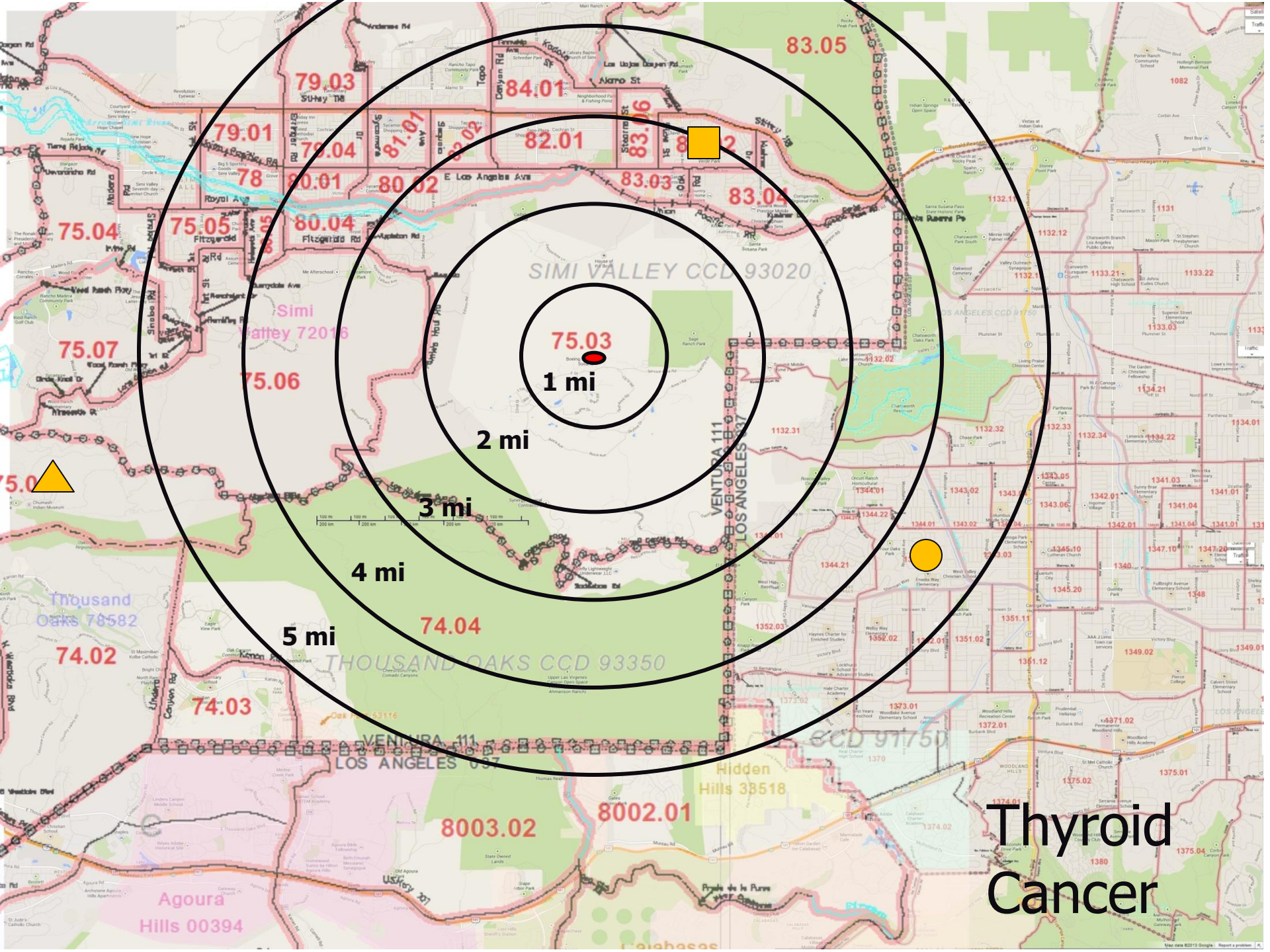


Female Breast Cancer



FEMALE BREAST




Thyroid Cancer
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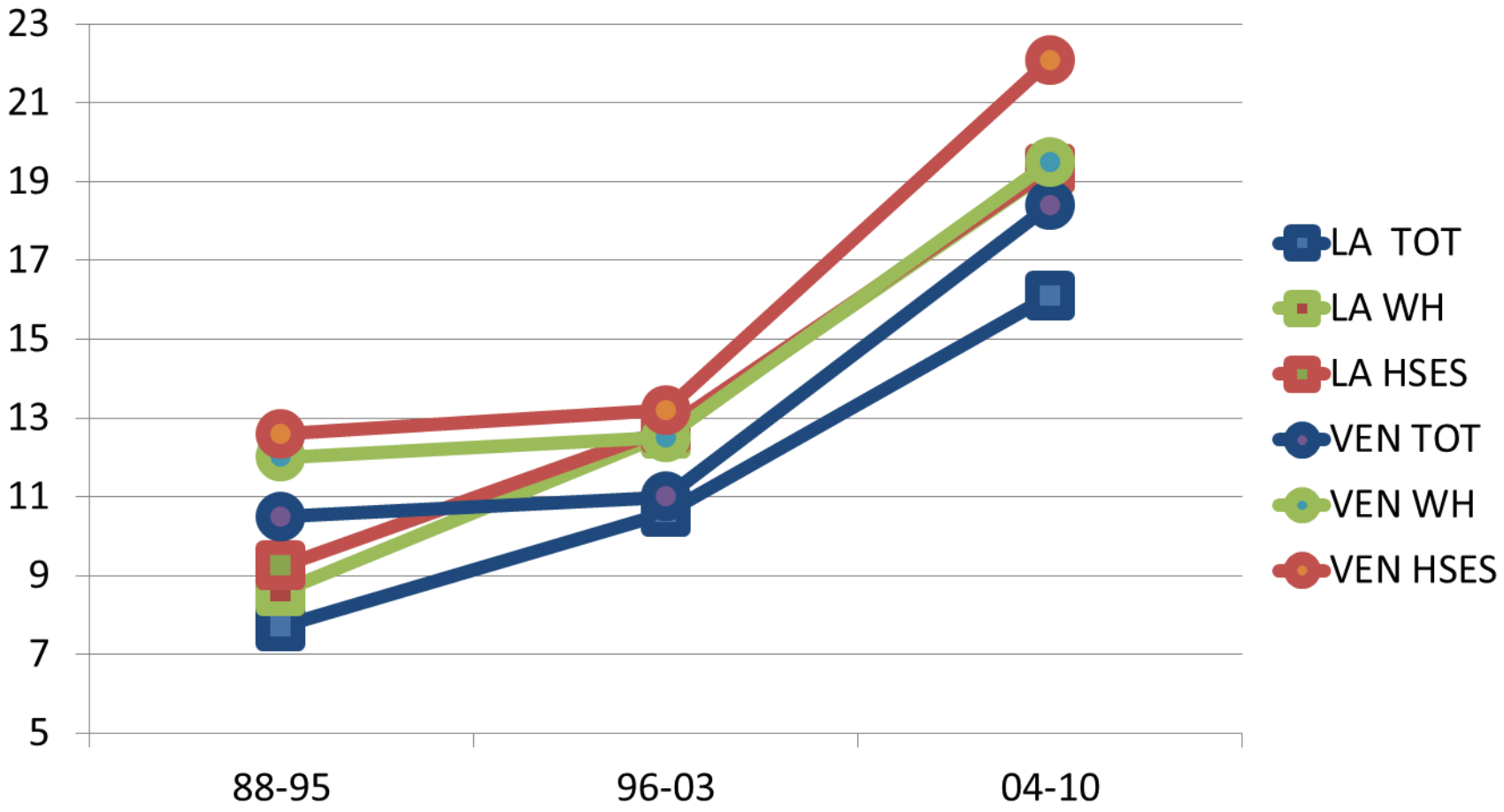
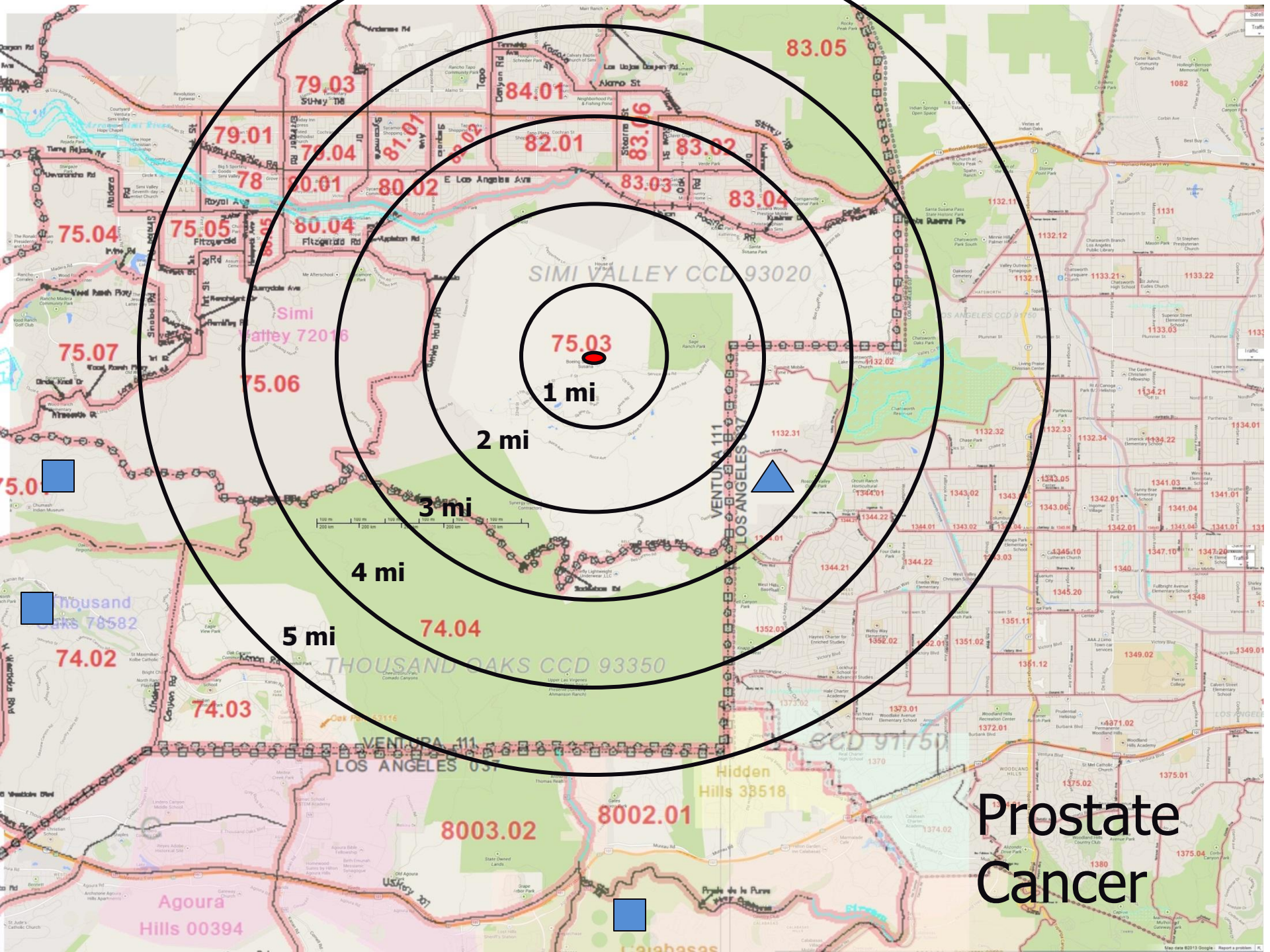
FEMALE THYROID




Prostate Cancer
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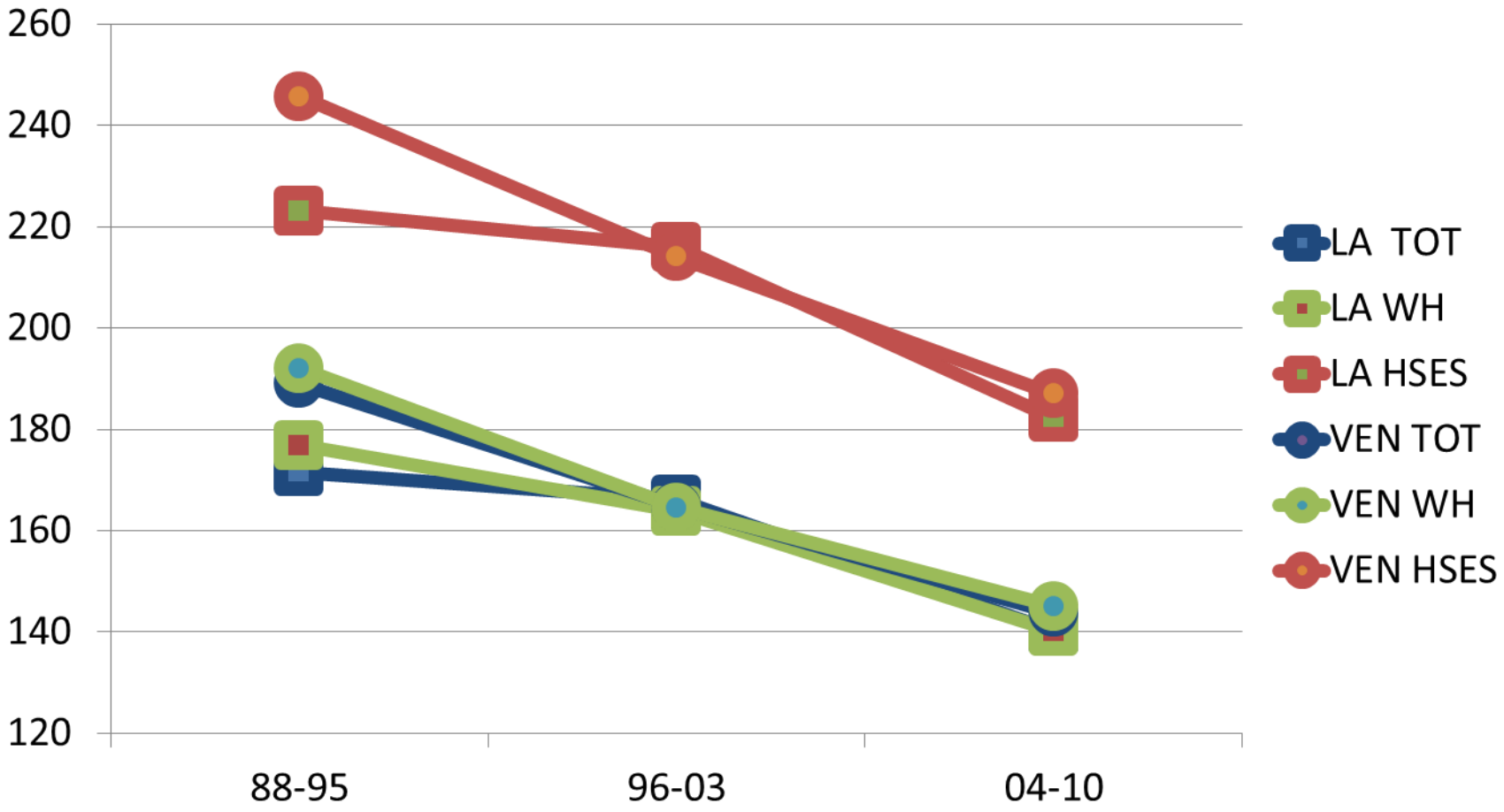
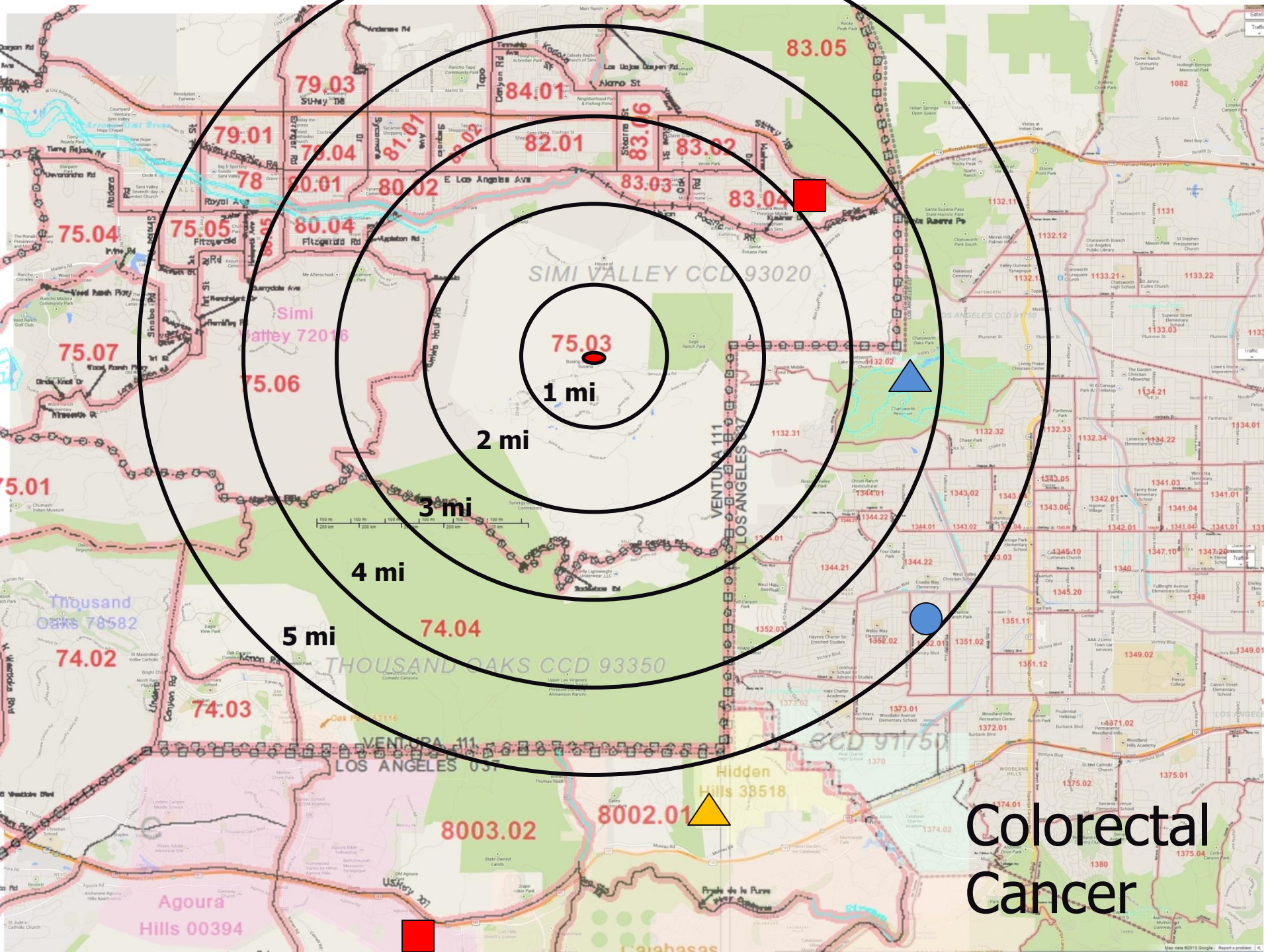
MALE PROSTATE




Colorectal Cancer
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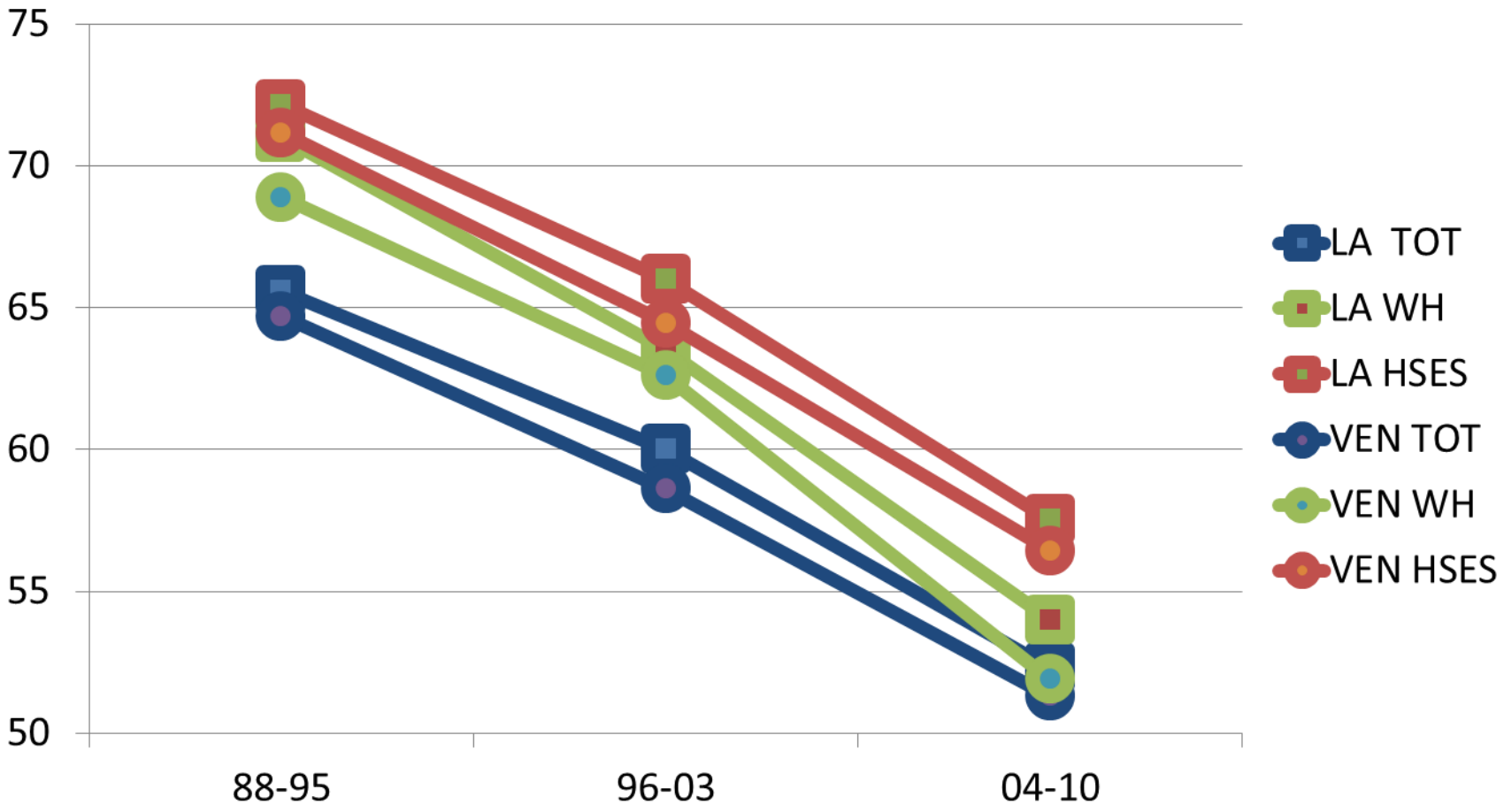
MALE COLORECTAL



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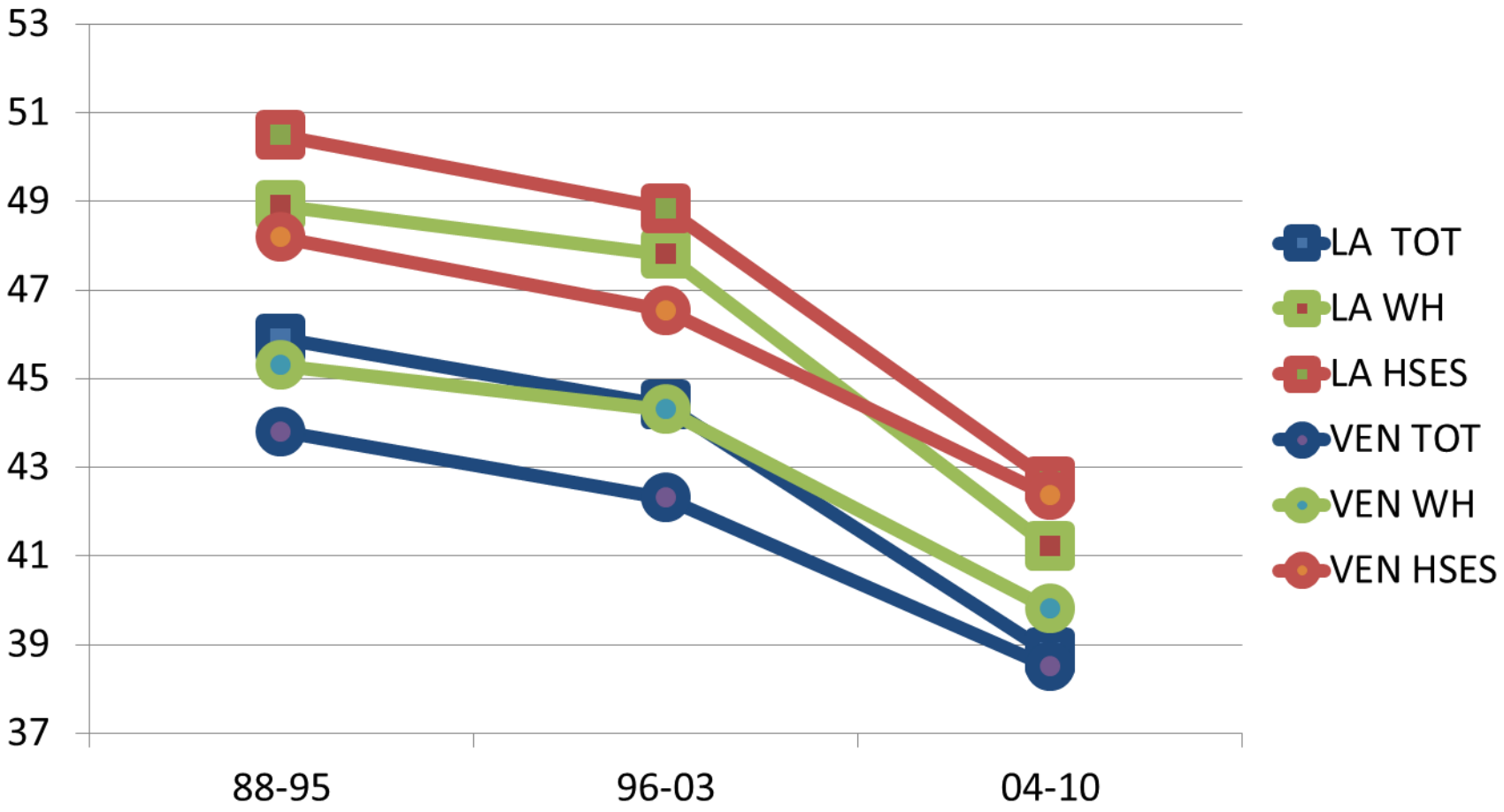

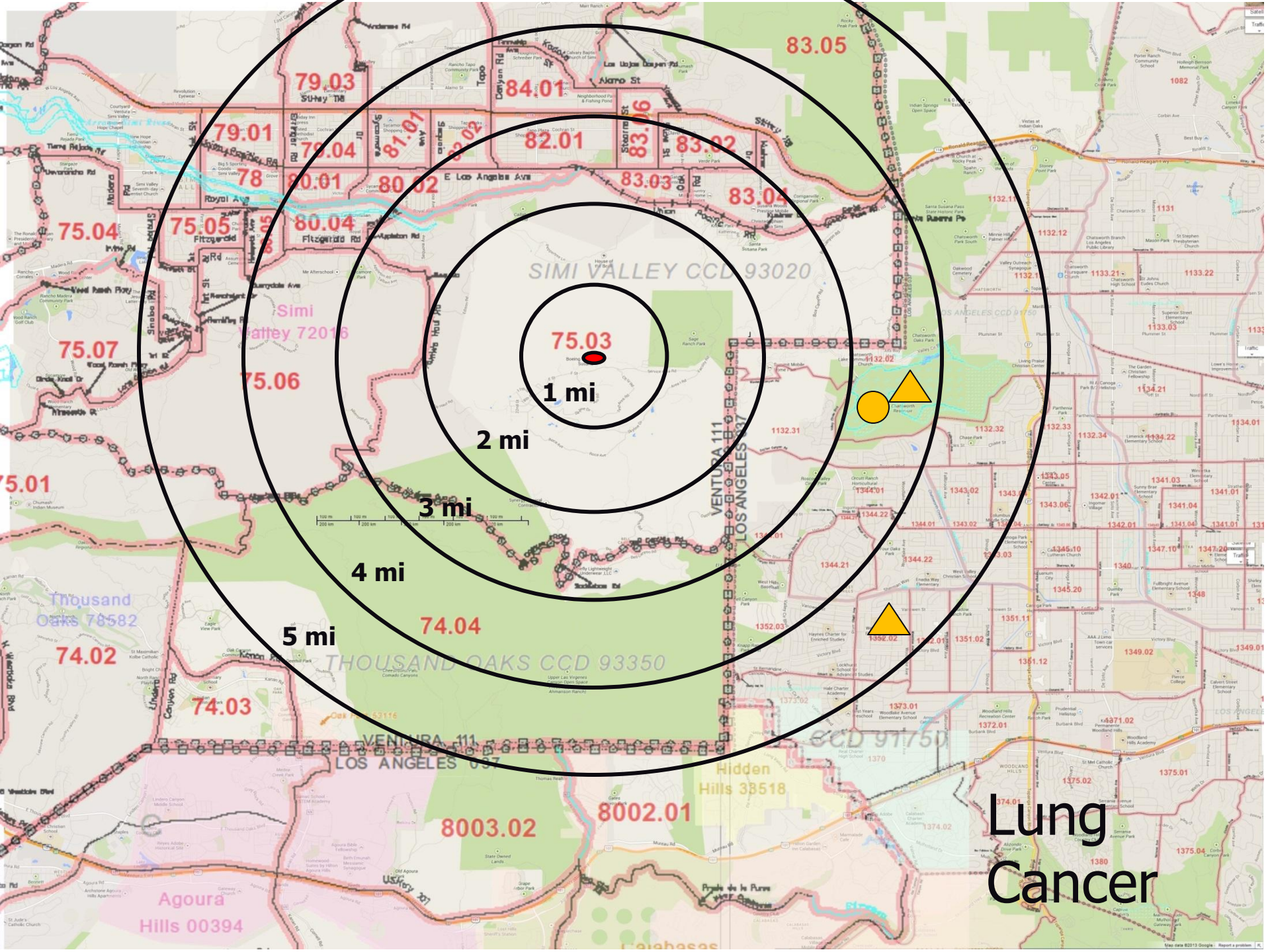
Lung Cancer
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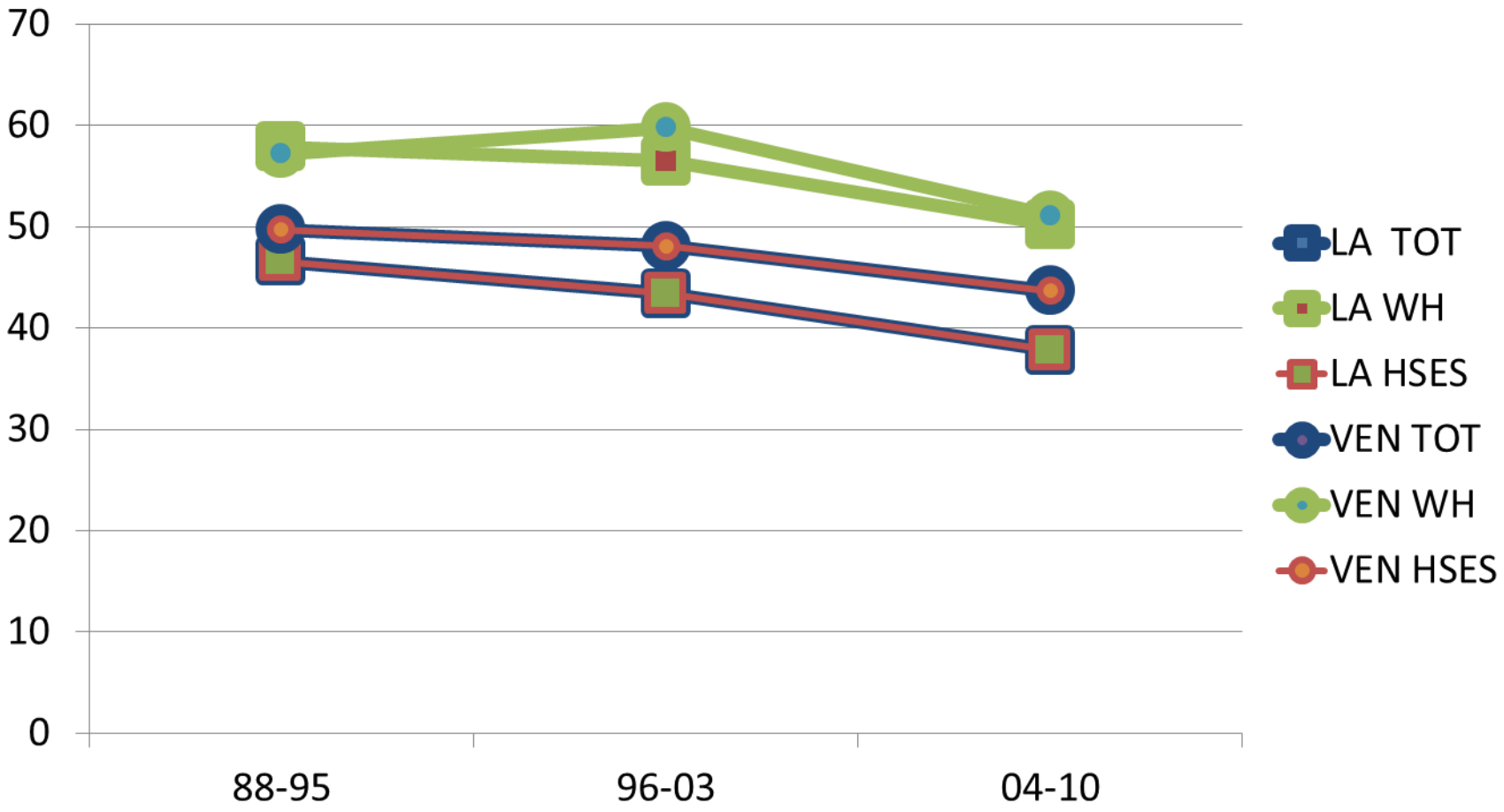
FEMALE LUNG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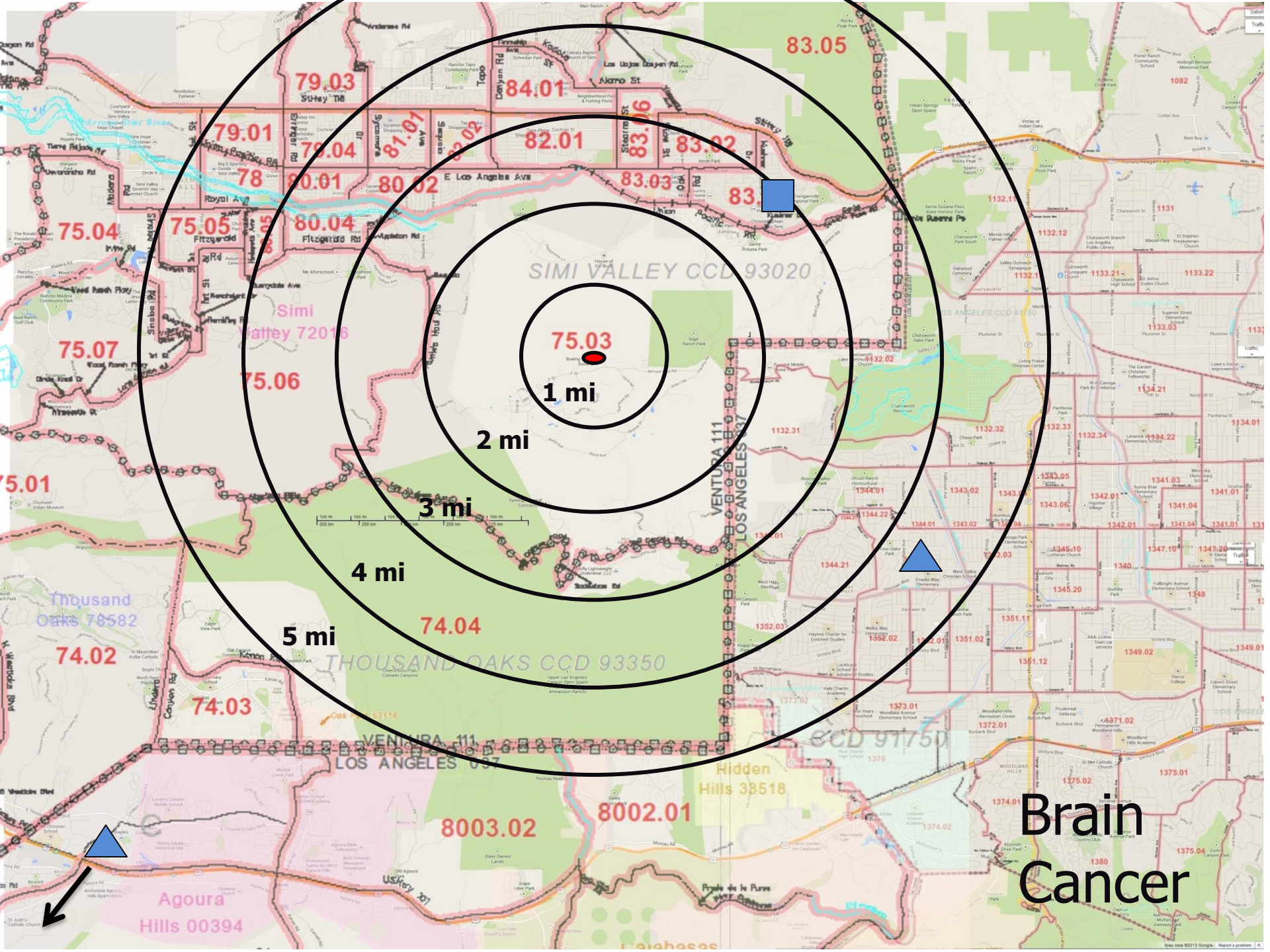
Likely effects of Lifestyle

Some clustering of risk is expected

- Breast and Malignant Melanoma
  - Known strong risk of race and high income/education
- Prostate and Thyroid cancers
  - Known to often not progress; commonly found by asymptomatic screening (PSA, ultrasound) with high access to care (high income/education)
- Lung and Colorectal cancers
  - Strongly determined by habitual factors:
    - Smoking for lung, diet/physical inactivity for colorectal


Brain
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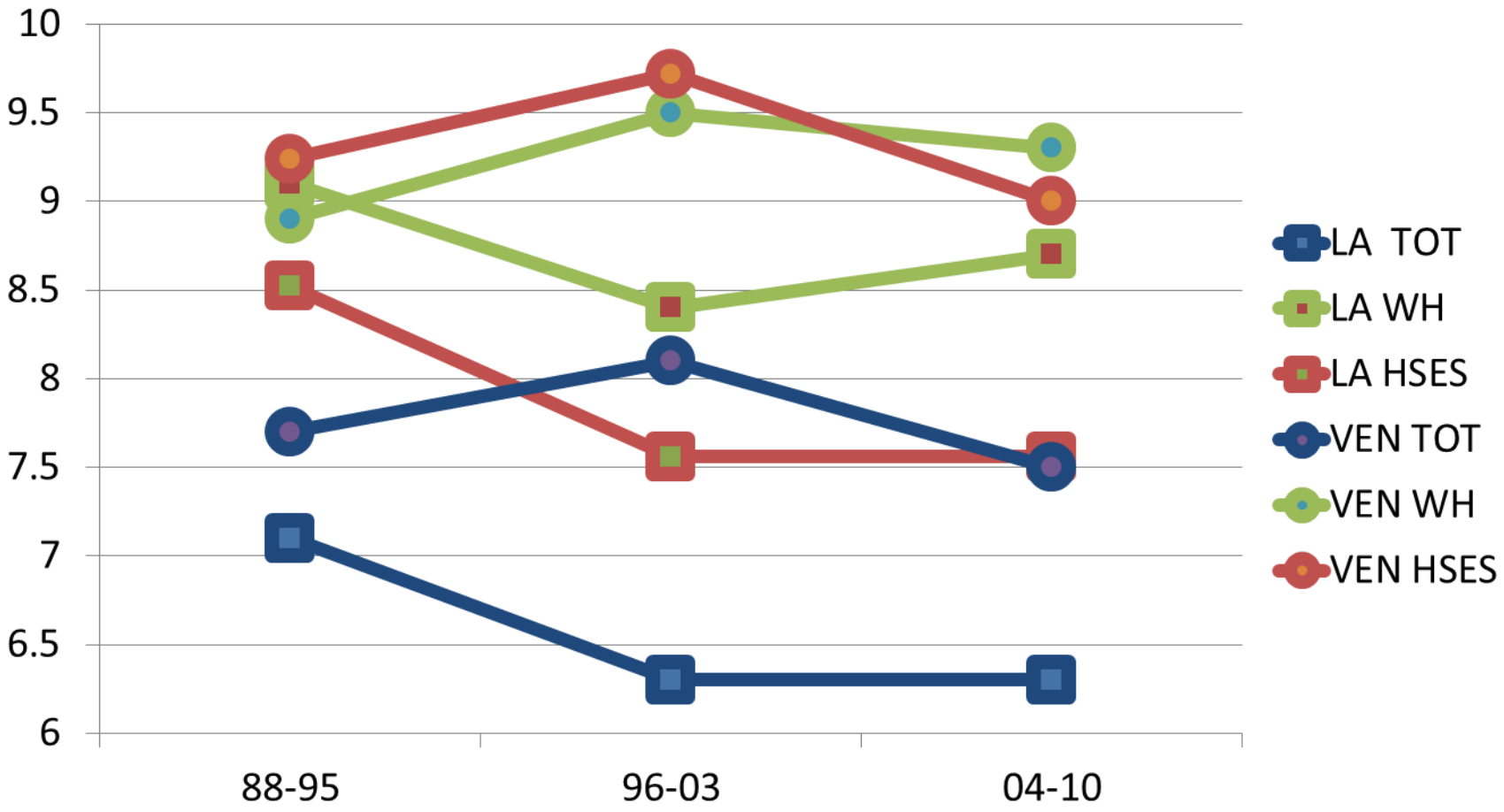
MALE BRAIN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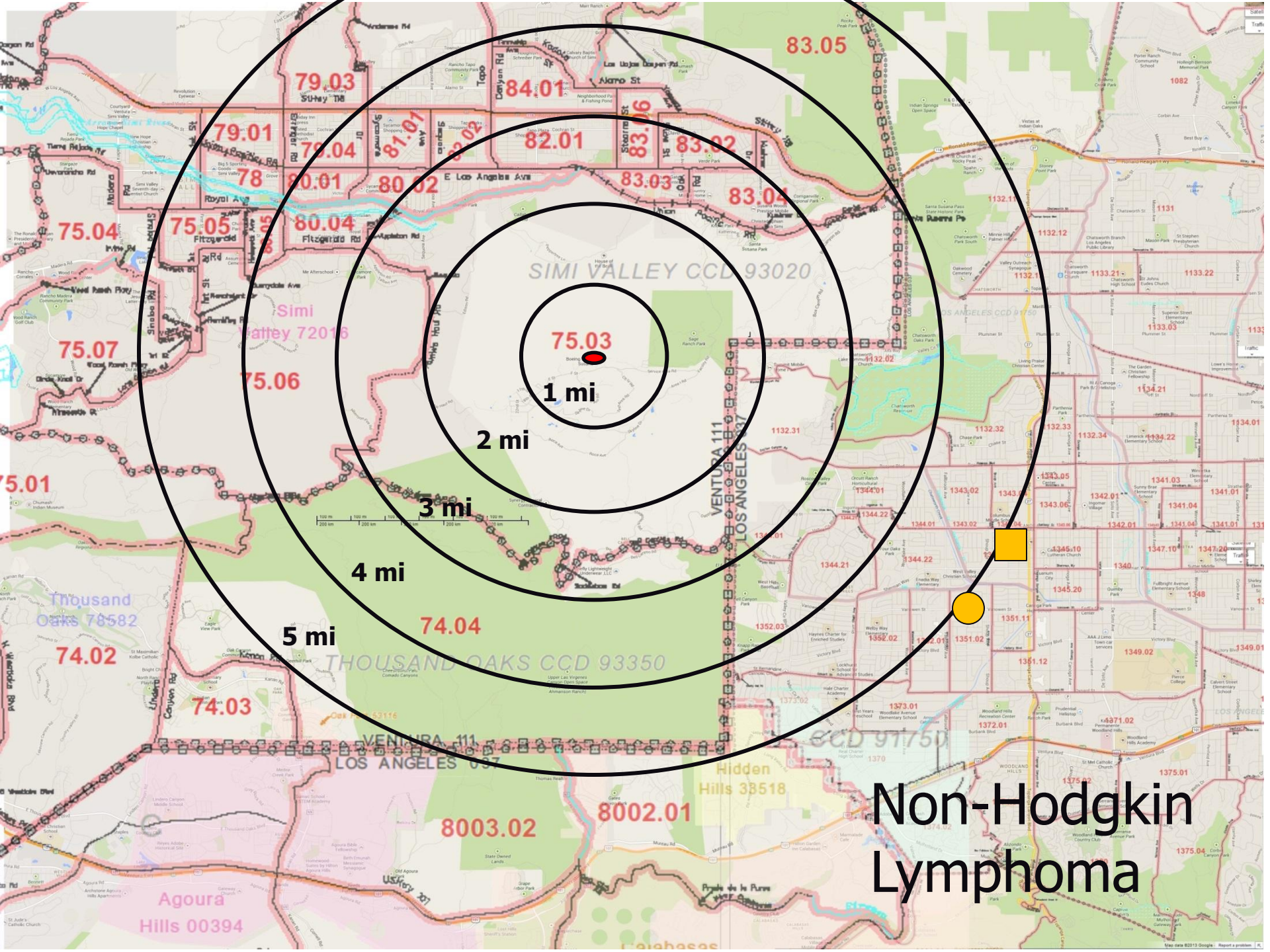
Non-Hodgkin Lymphoma
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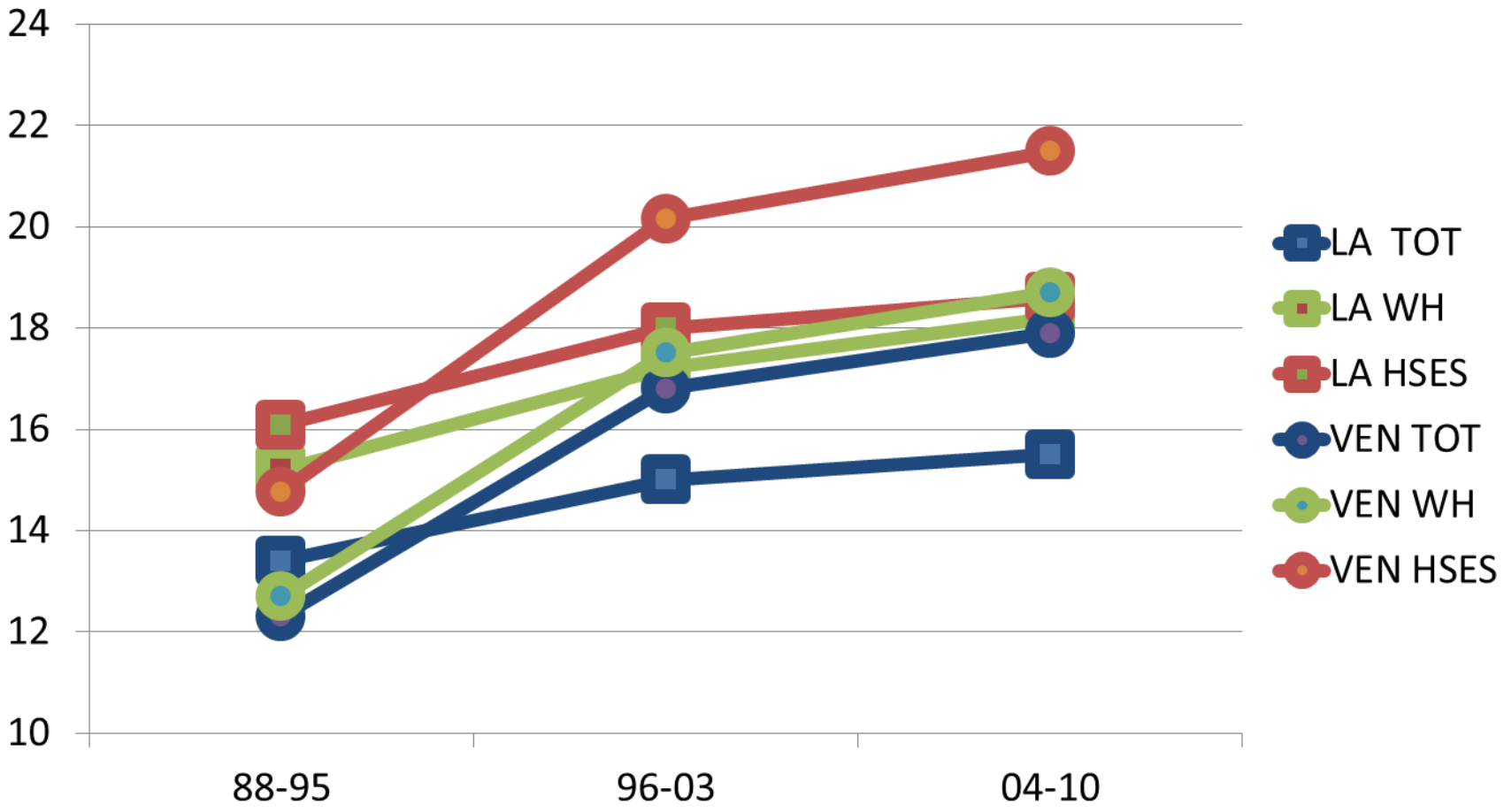
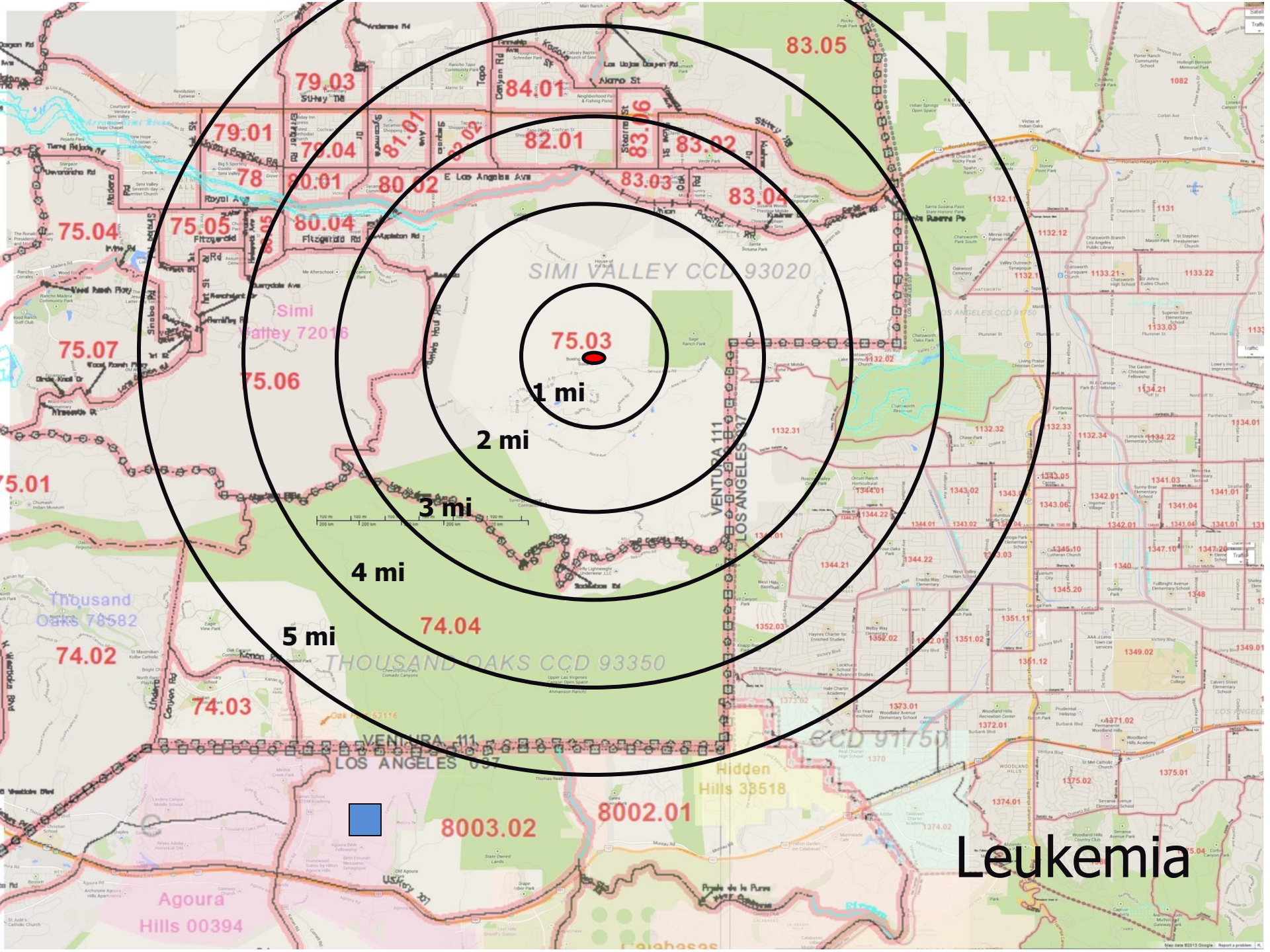
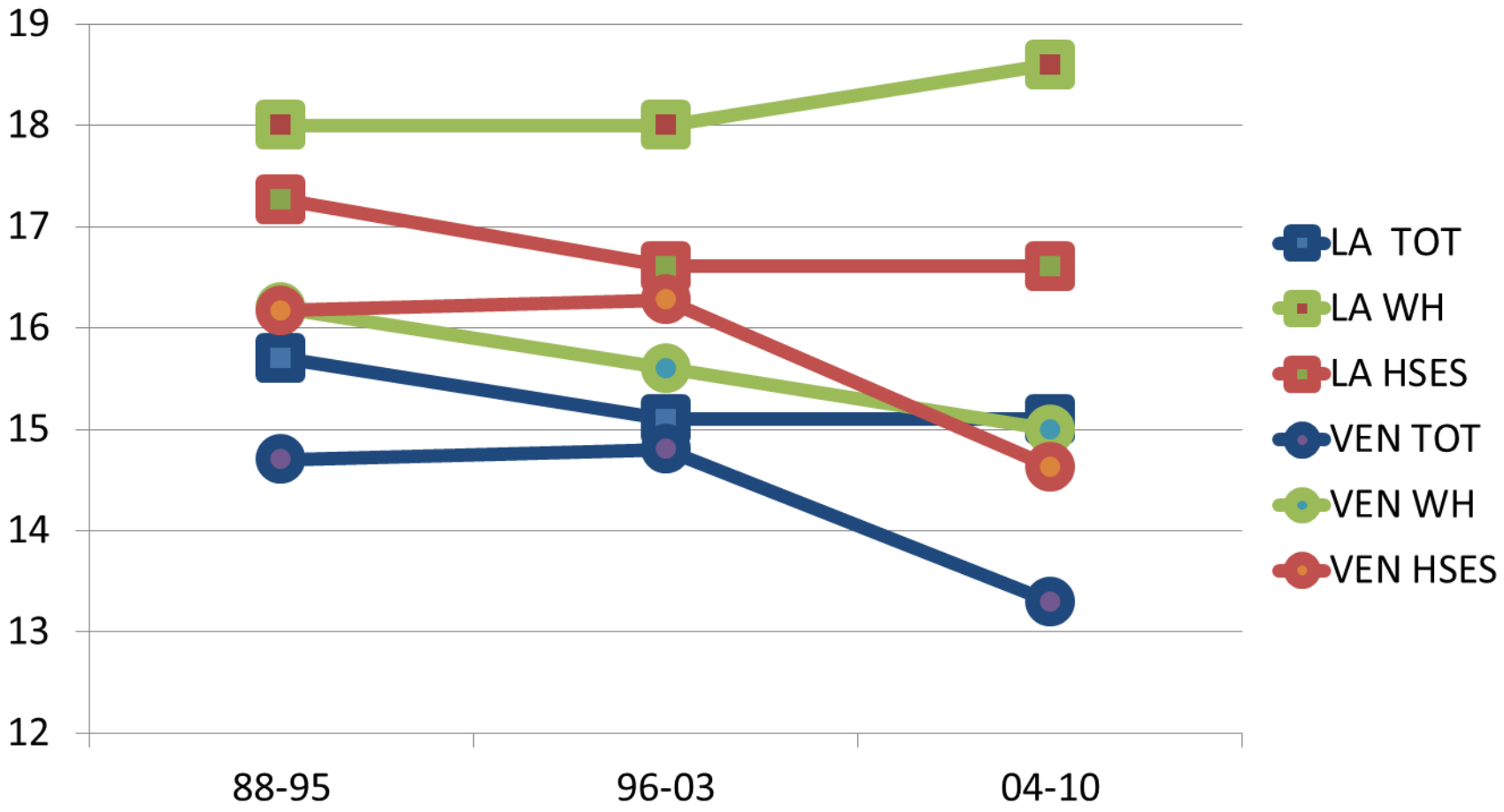
80.01
80.02
83.03
83.04
75.04
75.05
80.04
75.07
75.06
75.01
74.02
74.03
8002.01
8003.02

FEMALE NON-HODGKIN'S LYMPHOMA



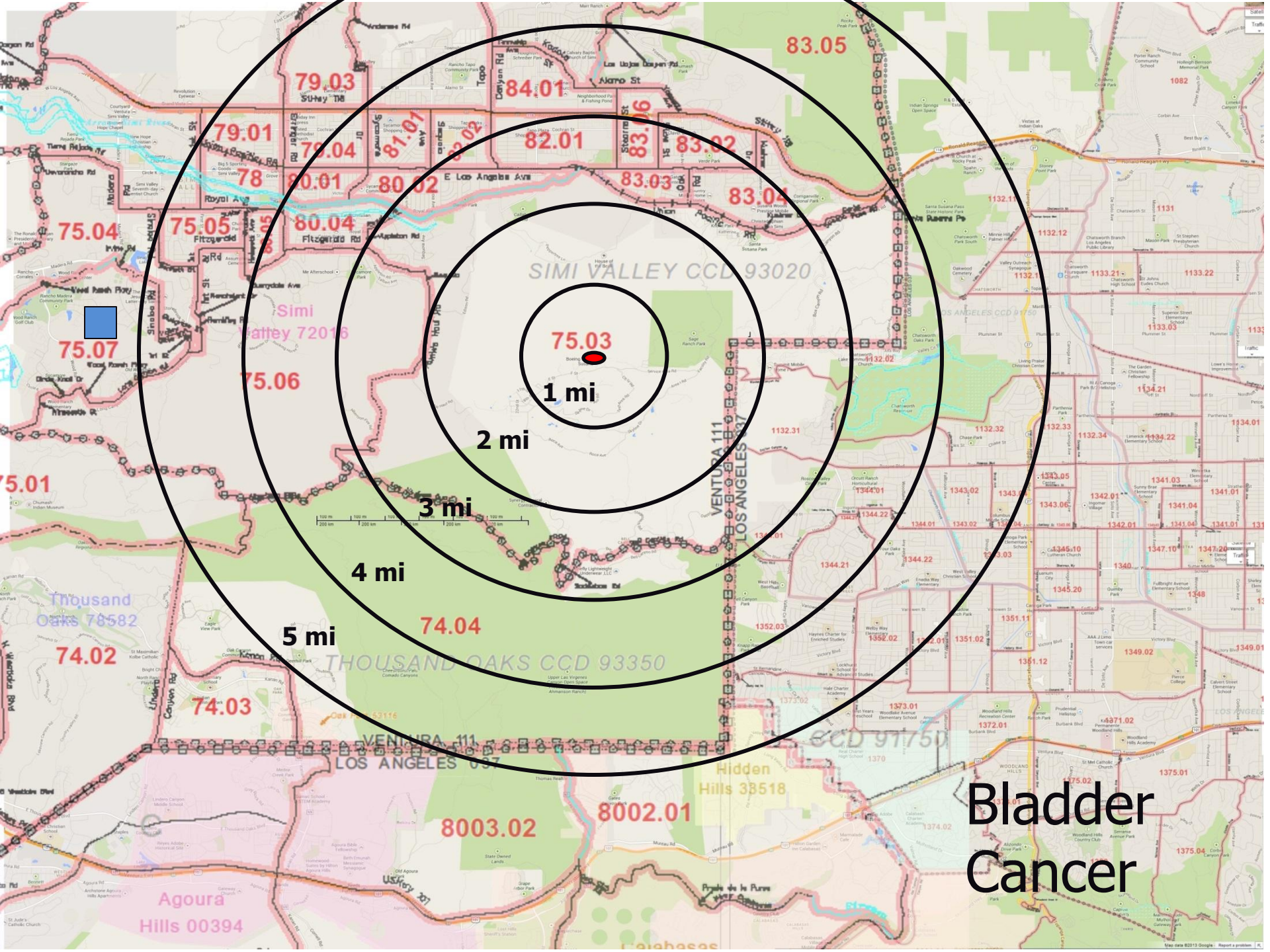

Leukemia
1 mi
2 mi
3 mi
4 mi
5 mi
75.03
74.04
74.02
74.03
75.04
75.05
75.06
75.07
79.01
79.03
78
80.01
80.02
80.04
81.01
82.01
84.01
83.02
83.03
83.04
83.05
8002.01
8003.02
SIMI VALLEY CCD 93020
THOUSAND OAKS CCD 93350
Simi Valley 72016
Thousand Oaks 78582
Hidden Hills 33518
Agoura Hills 00394
VENTURA 111
LOS ANGELES 037
E Los Angeles Ave

MALE LEUKEMIA

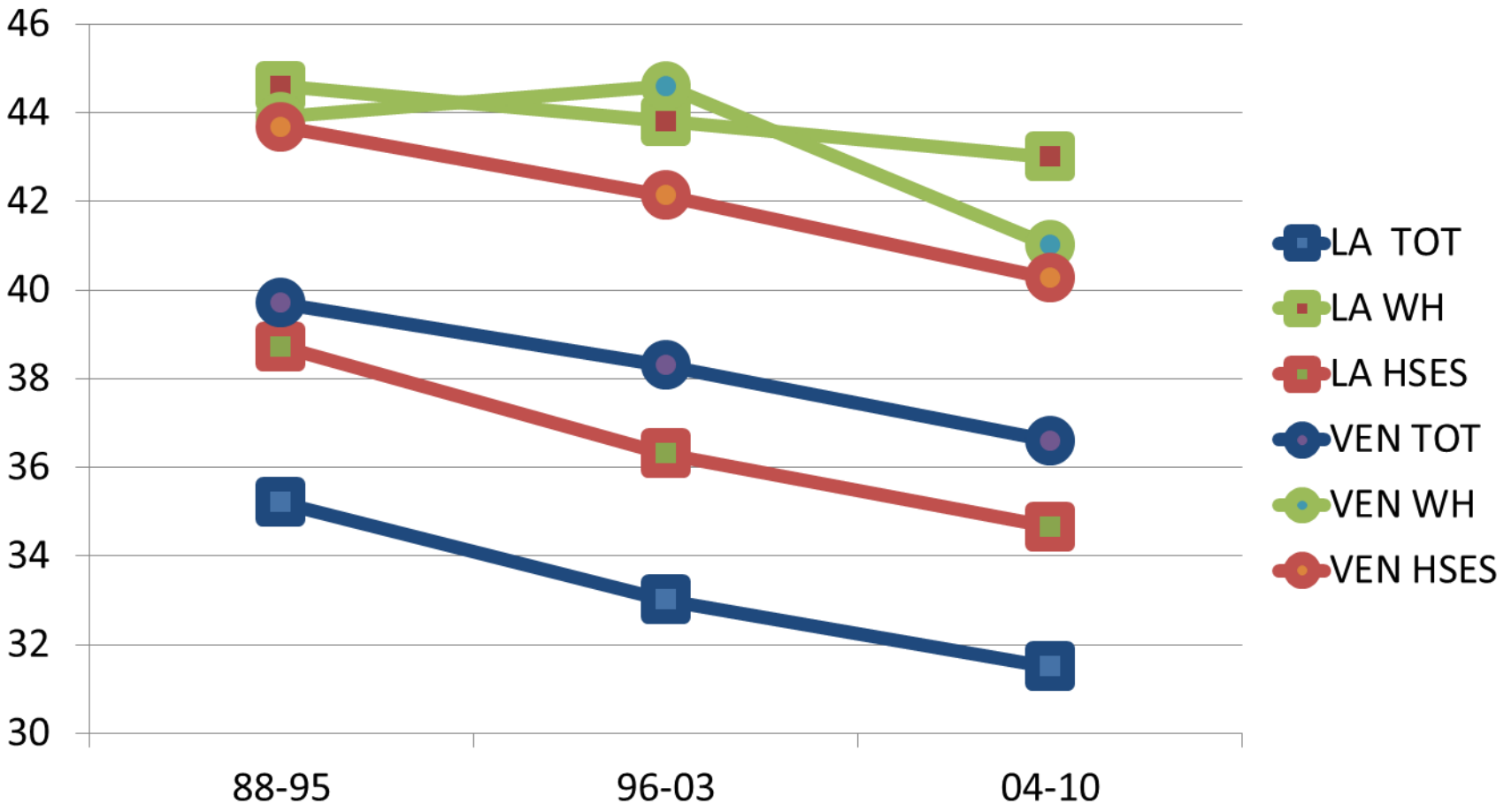


These cancer rubrics oversimplify causal heterogeneity

- Brain: several excess cases are benign, slow-growing tumors with different causes
- Non-Hodgkin lymphoma excess includes at least five different malignancies known to have different causes
- Leukemia excess also is made up of three common and several uncommon varieties
- In each of these, the “high-risk” tracts identified were no more numerous than was expected by chance, and included cases of diverse , most having no known environmental causation


Bladder Cancer
1 mi
2 mi
3 mi
4 mi
5 mi
75.03
75.07
75.06
75.04
75.05
75.01
74.02
74.03
74.04
79.03
79.01
79.04
78
80.01
80.02
80.04
81.01
82.01
84.01
83.05
83.06
83.02
83.03
83.04
8002.01
8003.02
SIMI VALLEY CCD 93020
THOUSAND OAKS CCD 93350
Simi Valley 72016
Thousand Oaks 78582
Agoura Hills 00394
Hidden Hills 33518
VENTURA 111
LOS ANGELES 037
E Los Angeles Ave
Alamo St
Fitzgerald Rd
Royal Ave

MALE BLADDER



Excess of bladder cancer in one tract in 2004-2010

- Extreme finding: RR >4
- Case tumors had the same common histology
- Most residences scattered, but several are within one mile
- The most prevalent cause of bladder cancer is smoking
- Environmental causes are industrial, waterborne arsenic
- Diagnoses were not clustered in time
- The tract is more than 5 miles to the west of SSFL
- Residential community: no known exposure, specifically no high arsenic in tap water, no local industry, no increase in kidney cancer (another arsenic outcome)

- 66% of the cases were >75 at diagnosis, and all but one of those was over 85.
- Census may have undercounted seniors

Neoplasm	"Significant" tract-periods	Observed/ Expected number per tract	Interpretation	Estimated number of CA tracts with that many or more cases
NHL	2 (3 exp. by chance)	8/2.5 12/5.3	No clustering of high-risk tracts No evidence of proximity to SSFL Mixture of cell types, no trend	50-100
Brain	3 (3 exp. by chance)	6/0.9 8/2.3 11/3.5	No clustering of high-risk tracts No consistent proximity to SSFL Mixture of cell types, no trend	10-50
Leukemia	1 (3 exp. by chance)	7/1.3	No clustering of high risk tracts No evidence of proximity to SSFL Mixture of cell types, no trend	10
Bladder	1 (3 exp. by chance)	11/2.5	No clustering of high risk tracts No evidence of proximity to SSFL No evidence of carcinogens Preponderance of elderly cases ? Smoking, census error	1-2

Conclusion

- It is not possible to completely rule out any offsite carcinogenic effects from SSFL

- No evidence of measureable offsite cancer causation occurring as a result of emissions from the SSFL was found.

- Further, no evidence of any cancer causation by any environmental factor was found.

Cancer Occurrence in Offsite Neighborhoods Near the Santa Susana Field Laboratory

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

Reasons for Concern

- Intensive testing of rocket fuels
- Usage of solvents, chemicals, metals, radionuclides
- Presumed carcinogen contamination
- Lymphomas and lung cancers among workers

- History of accidents, spills and releases
- Possible dispersion offsite by air and water

- Safety conditions relaxed, inadequate monitoring
- History of secrecy and non-responsiveness

Reasons for Scientific skepticism

- Lack of any clear risk found by previous searches

Previous searches were Inconclusive

Study	Periods	Locations	Cancers	Conclusions
Perkins-Wright	1978-82 1983-87	5 LA Tracts	11 Sites	Single Tract Bladder 1.5 83-7 Overall: Inconclusive
Coye-Goldman	1973-82 1983-88 1988-89	Aggregated Tracts by County	14 Sites aggregated	Bladder 1.3 83-88 LA tracts Lung 1.1 88-89 VEN Tracts Suspect Confounding
Nasseri	1988-95	Aggregated VEN Co Tracts	12 Sites aggregated	No positive findings
Morgenstern	1988-95 1996-02	Aggregated LA, VEN Blocks in 3 belts by Distance	9 Sites aggregated	Lung 1.1 Middle Belt 88-95 Melanoma 1.2 Middle Belt 96-02 Thyroid ? Proximity effect Aerodigestive? Proximity effect

Problems with Previous searches

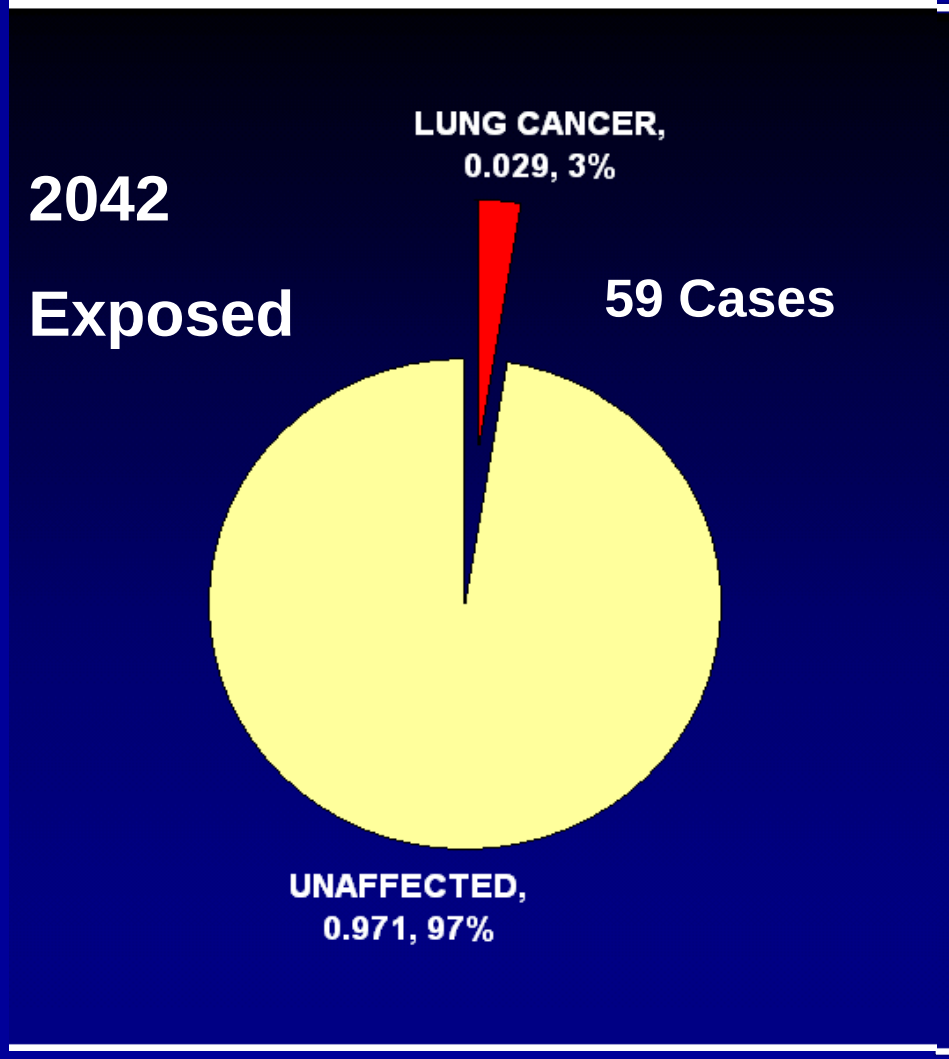
Study	Problems
Perkins-Wright	Multiple comparisons without adjustment Weak associations Bias: response to cluster report Confounded by Race and Social Class
Coye-Goldman	Multiple comparisons without adjustment Weak associations Aggregation obfuscates location Confounded by Social Class
Nasseri	Multiple comparisons without adjustment Aggregation obfuscates location Low statistical power Confounded by Social Class
Morgenstern	Multiple comparisons without adjustment Weak associations Aggregation obfuscates location; Distance is not dose Confounding by Social Class

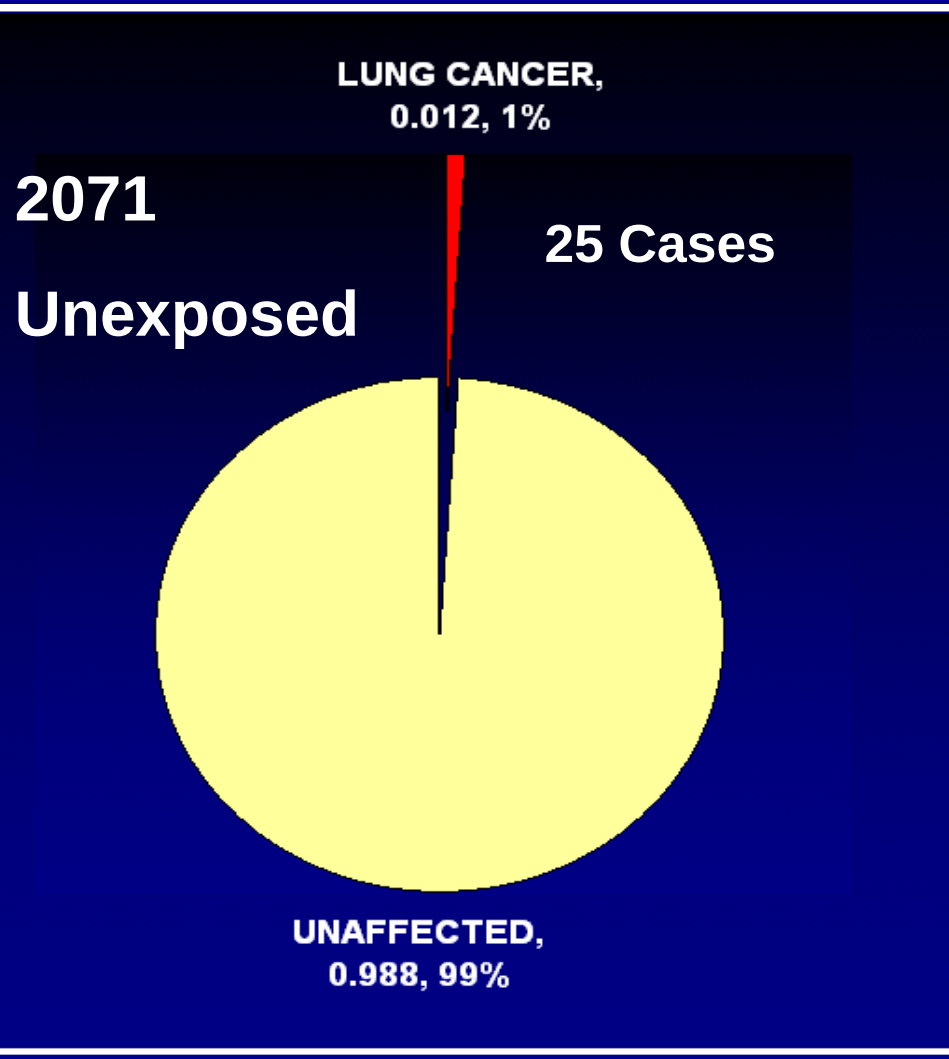
Reasons for Scientific skepticism

- Ambiguous and controversial exposure estimates
- The presence of a carcinogen, especially when technology permits detection of very low levels, does not necessarily constitute a major hazard
- High dose levels are needed to produce a measurable cancer excess

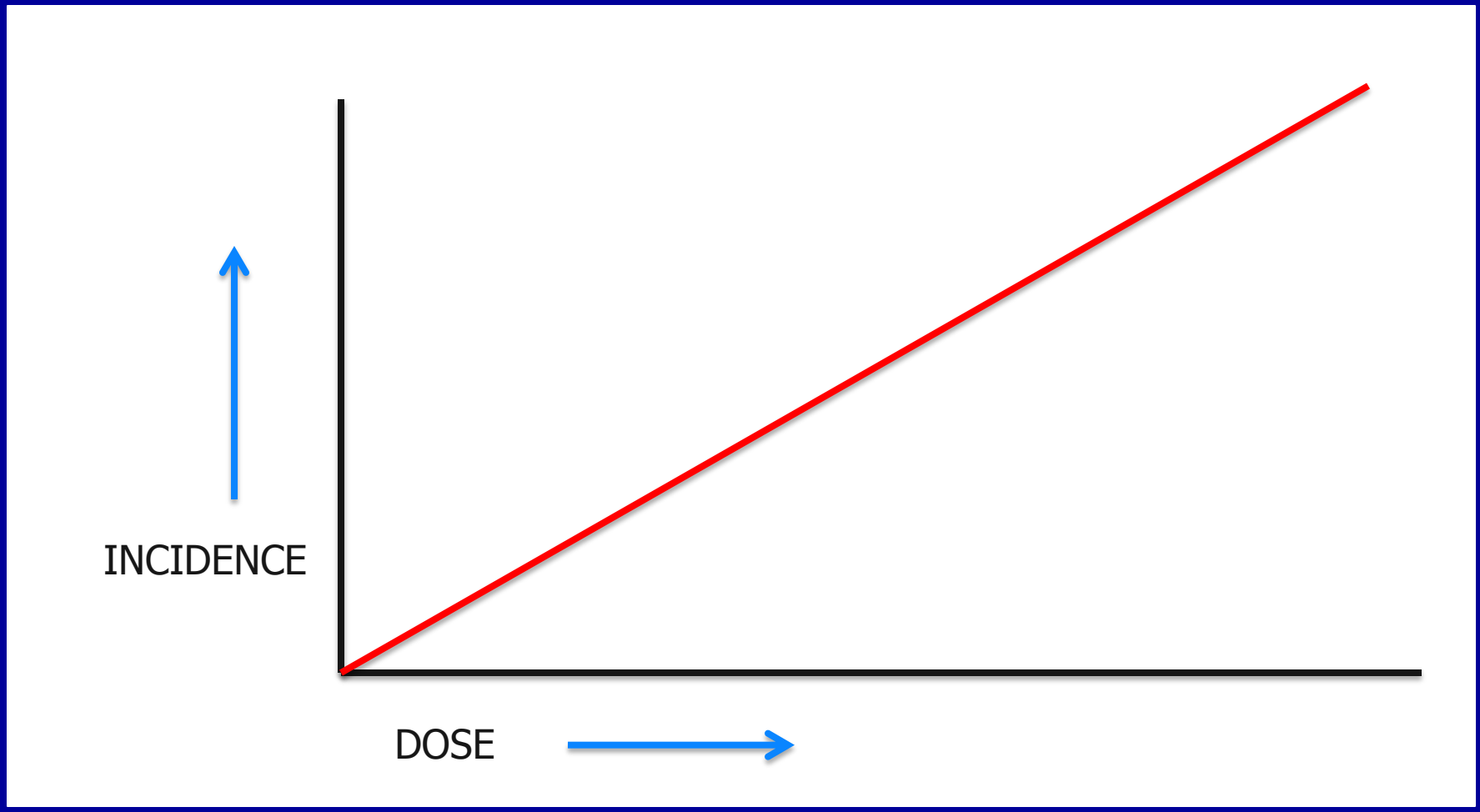
Effect of Industrial exposure to hexavalent chromium:

Mean level 790 micrograms/cubic meter of air





Carcinogenesis increases linearly with dose

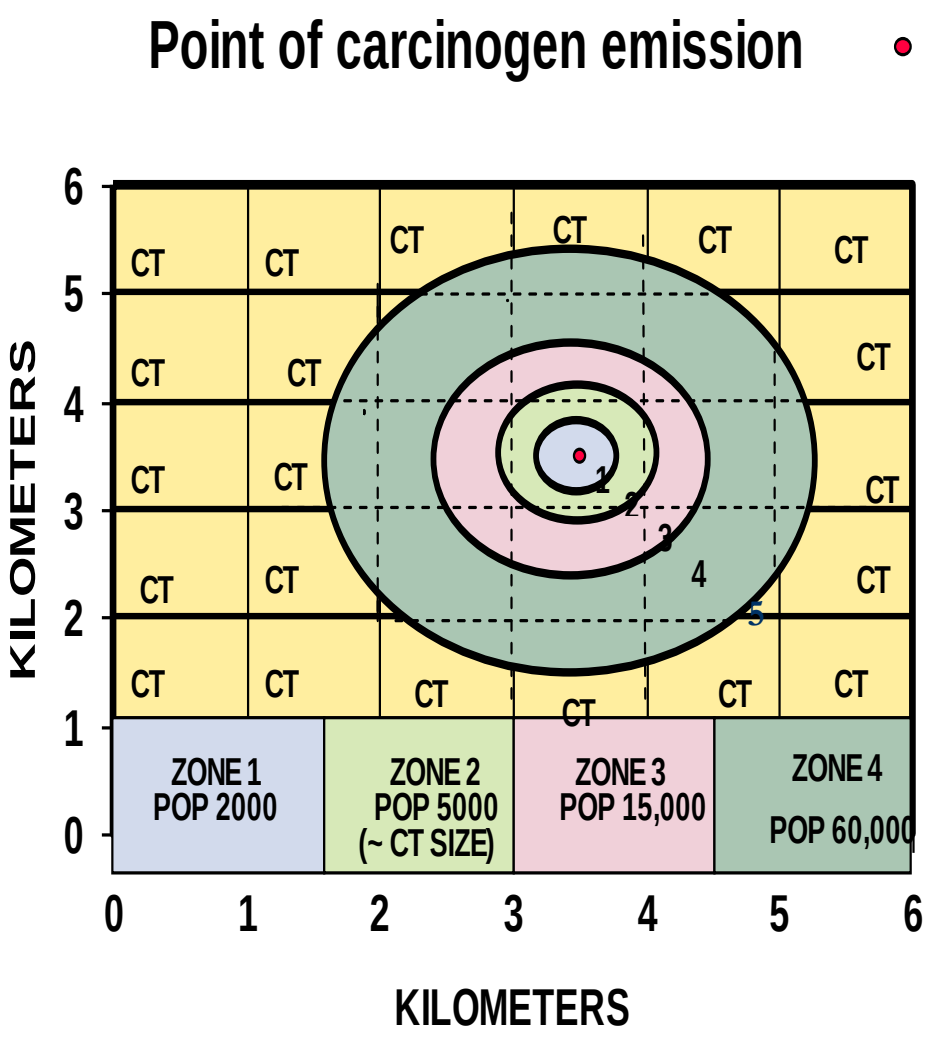


Projected effect of Strongest Community Exposure to Hexavalent Chromium

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

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

Dispersion of carcinogen emissions



Emission dose level to individuals is variable

- Chemicals rapidly disperse into air/water
- As the distance from the site increases:
  - More people are exposed
  - Exposure dose is lower
  - Dispersion results in dilution: dose is inversely proportional to distance

Impact of point emission if dose is thought to double the 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

No more than a single additional case would be expected

Reasons for Scientific skepticism

- Absence of historical precedents

Precedents: Environmental cancer clusters do occur (other than occupational risks)

Fallon, NV: 2000-2001, 16 ALL cases occurred, 0.3 expected

Host to thousands of diverse visitors

Libby, MT: Multiple cases of mesothelioma in a small town

Tailings of asbestos-containing vermiculite

Cappadocia, Turkey: Cluster of cases of mesothelioma

Greece, Italy, New Caledonia: Clusters of mesothelioma

From building materials or whitewash with asbestos

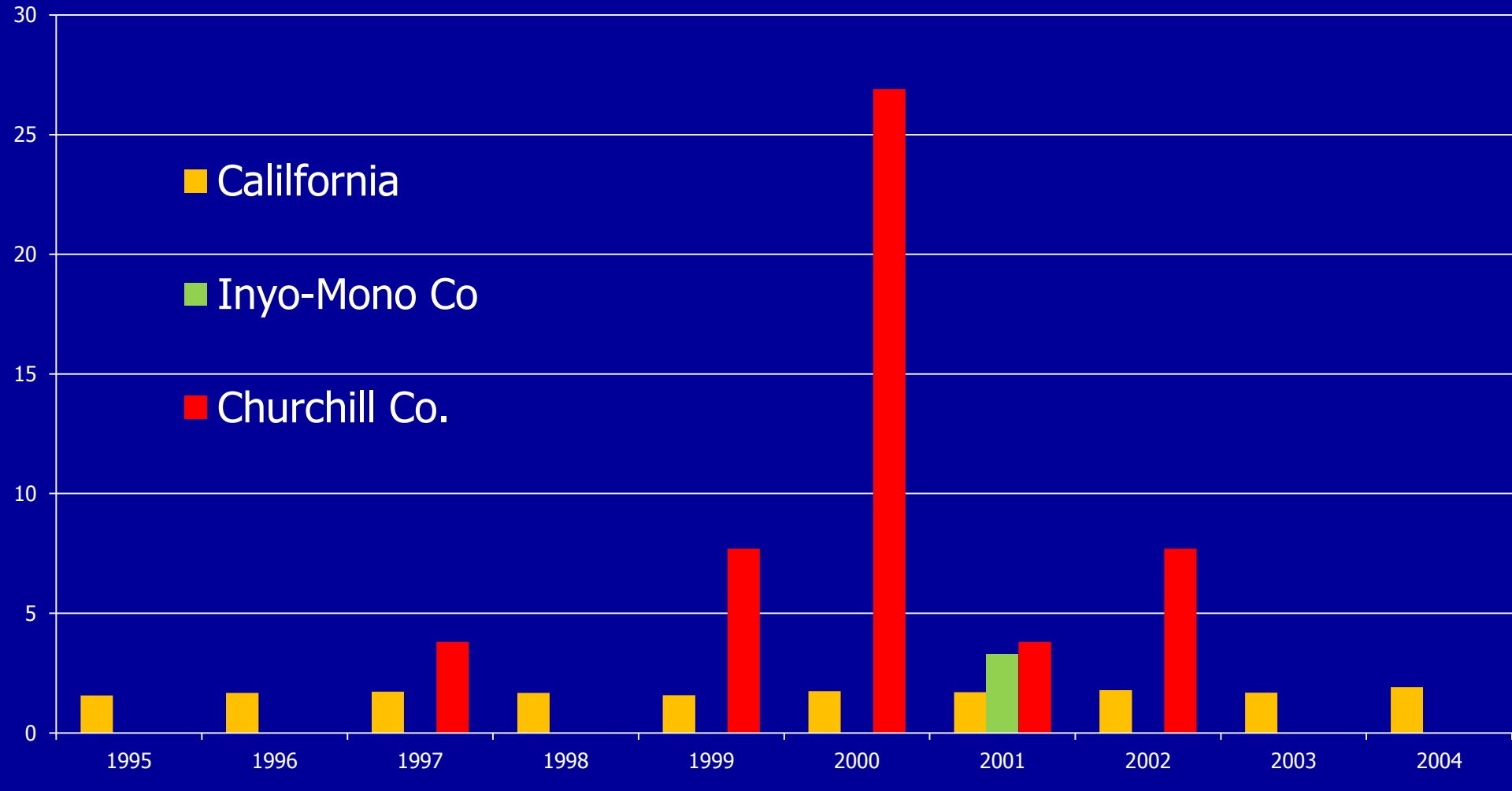
Ukraine/Belorus: Localized thyroid cancer in young persons

From nuclear fallout

Taiwan, Chile, Argentina, Bangladesh: Localized bladder cancer

Groundwater contaminated with natural arsenic deposits

Churchill County (Fallon) ALL Cluster Rate compared to California Rates



If dose is usually weak, why are “clusters” found?
Two different circumstances

Strong direct exposure, highly targeted at close quarters

Household asbestos, person to person virus

Sufficient dose by *short-term but intense* exposure

Sufficient dose to ***single families or compounds***

Strong indirect or distant exposure, disseminated by air/water/soil

Chernobyl, waterborne arsenic, asbestos tailings

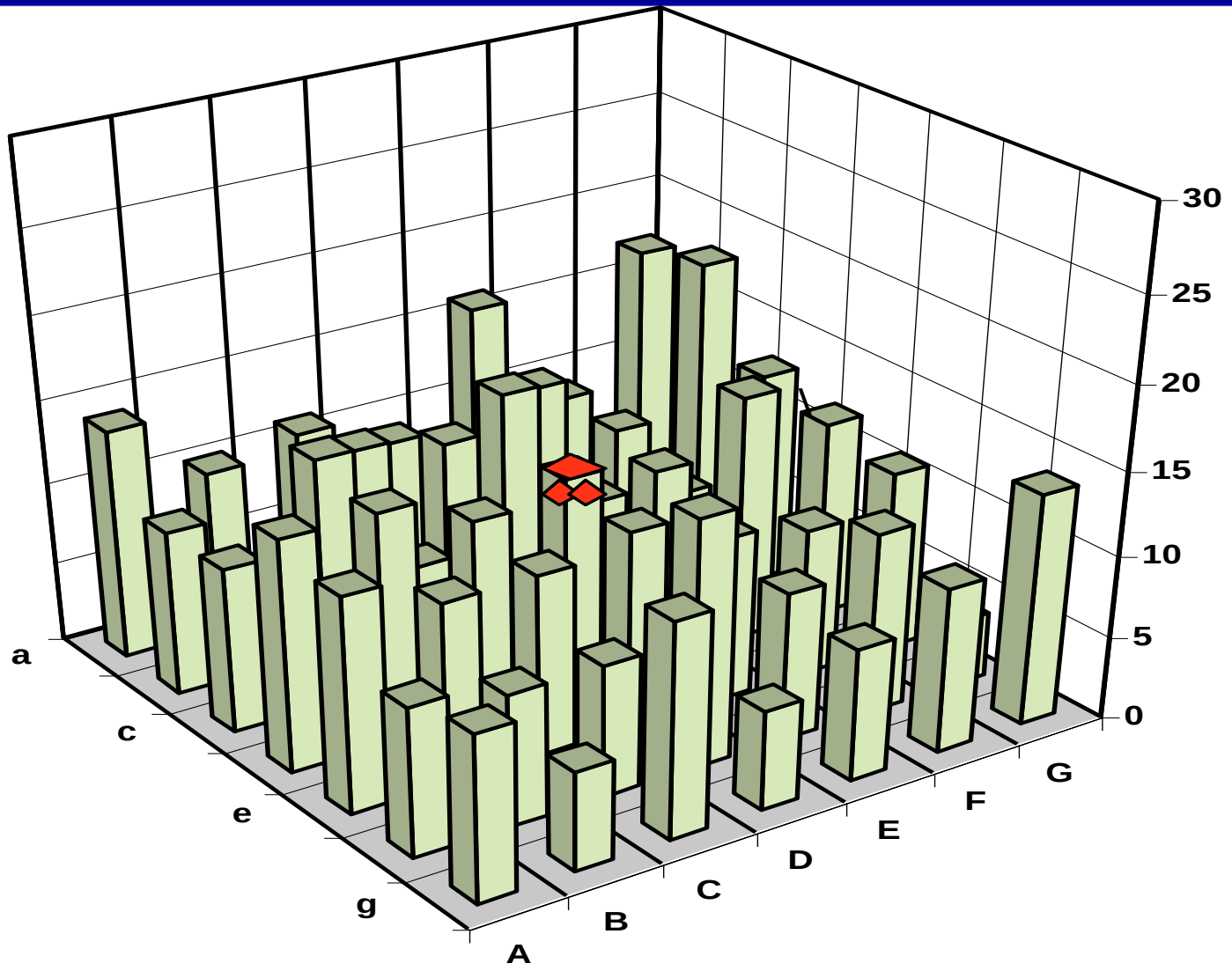
Sufficient dose by ***continuous cumulative*** exposure over the long-term

Sufficient dose disseminated to ***multiple adjacent localities***

Weak exposure

Rare cancers undetectable, common ones lost within random variation

If the cancer is not rare, the usual cases outnumber the added ones (and vary in number by chance)



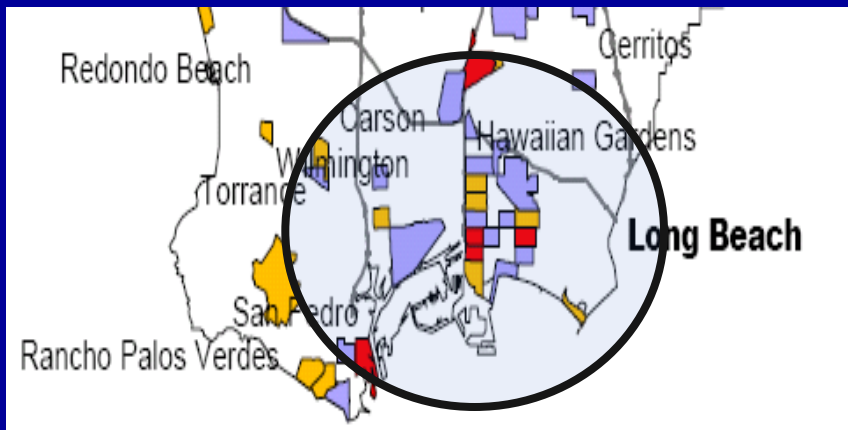
The Challenge

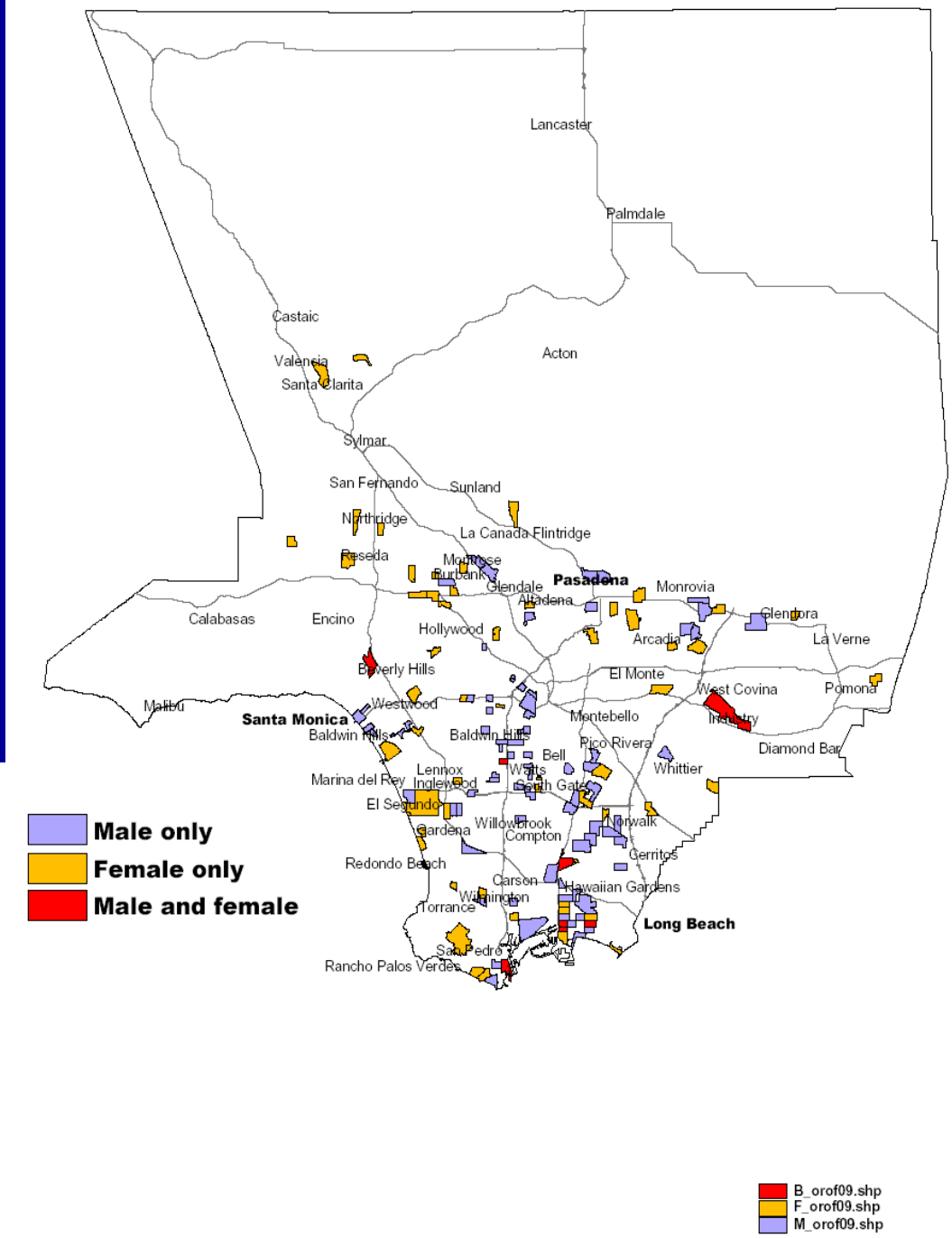
- Some offside residents may have been exposed to carcinogens at ***some*** dose
- They may well have ***some*** added cancer risk.
- The challenge is to see if a ***measureable and unambiguous*** increase in risk has been produced.
- Must examine ***individual*** neoplasms and ***individual*** tracts

To demonstrate an unambiguous association:

- Increase must be at least 50%, a relative risk of 1.5 (there are too many alternative explanations for a weaker link)
- Chance must be excluded
- Adjacent tracts (localities) offsite should have high exposure in common
- Here is a local example

Carcinoma of the Oropharynx





Steps in Linking Environmental Carcinogenicity to a Particular Locality

1. Assess the likelihood that any association between cancer incidence and a residential locality could be explained ***by chance***

2. Ensure that any such association cannot be explained by ***a bias***

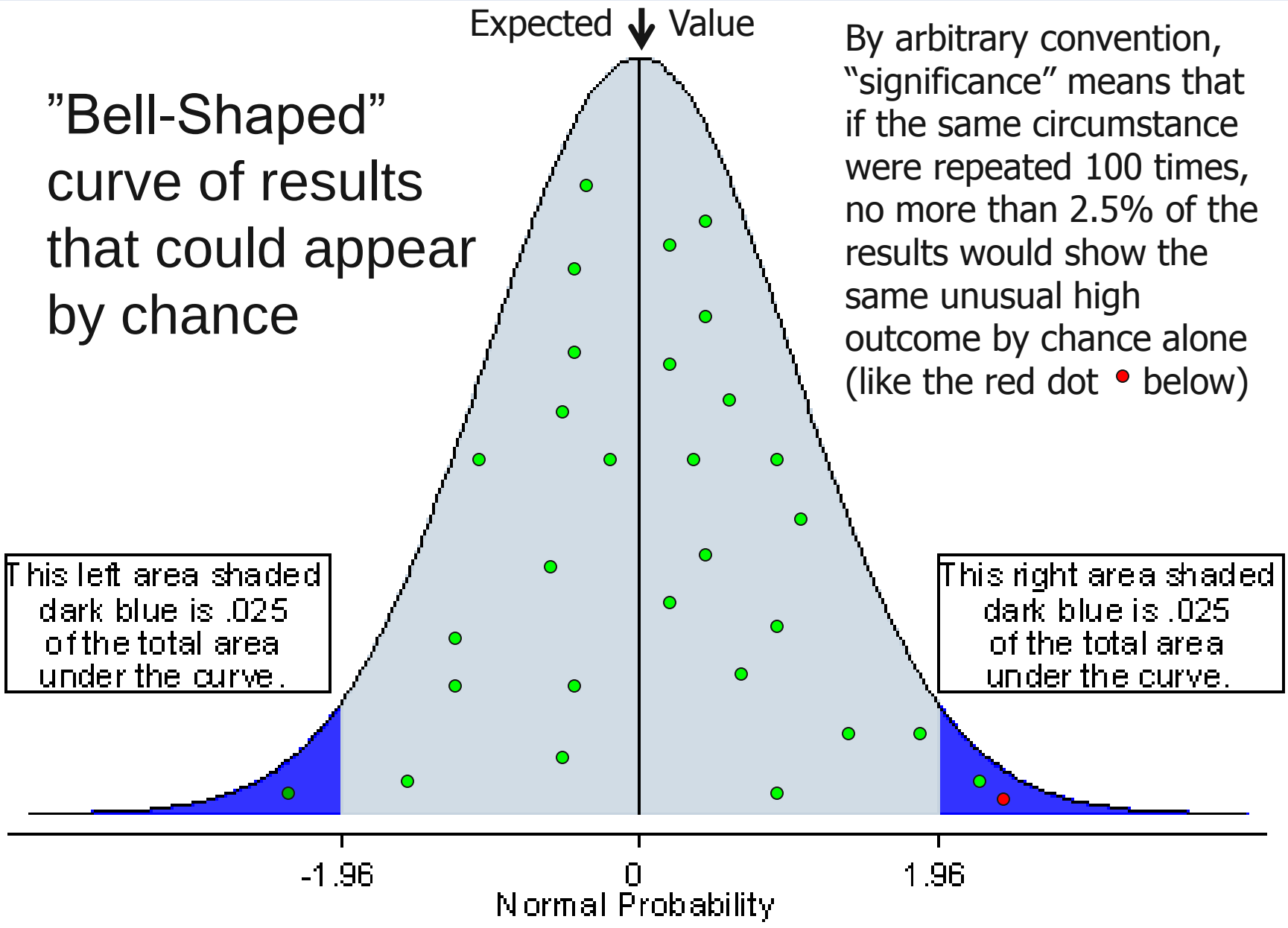
3. Ensure that any such association cannot be explained by the ***characteristics of local residents?***.

1. Assessing chance

- The conventional method is to identify by computation any excess difference which is statistically significant at the level of 95% confidence

- Method is based on the appropriate distribution of random possible results—chance can never be ruled out, just quantified at an arbitrary level.

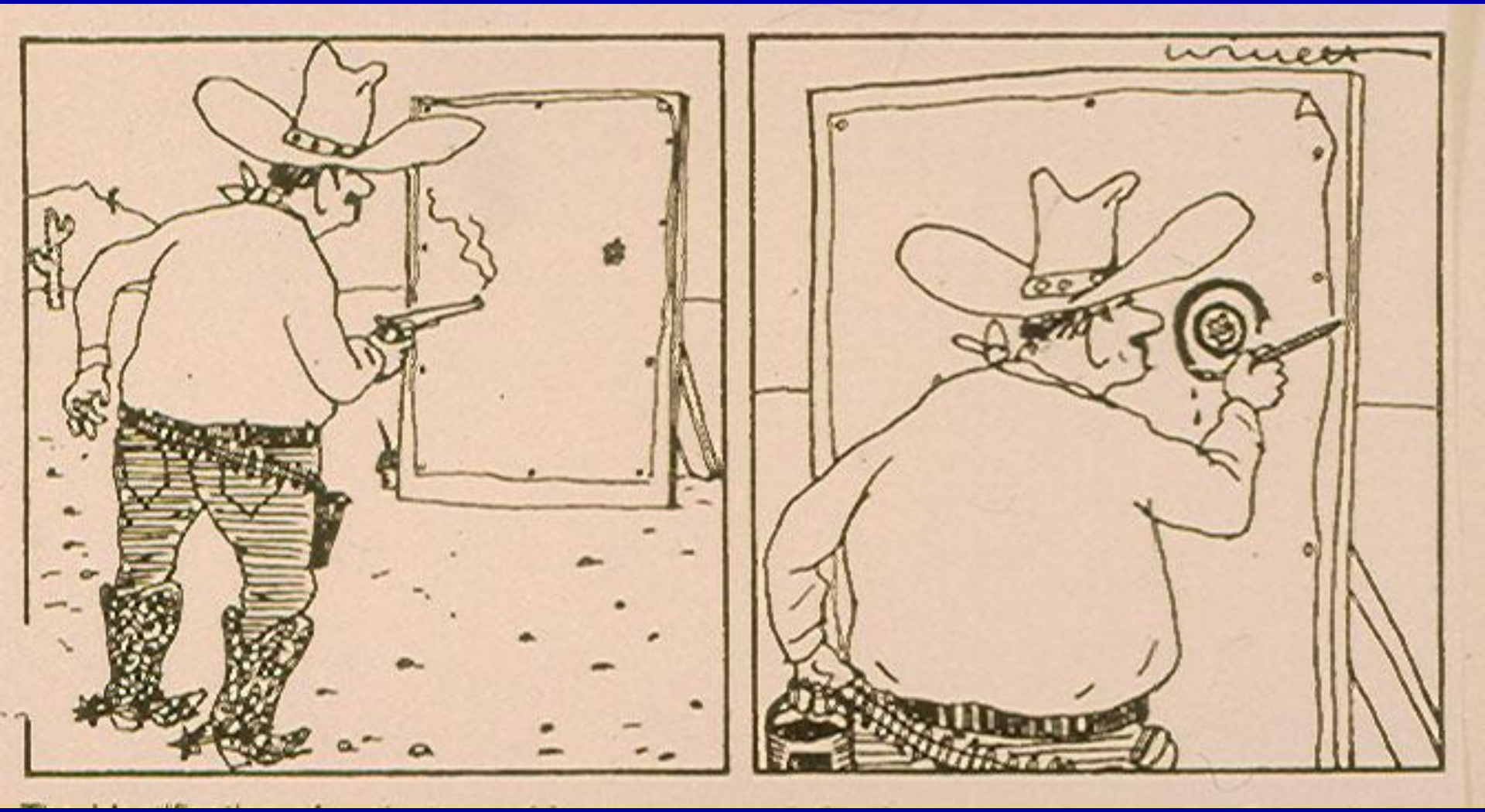
- We perform this exercise to screen tract/cancers


Expected Value
"Bell-Shaped" curve of results that could appear by chance
By arbitrary convention, "significance" means that if the same circumstance were repeated 100 times, no more than 2.5% of the results would show the same unusual high outcome by chance alone (like the red dot • below)
This left area shaded dark blue is .025 of the total area under the curve.
This right area shaded dark blue is .025 of the total area under the curve.
-1.96
0
1.96
Normal Probability

2. Bias comes in several forms

- Registry errors: unlikely, because ascertainment is very complete and in effect done blindly to place, age, race, etc.
- Census errors: underestimation of the number of persons, especially high risk persons, makes the excess look too large. This is a common problem in rapidly changing neighborhoods
- Texas sharpshooting: If investigation is initiated by a reported “cluster”, we already know the rate is not going to be low, and the statistical test is meaningless

“TEXAS SHARPSHOOTING”



AIM, SHOOT, AND ONLY THEN--
DRAW THE TARGET

Multiple Comparisons

- .
- The more cancers, periods, and tracts tried, the more likely are extreme findings

- Solution: instead of relying upon “significance” for each tract/cancer, we screen all tract-cancer combinations by significance, then calculate how often each extreme result could occur by chance among all CA tracts

- The following Poisson table gives this percentage for selected observed numbers given the number expected.

Percent of searches expected to find N or more cases observed according to the mean expected

Mean expected	1 Obs	2 Obs	3 Obs	4 Obs	5 Obs	6 Obs	7 Obs	8 Obs	9 Obs	10 Obs	11 Obs	12 Obs
1	63.2%	26.4%	8.0%	1.9%	0.4%	0.1%	0.01%					
2		59.3%	32.2%	14.2%	5.2%	1.6%	0.4%	0.1%	0.02%	0.01%		
3			58.4%	36.0%	19.2%	9.1%	3.4%	1.2%	0.4%	0.1%	0.03%	
4				56.7%	37.1%	21.5%	11.1%	5.1%	2.1%	0.8%	0.3%	0.1%
5					55.8%	38.3%	23.7%	13.3%	6.8%	3.2%	1.3%	0.5%
6						55.4%	39.3%	25.5%	15.2%	8.3%	4.2%	1.9%
7							54.9%	40.0%	27.0%	16.9%	9.8%	5.3%
8								54.8%	40.8%	28.4%	18.4%	11.3%
9									54.3%	41.1%	29.2%	19.5%
10										45.3%	32.8%	21.4%

For example:

- When 2 cases are expected and 6 are observed, 1.6% of localities of that size would find as many or more than 6 by chance.

- That means in160 California localities

3. Explore alternative explanations for any cluster: ***They are important considerations***

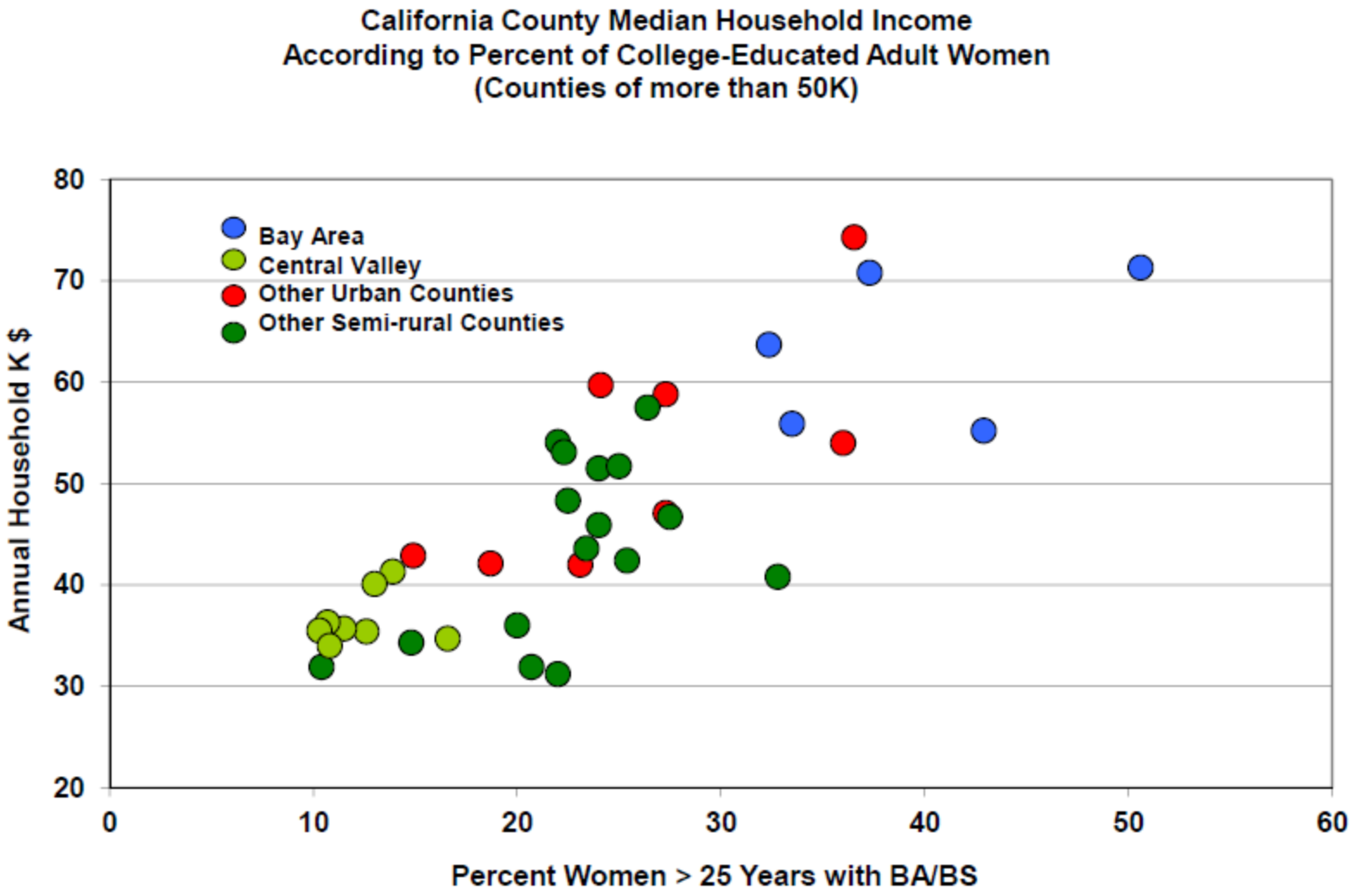
- Other known causes of that particular cancer
  - Rarely measureable by locality: example--smoking
- Race/Ethnicity, (approximate by tract)
  - Measureable surrogate causes like—skin color
- Education and Income (approximate by tract)
  - Measureable surrogate for causes like—sexual and reproductive history

A rough commonality of lifestyle characterizes the residents of any neighborhood

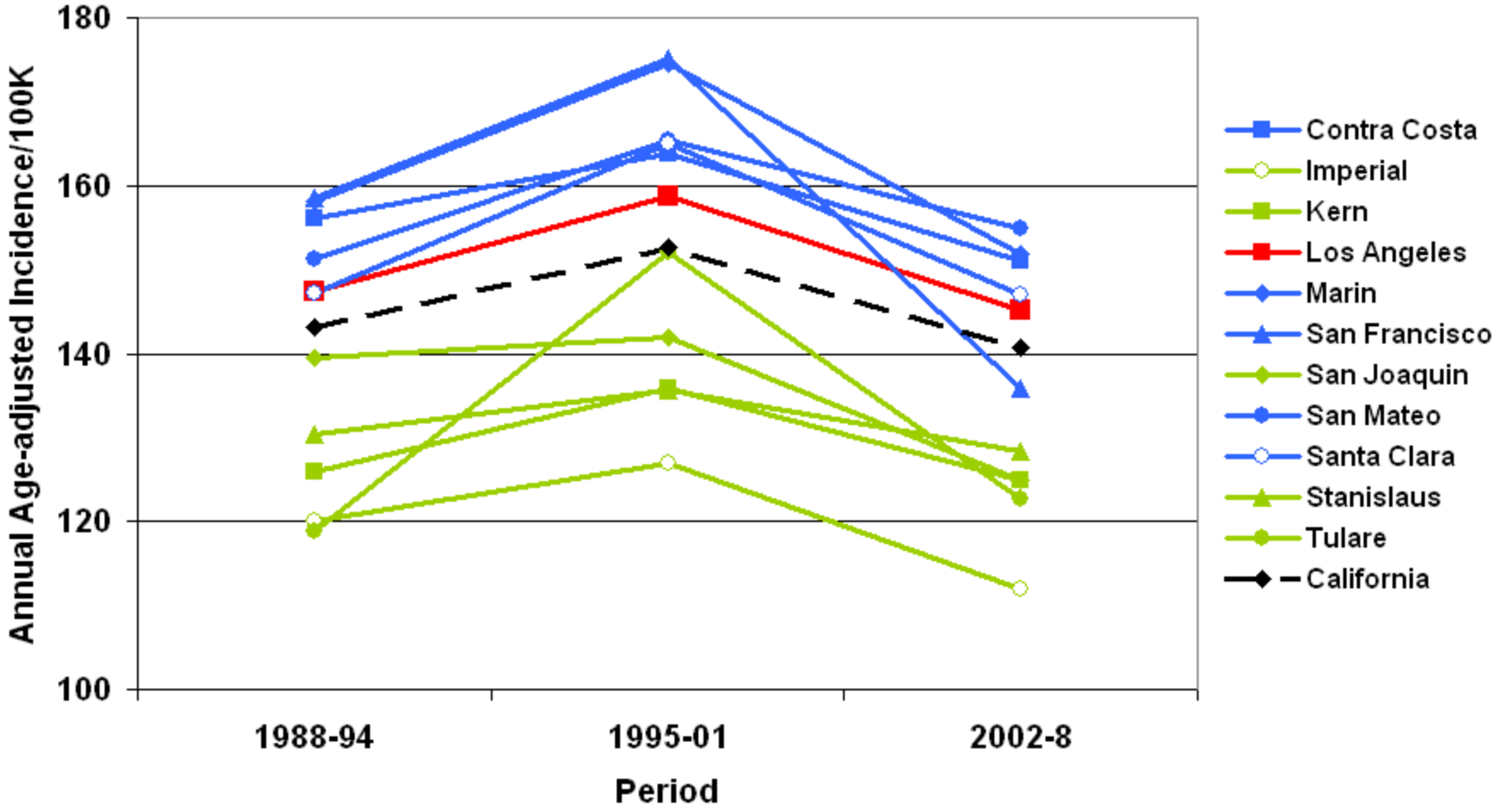
- Neighborhood choice is personal and particular
  - Preferred location, location, location
- Thus birds of a feather tend to flock together

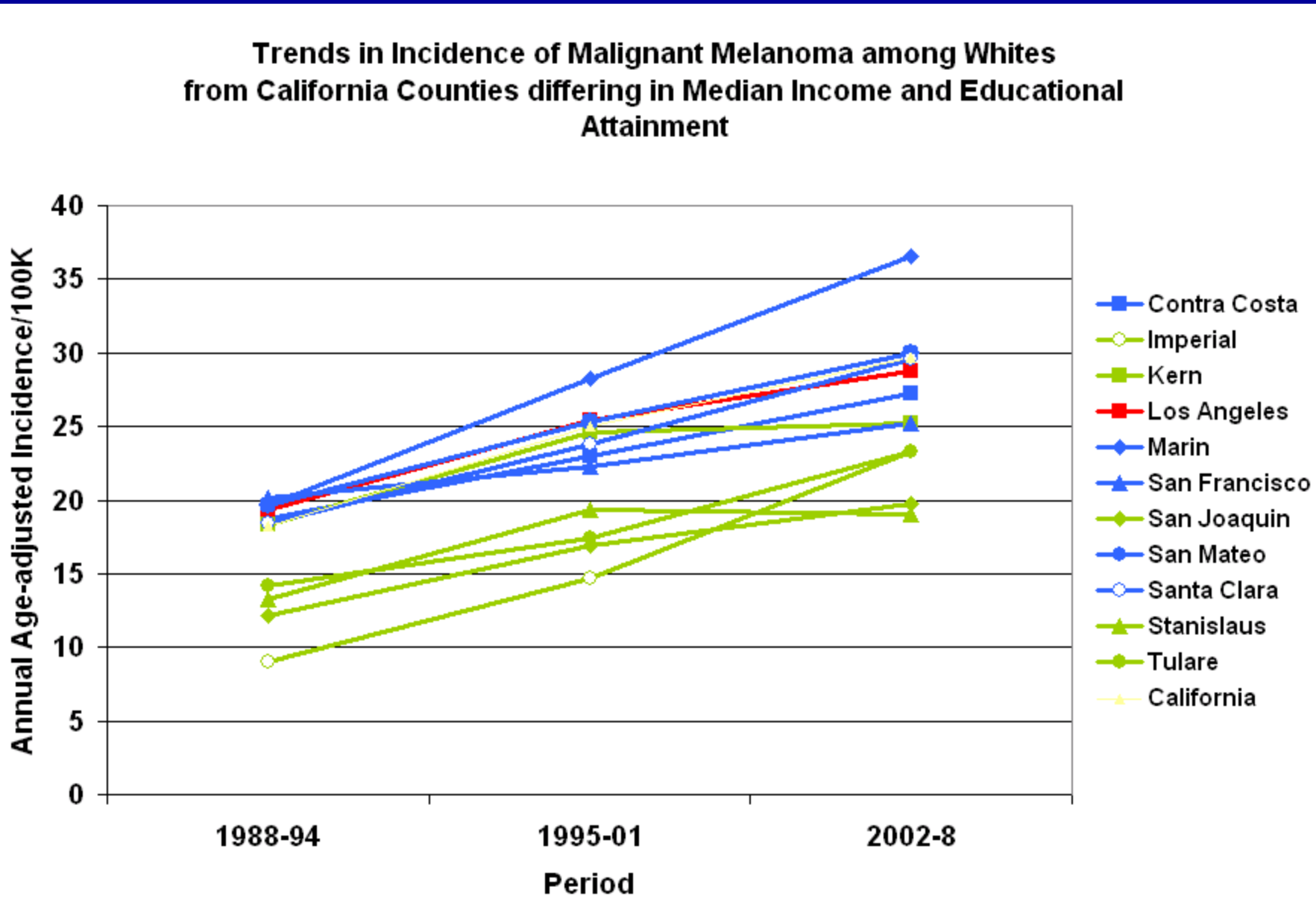
- Obvious on both County and Census tract levels
  - Ethnicity, education, friends, habits, occupation

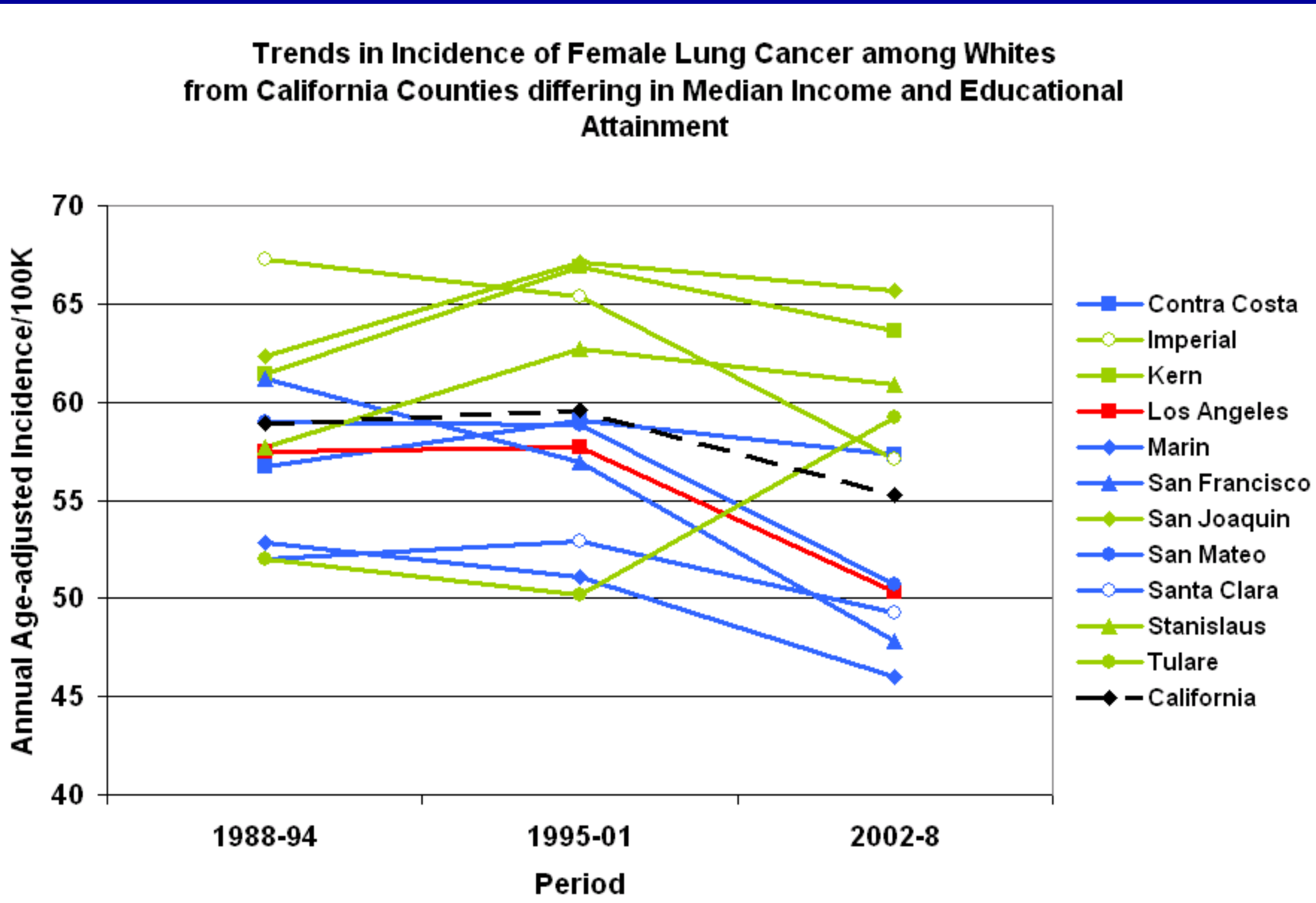
- Shows up in cancer patterns


California County Median Household Income
According to Percent of College-Educated Adult Women
(Counties of more than 50K)
Bay Area
Central Valley
Other Urban Counties
Other Semi-rural Counties
Annual Household K $
80
70
60
50
40
30
20
0
10
20
30
40
50
60
Percent Women > 25 Years with BA/BS

Trends in Incidence of Breast Cancer among White Females from California Counties differing in Median Income and Educational Attainment



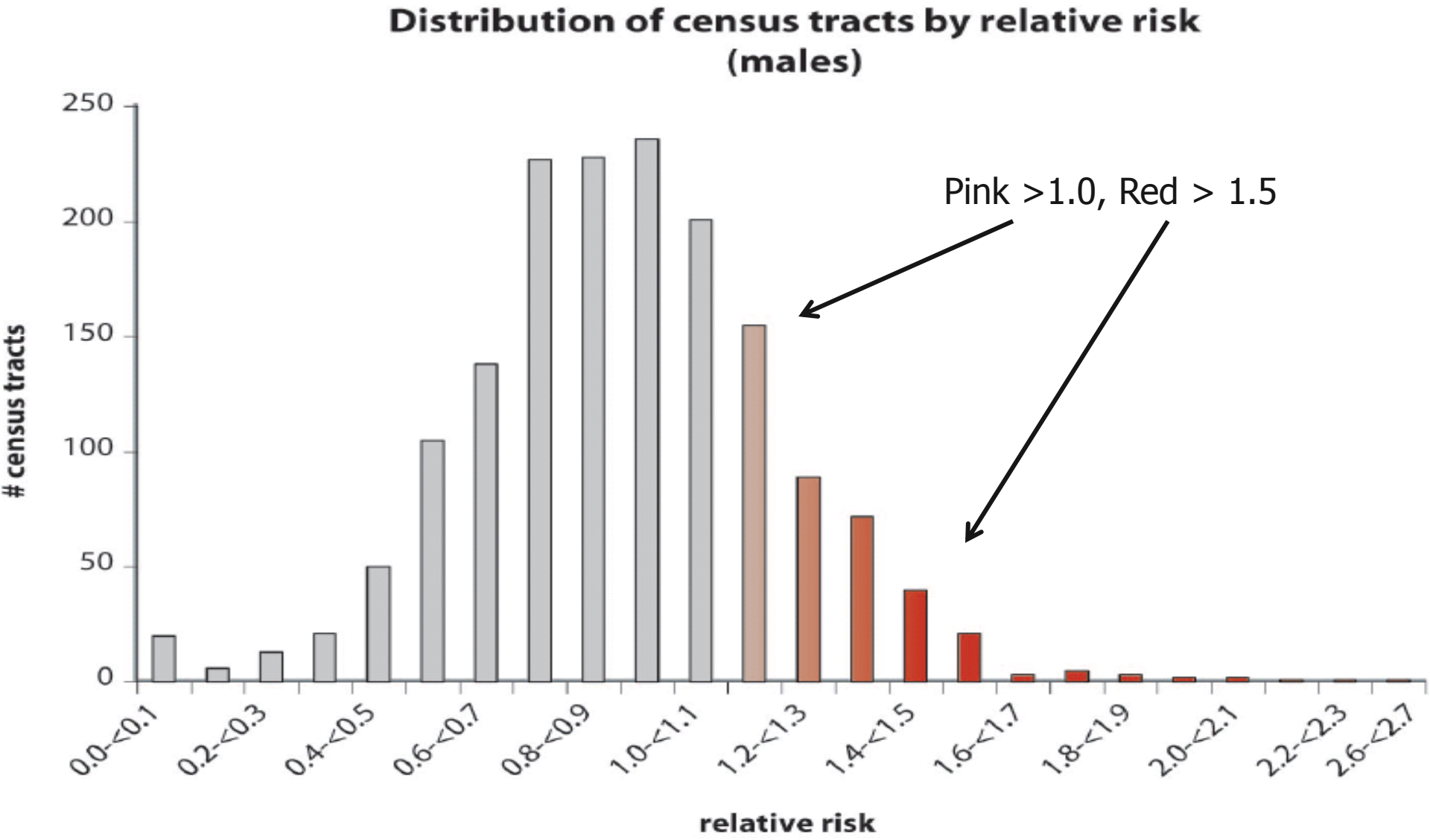

Trends in Incidence of Malignant Melanoma among Whites from California Counties differing in Median Income and Educational Attainment
Annual Age-adjusted Incidence/100K
40
35
30
25
20
15
10
5
0
1988-94
1995-01
2002-8
Period
Contra Costa
Imperial
Kern
Los Angeles
Marin
San Francisco
San Joaquin
San Mateo
Santa Clara
Stanislaus
Tulare
California


Trends in Incidence of Female Lung Cancer among Whites from California Counties differing in Median Income and Educational Attainment
Annual Age-adjusted Incidence/100K
70
65
60
55
50
45
40
1988-94
1995-01
2002-8
Period
Contra Costa
Imperial
Kern
Los Angeles
Marin
San Francisco
San Joaquin
San Mateo
Santa Clara
Stanislaus
Tulare
California

From Counties to Census tracts

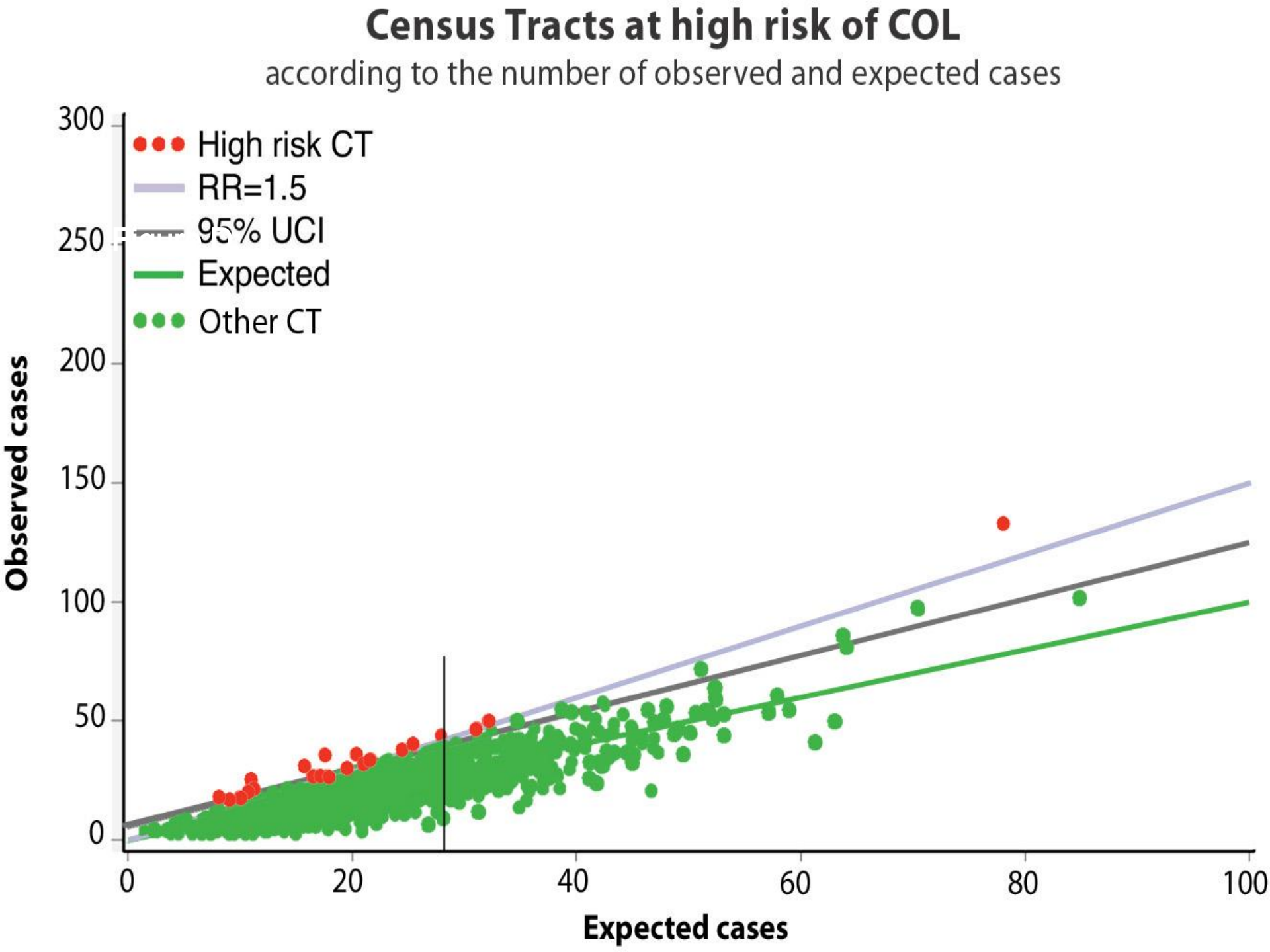
- We define localities as census tracts because the census gives us accurate populations by age and sex
- Census tracts are smaller than counties, averaging about 5000 persons but varying in size from hundreds to tens of thousands
- Thus variation in cancer occurrence comes from three factors, usually in this order:
  - Size of the tract population
  - Chance
  - Prevalence of causal factors

Colon Carcinoma in LA

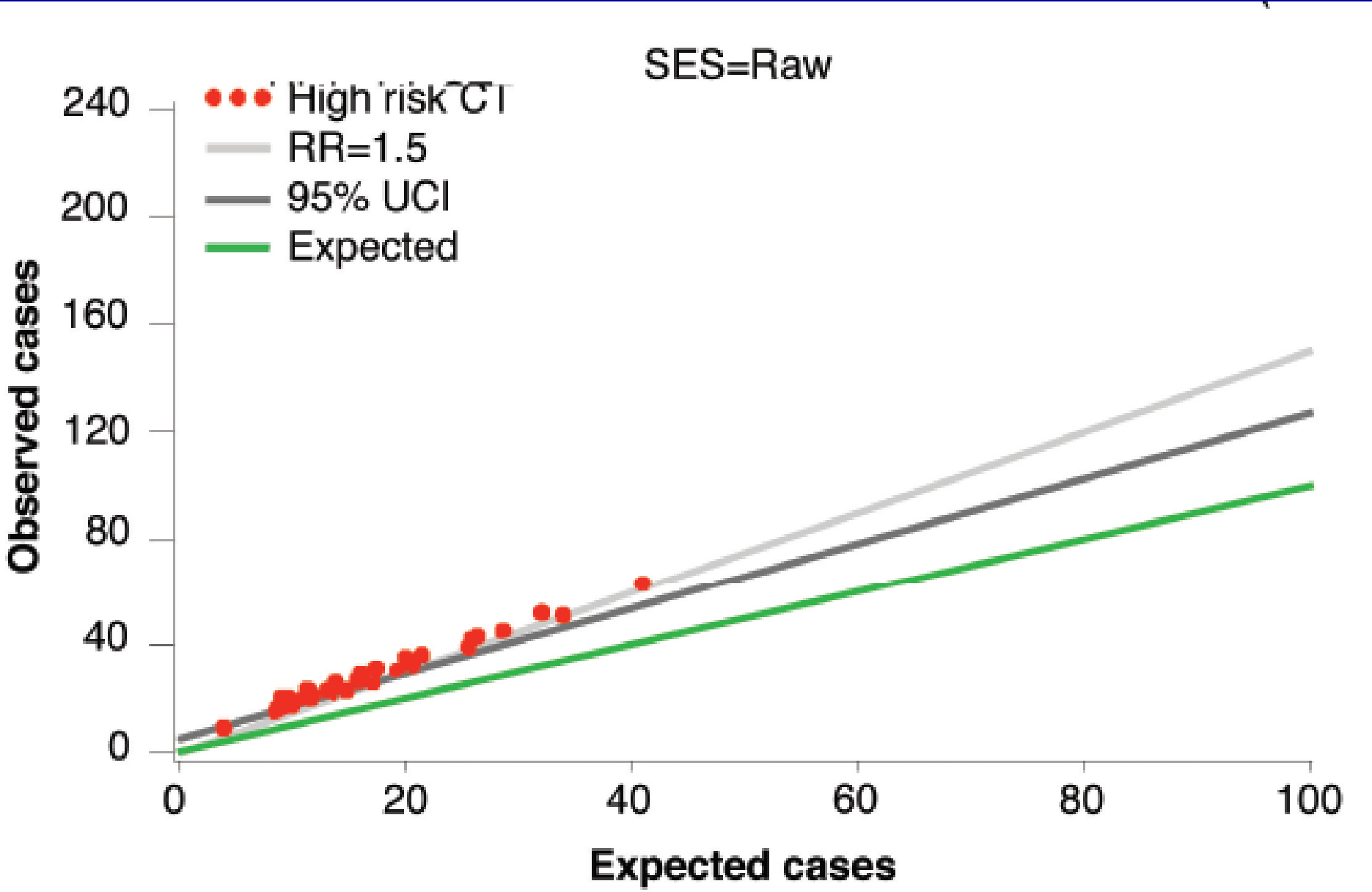


Because the tract size varies, we can describe the tracts by the number of cases expected and observed rather than by rate

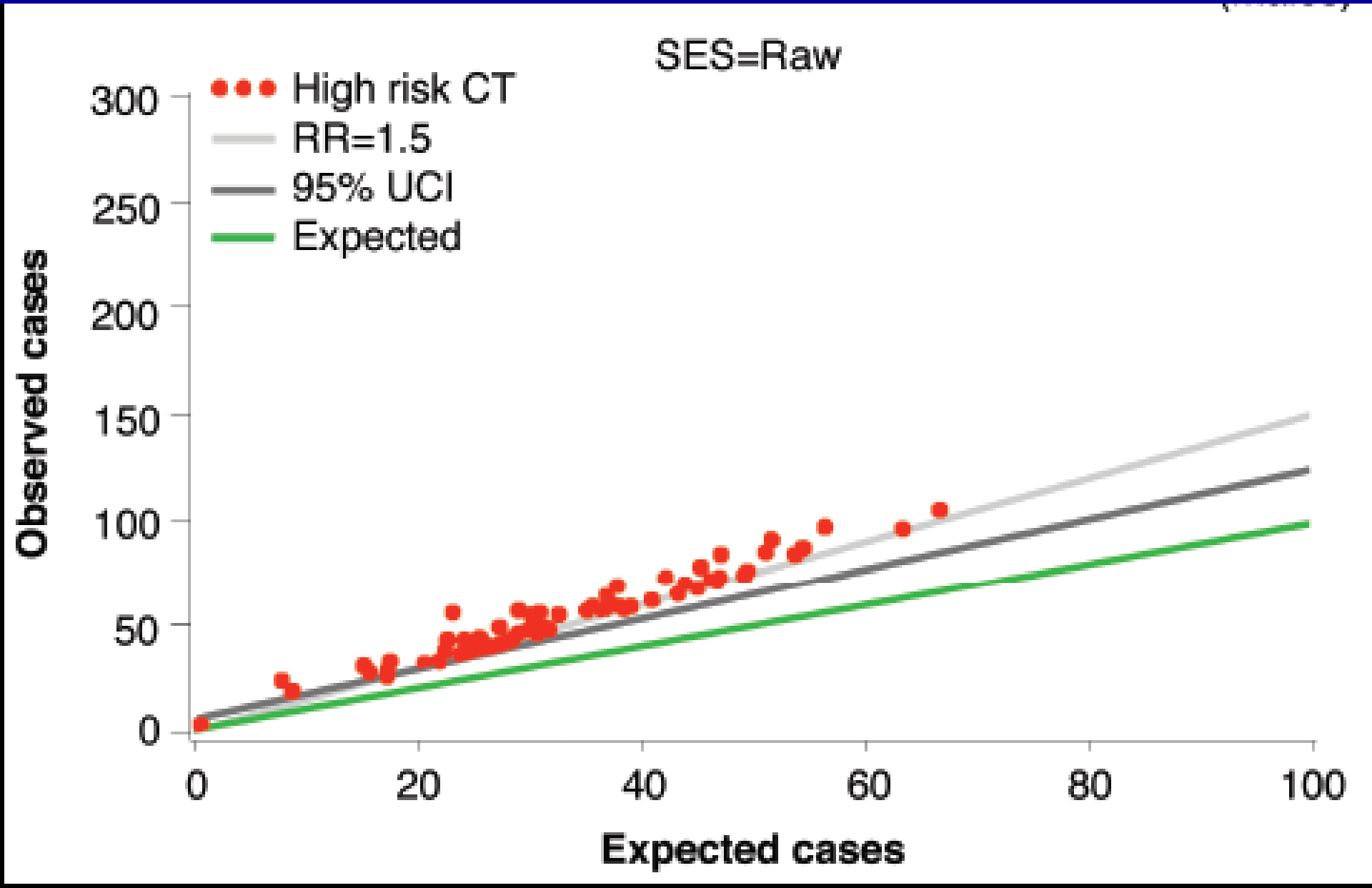
- For a given expected case number horizontally, we represent each tract vertically by a dot for the observed case number
- Lines showing both a standard risk (50% increase) and a measure of “significance” are shown.
- A dot above the lines in red represents a “significant” increase.
- Those occurring by chance will usually touch a line. The higher the red dot, the higher the incidence.
- Different cancers show different patterns depending on how localized high risk is found


Census Tracts at high risk of COL
according to the number of observed and expected cases
High risk CT
RR=1.5
95% UCI
Expected
Other CT
Observed cases
Expected cases
300
250
200
150
100
50
0
0
20
40
60
80
100

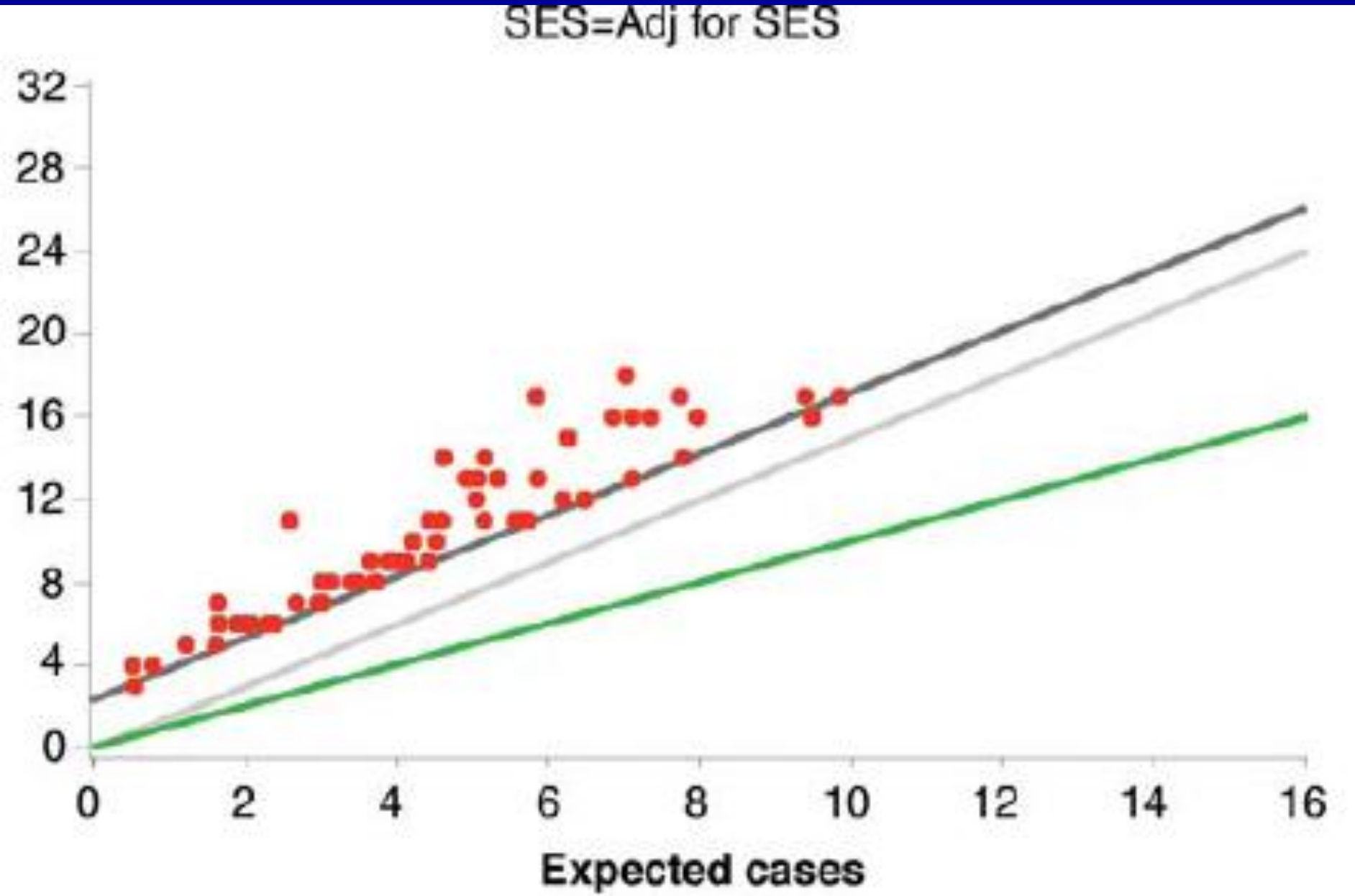
Female Colon Cancer



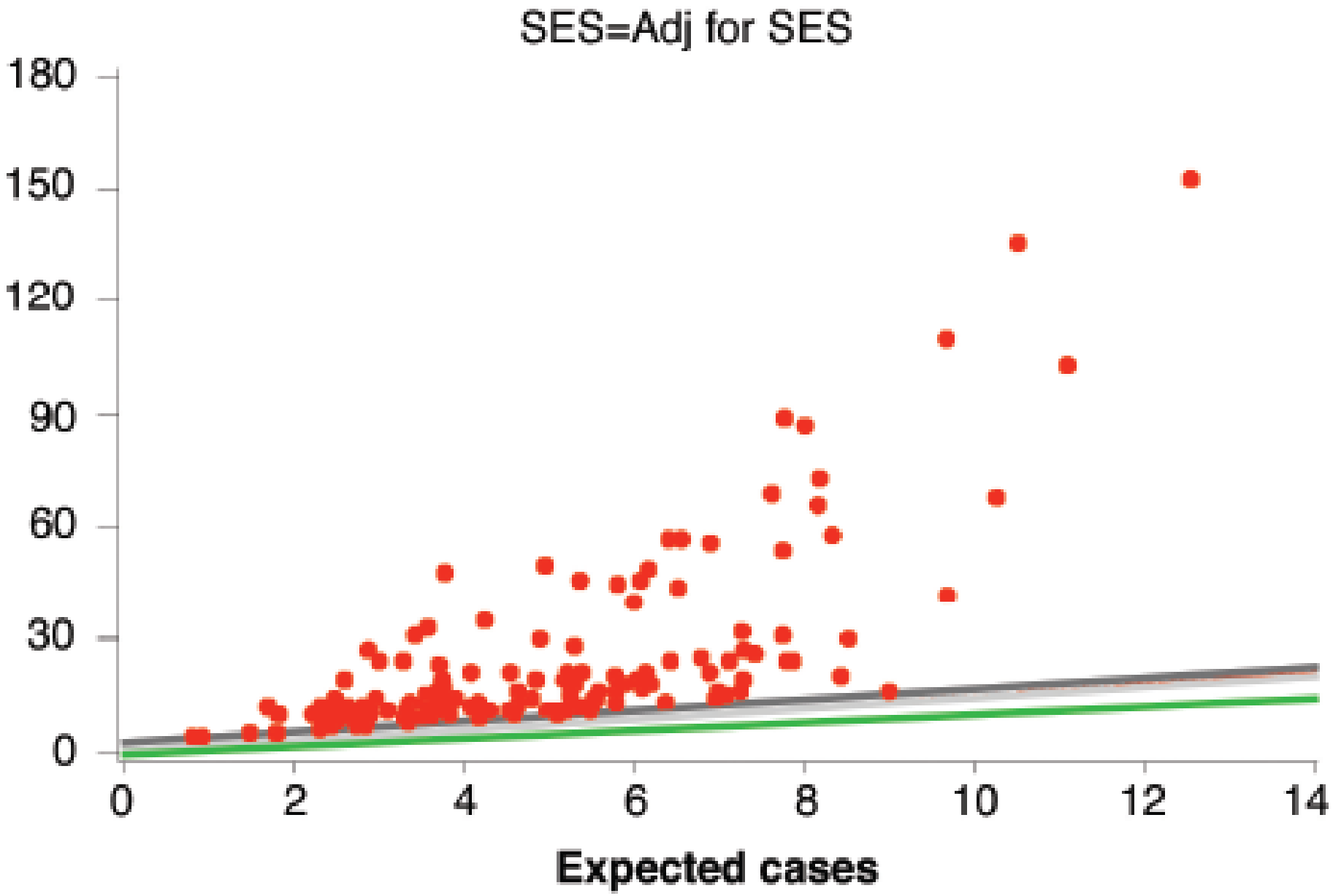
Male Lung Cancer



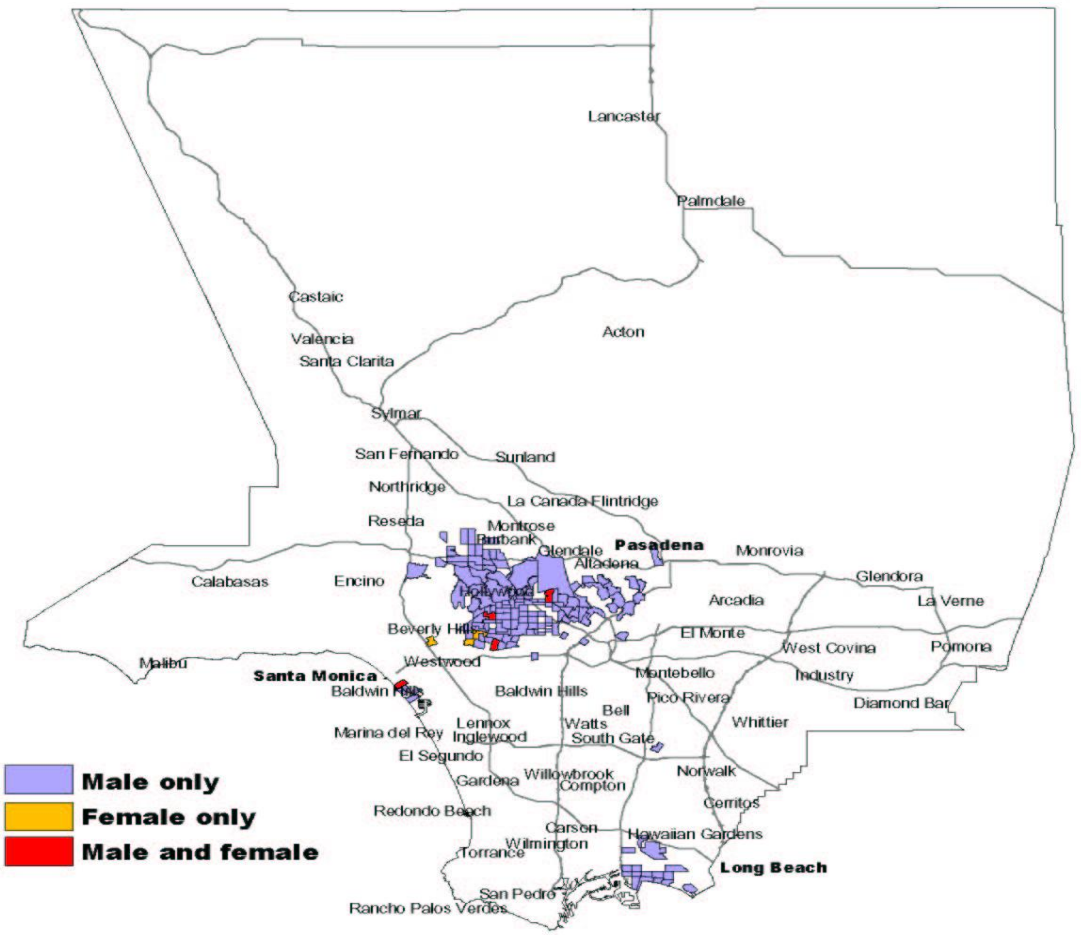
Female Oropharyngeal Cancer



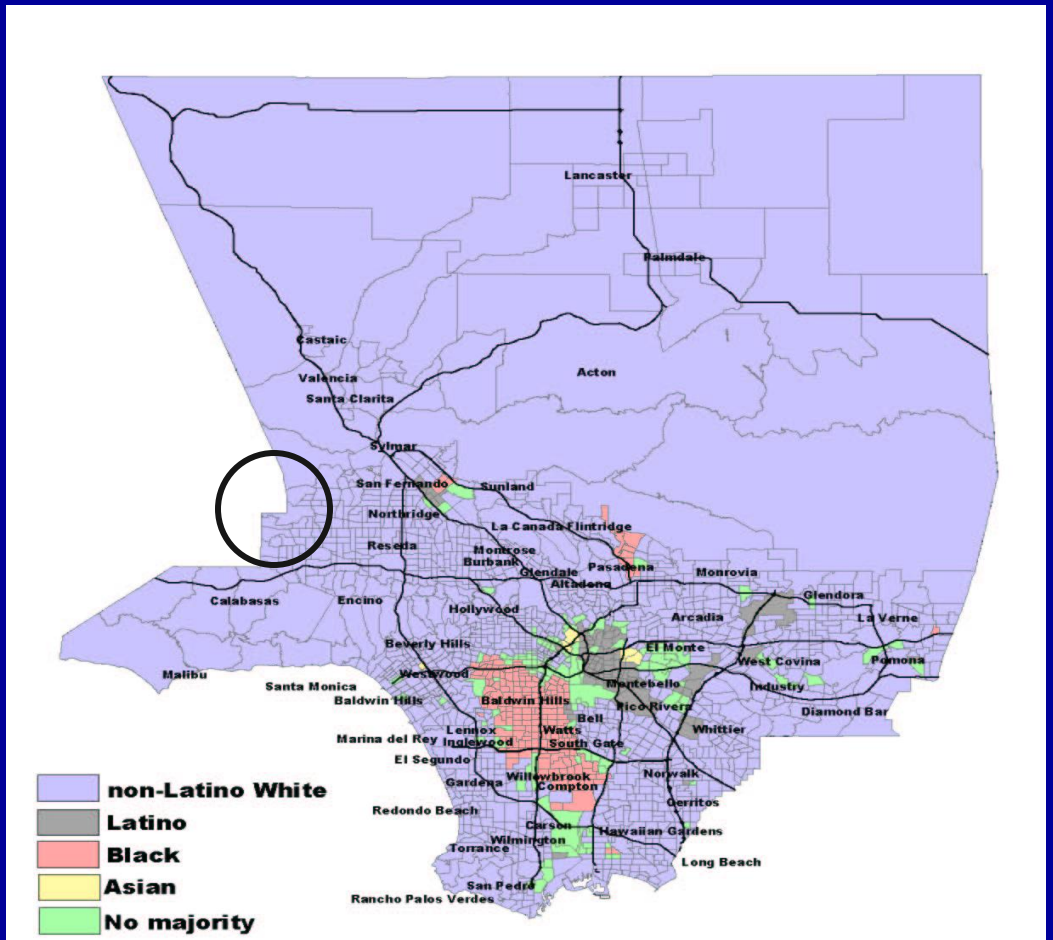
Male Kaposi Sarcoma



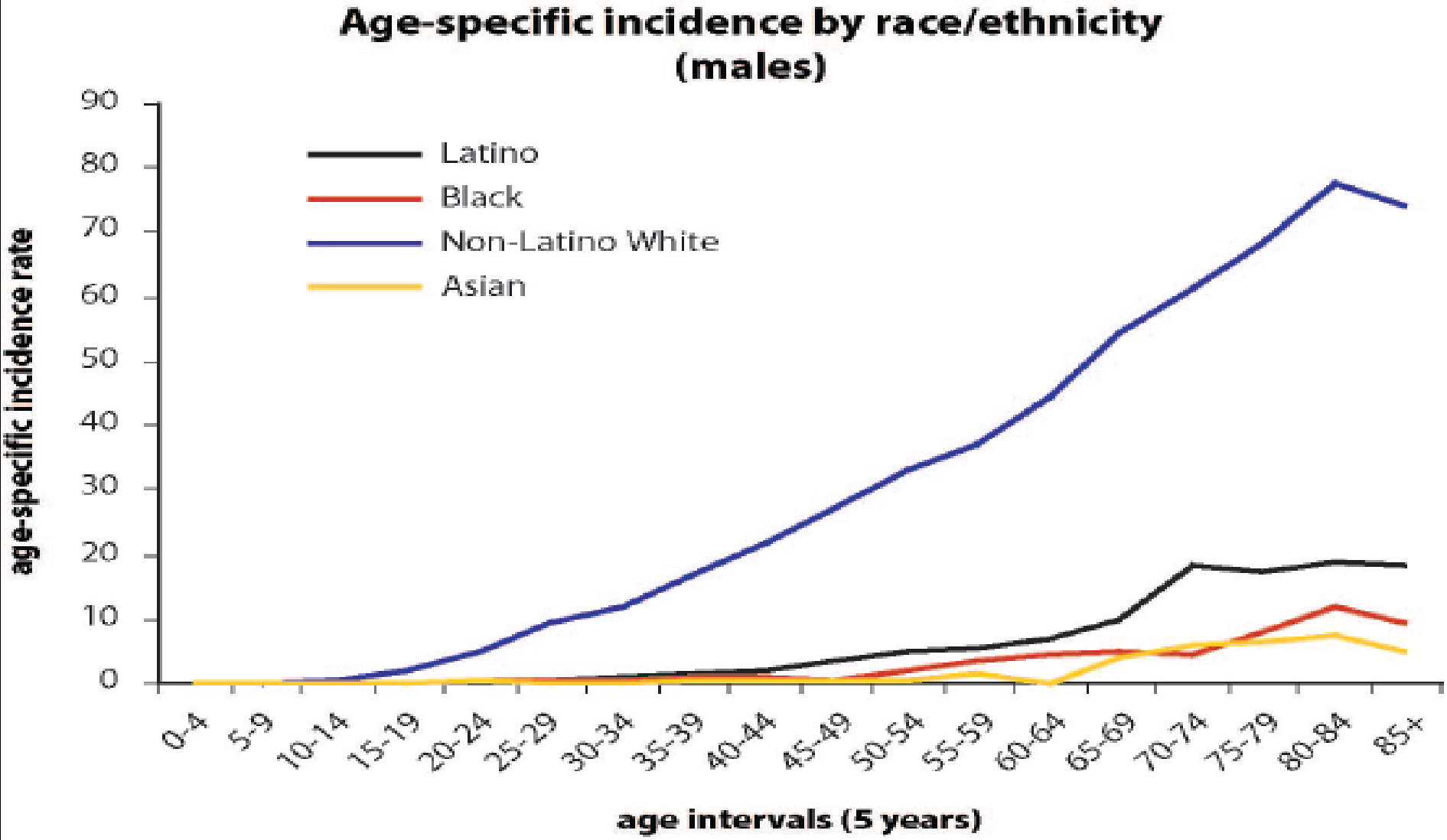
KAPOSI SARCOMA



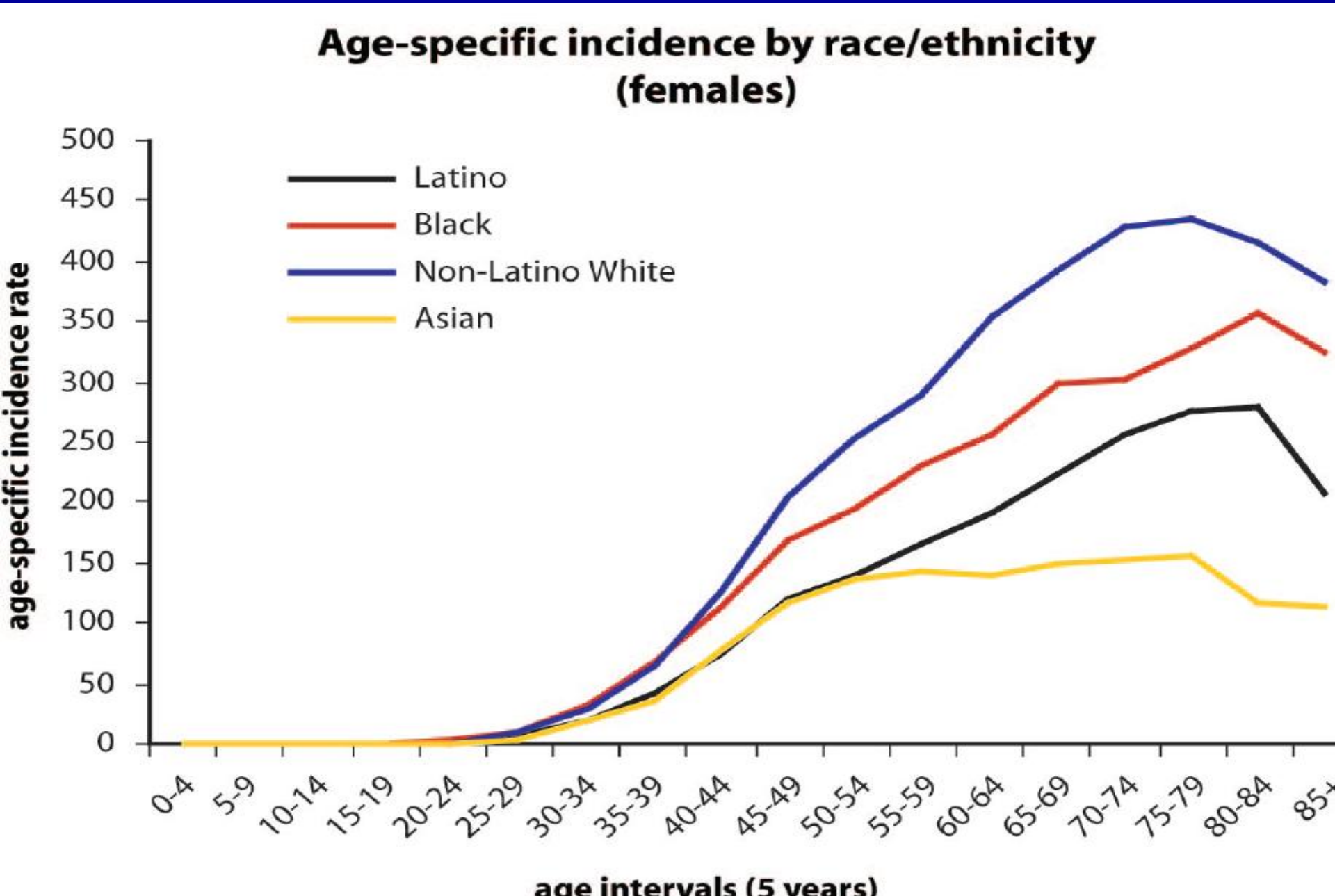
CENSUS TRACTS BY MAJORITY CASE RACE/ETHICITY



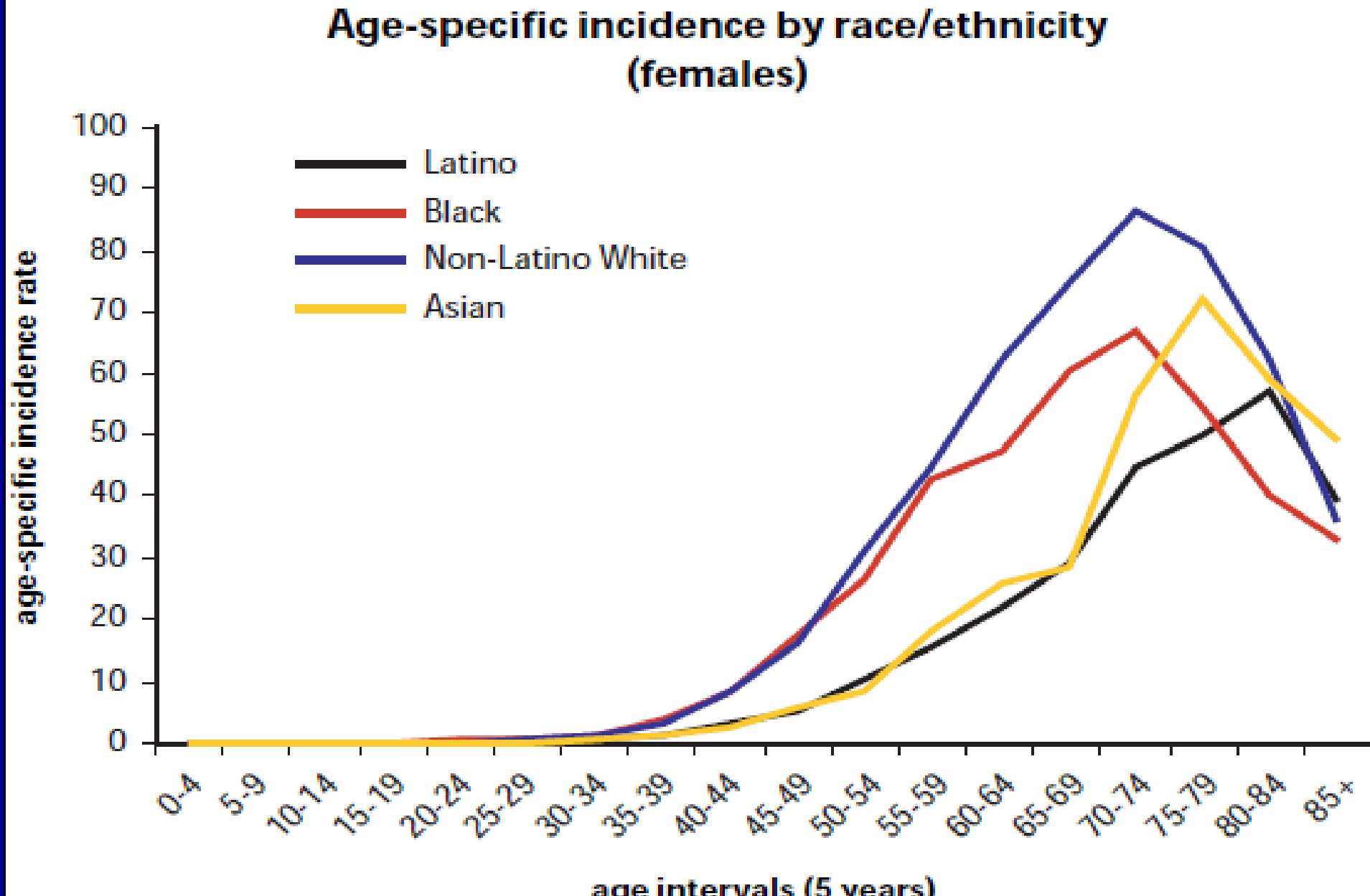
Malignant Melanoma



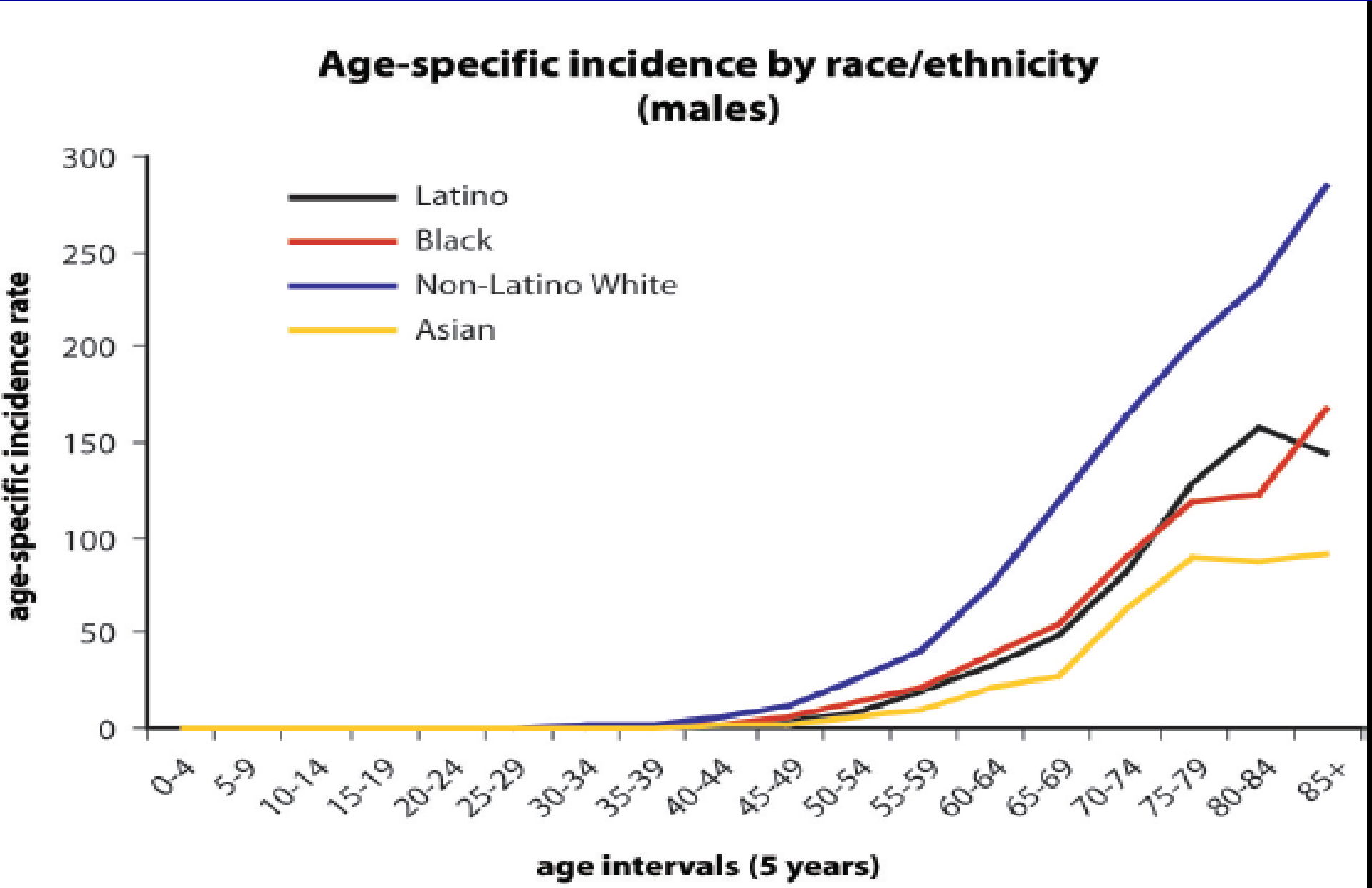
Female Breast Cancer



Female Lung Adenocarcinoma



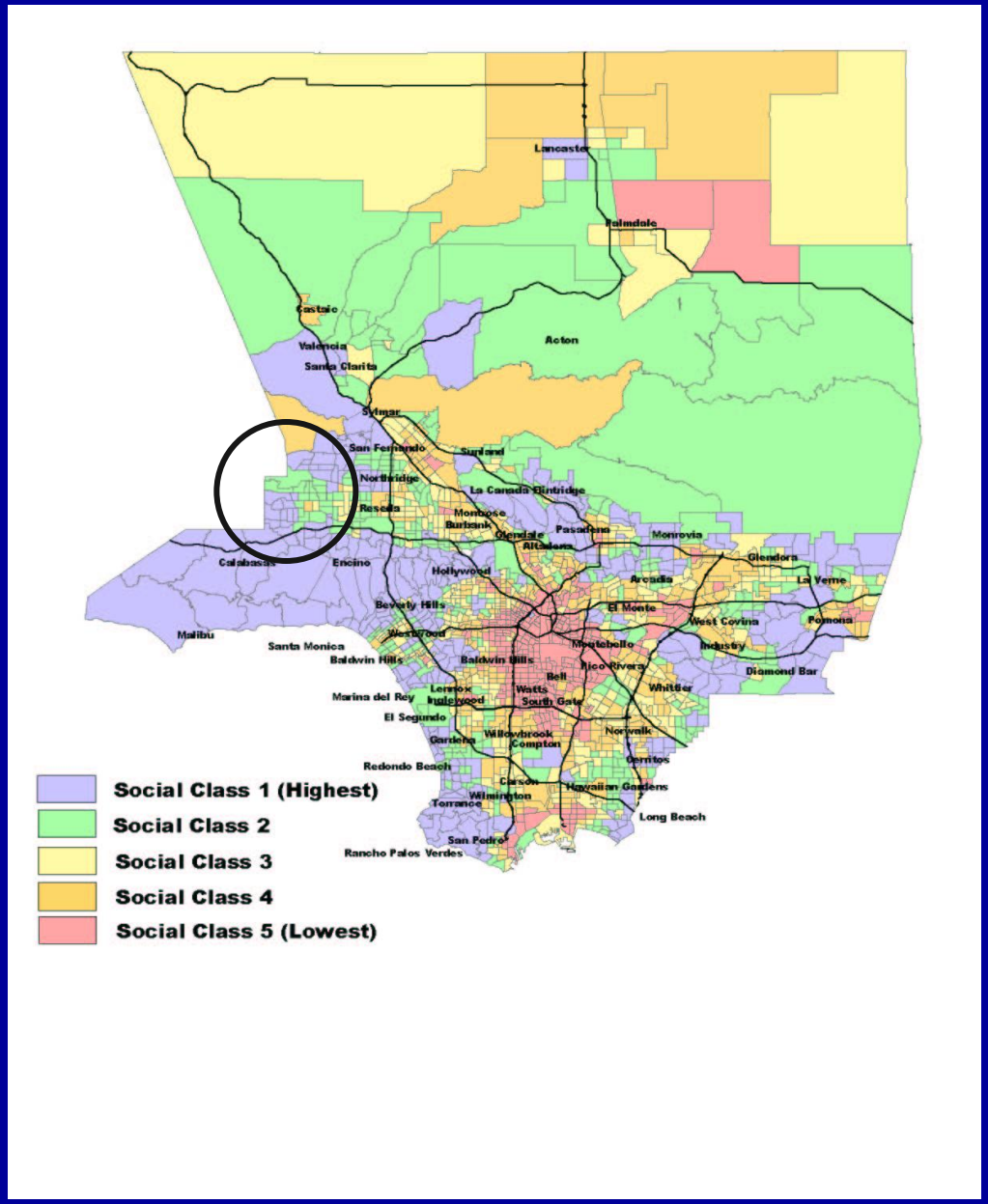
Bladder Cancer



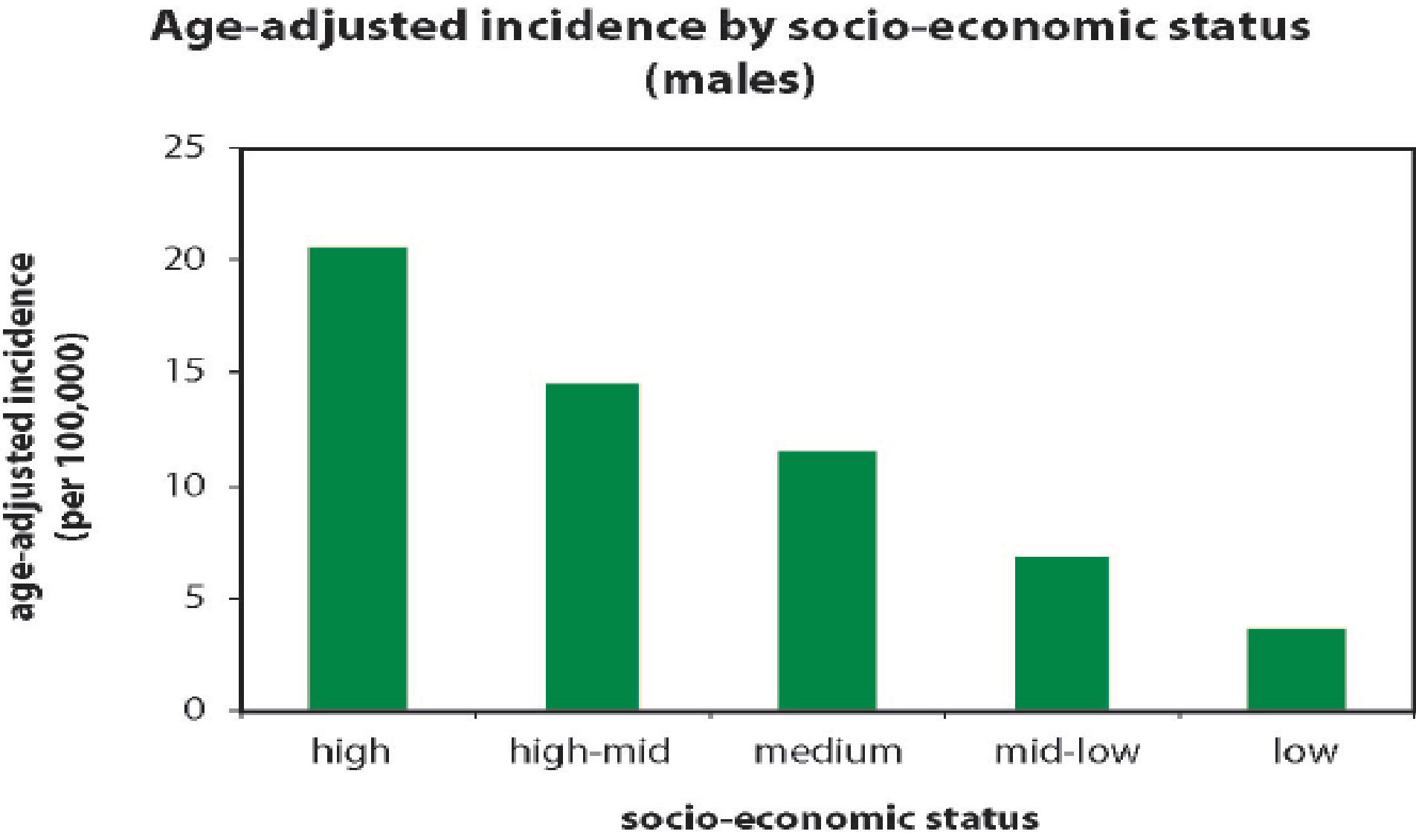
Other cancers higher in other Race/Ethnicity groups

- Prostate cancer higher in African-Americans
- Liver cancer higher in East Asian-Americans
- Gall Bladder and stomach cancer higher in Latino-Americans

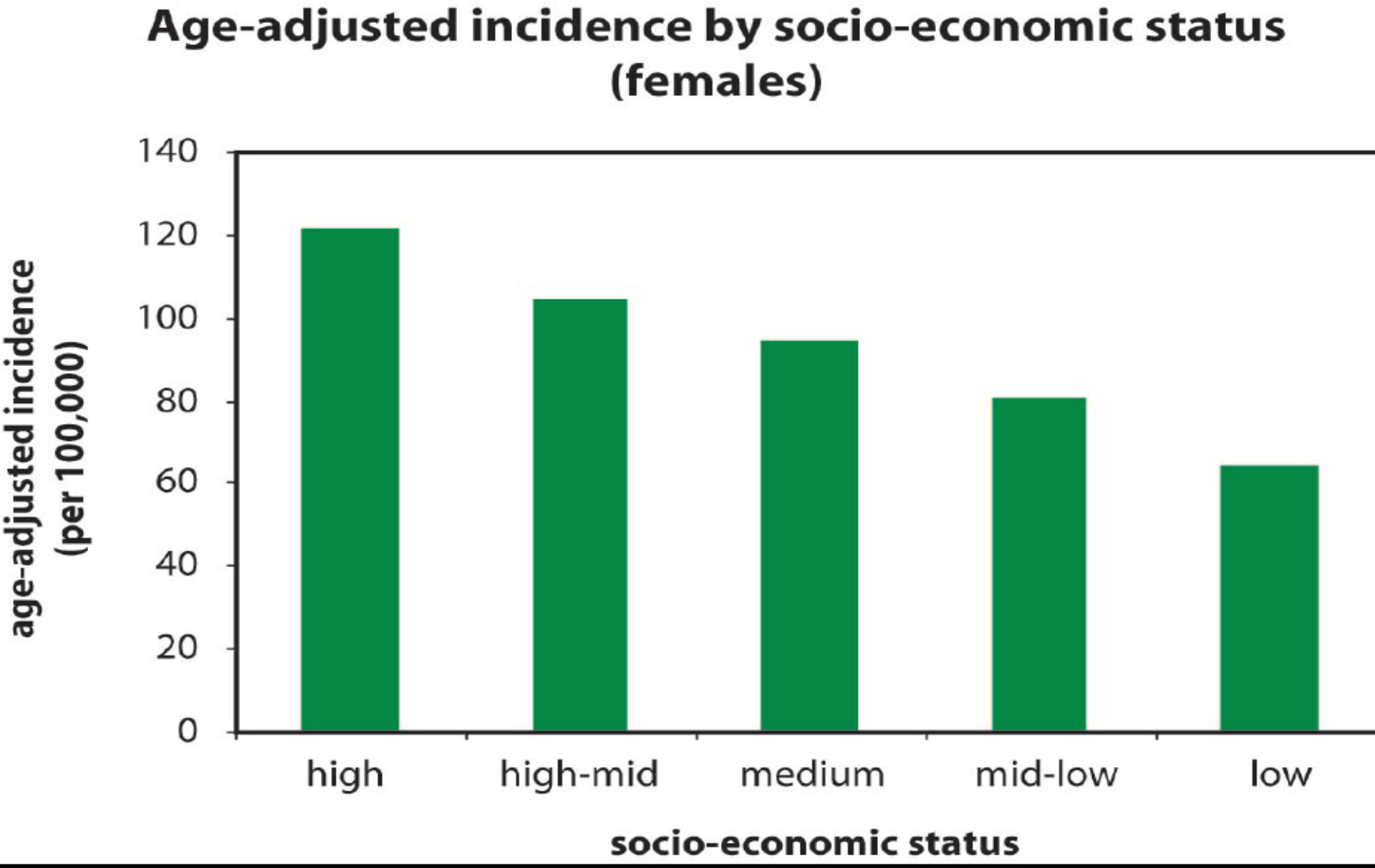
CENSUS TRACTS BY SOCIAL CLASS



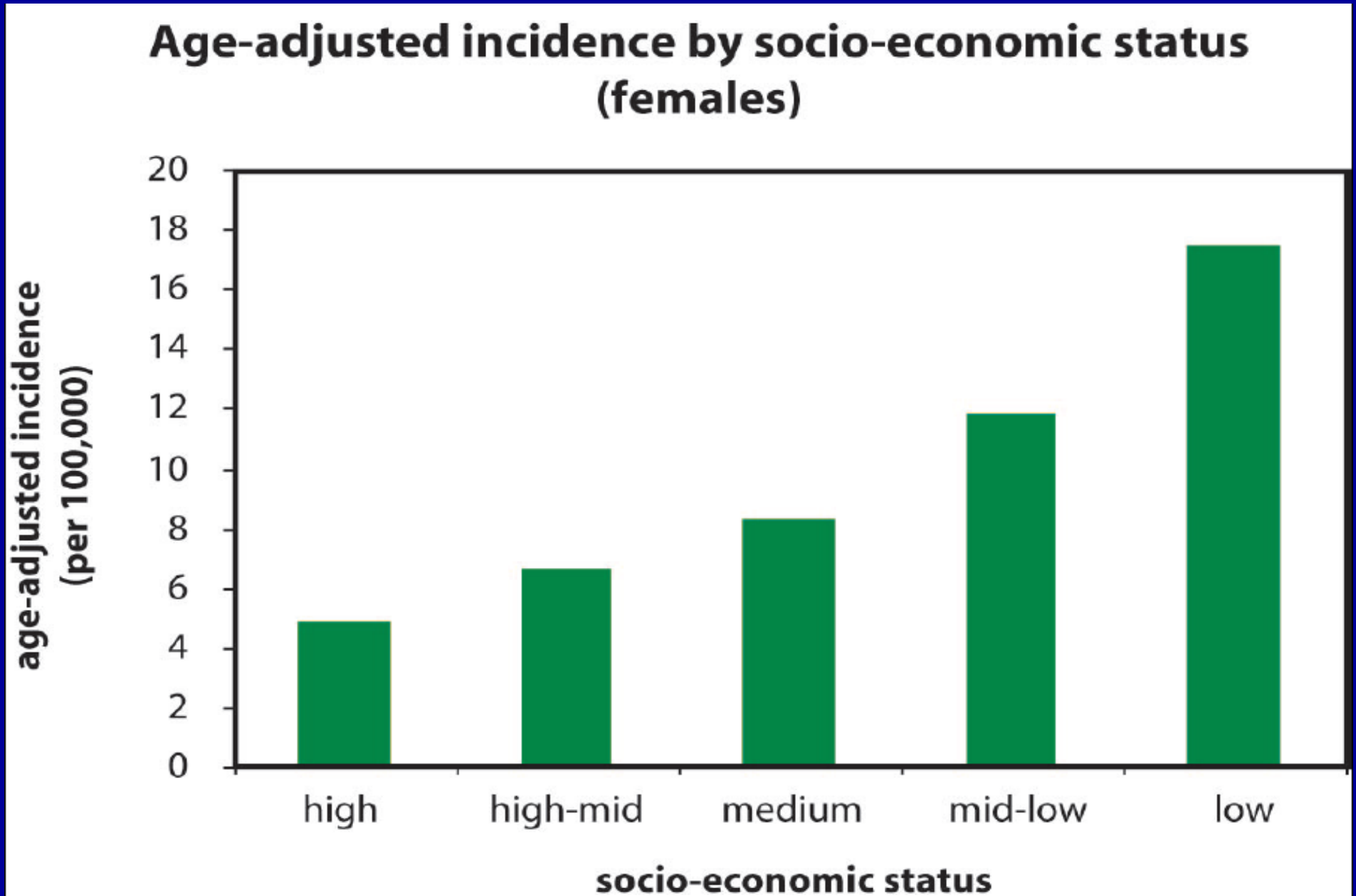
Malignant Melanoma



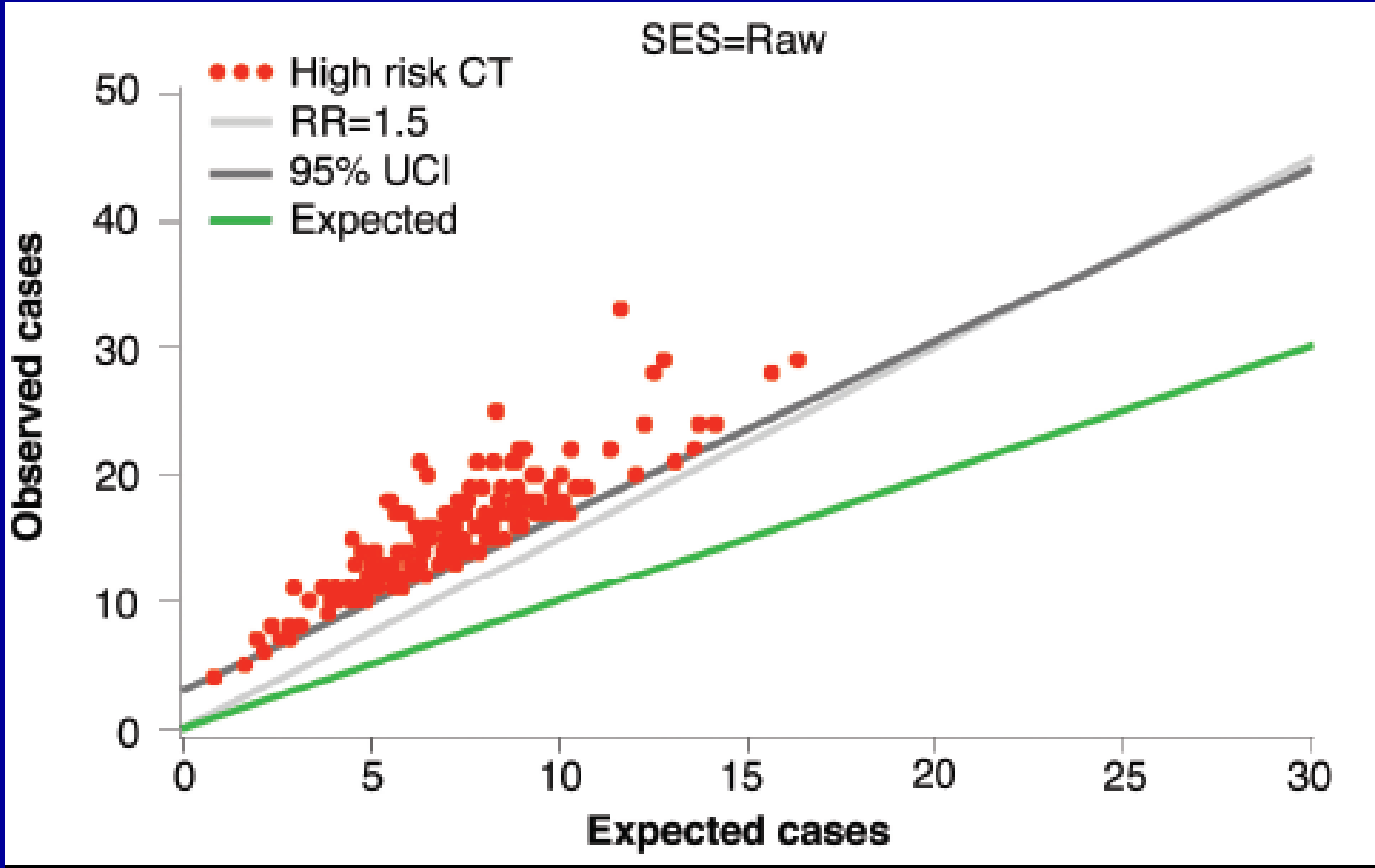
Female Breast Cancer



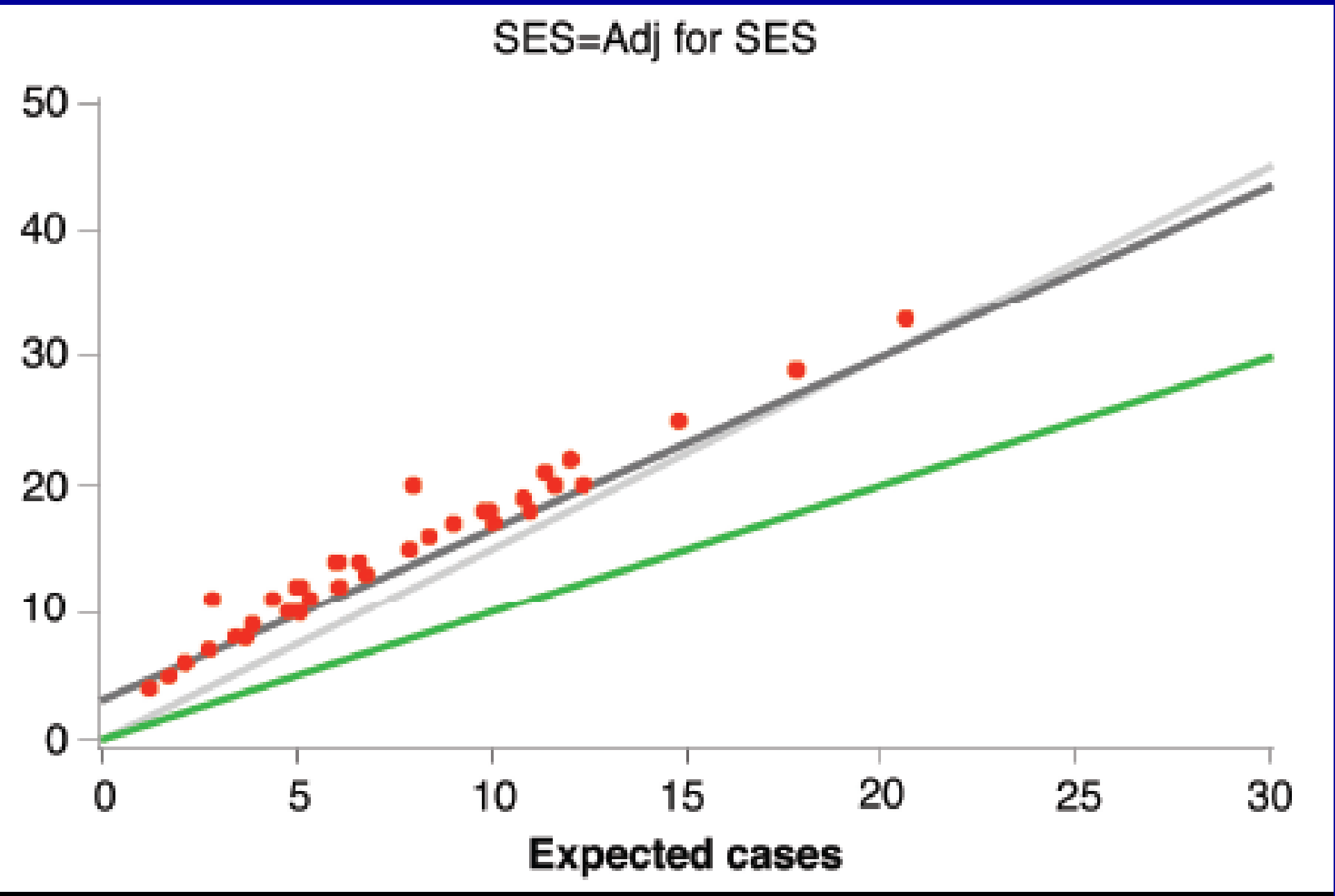
Cancer of the Cervix



Female Cancer of the Cervix



Female Cancer of the Cervix

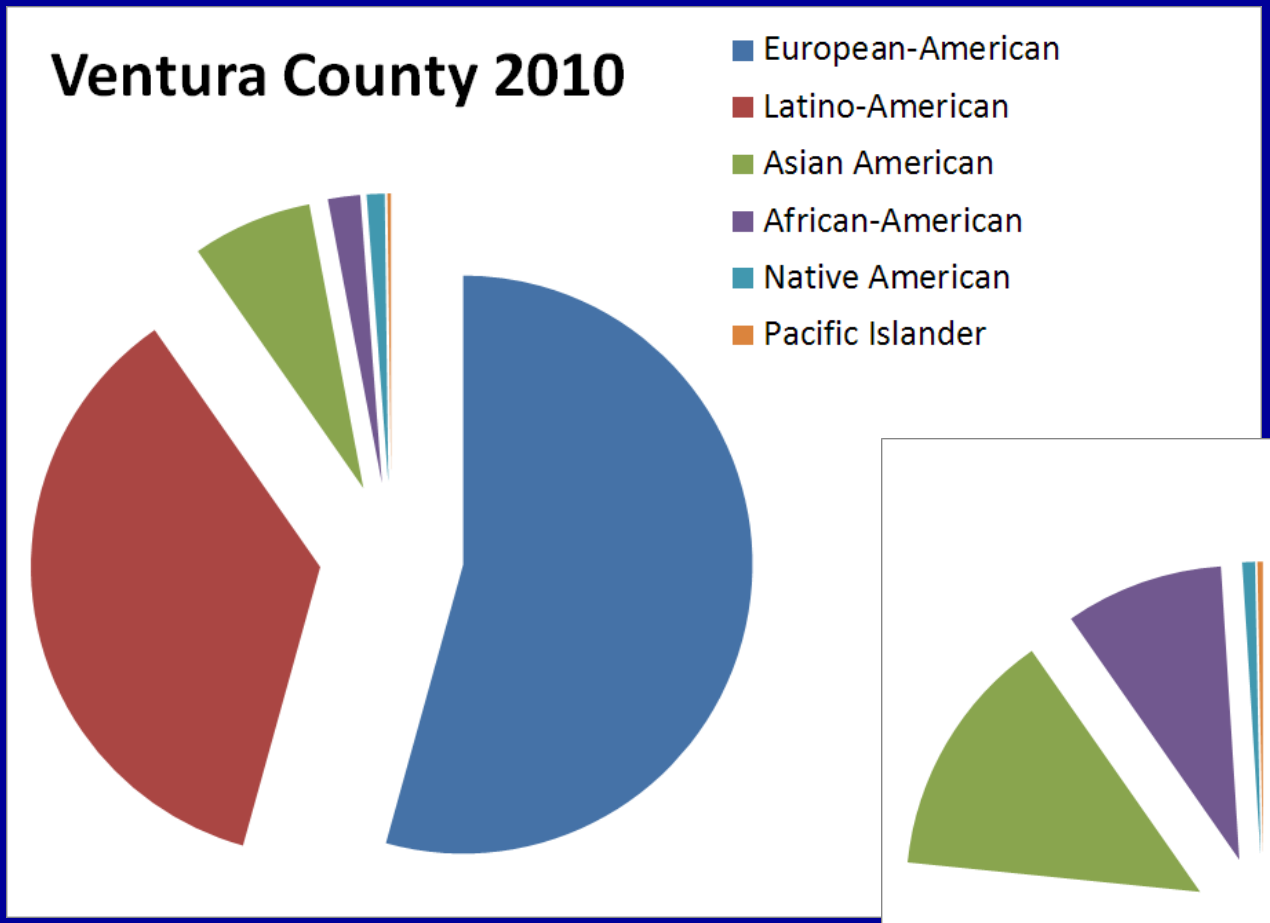


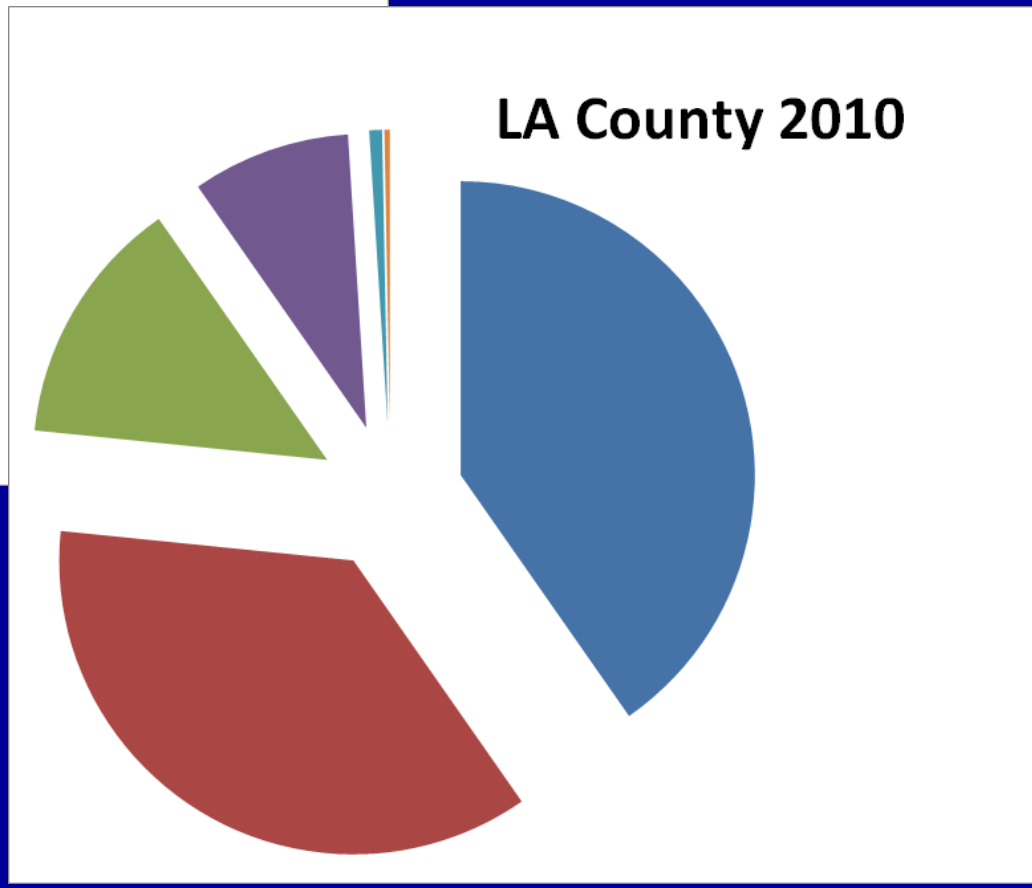
Cancers “cluster” for different reasons

- Lung cancer clusters by smoking, race, education
- Oropharynx cancer by smoking/drinking
- Cervical cancer by self/partner’s sexual activity
- Kaposi sarcoma clustered by sexual preference
- Prostate cancer clusters by race, access to care
- Stomach cancer clusters by history of poverty
- Liver cancer clusters by parental ethnicity
- Thyroid cancer clusters by access to screening
- Mesothelioma clusters by occupation
- Melanoma clusters by race and education
- Breast cancer clusters by education/occupation

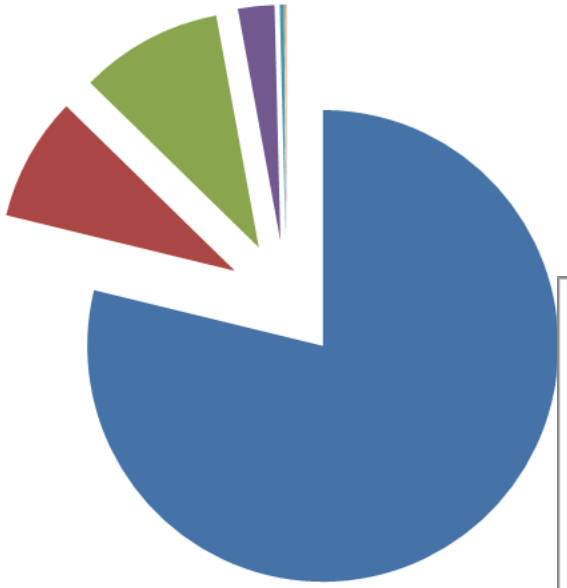
Characteristics of SSRL Offsite Tracts

- They are not characteristic of their respective Counties in terms of:
  - Income and, doubtless, education
  - Race/ethnicity

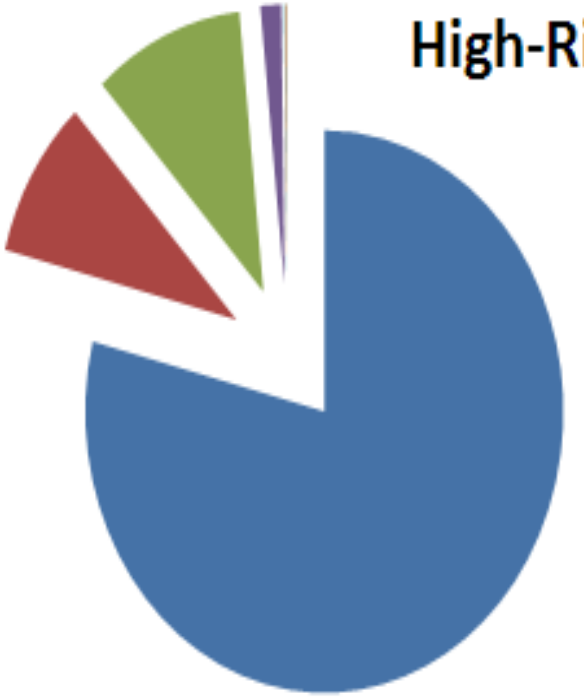

Ventura County 2010
European-American
Latino-American
Asian American
African-American
Native American
Pacific Islander


LA County 2010

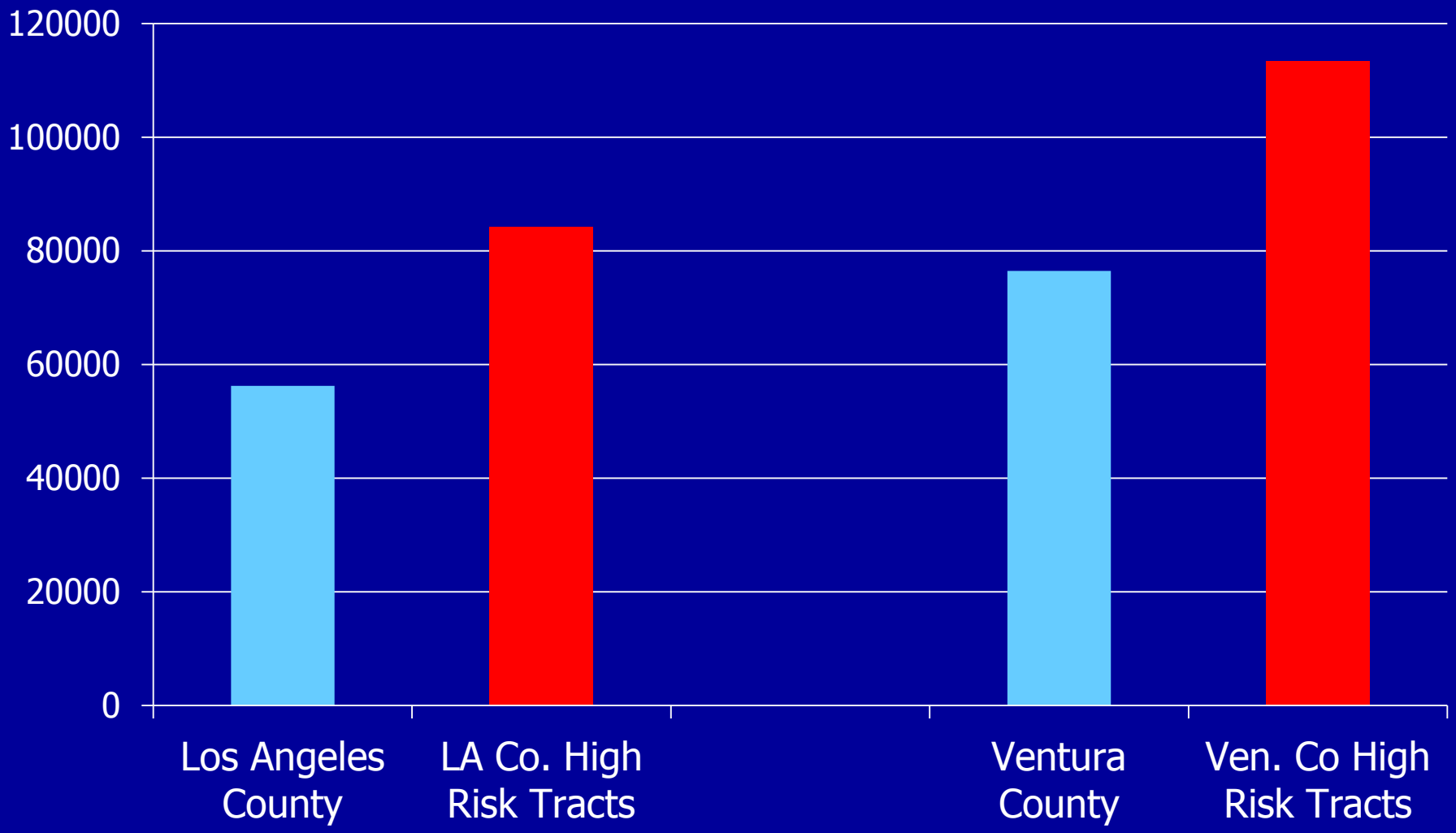
LA County High-Risk Tracts



Ventura County High-Risk Tracts



Median Family Income of Counties and of High Risk Tracts



From where do case reports come?

- Cancer reporting is mandatory since 1988
- California Cancer Registry covers the State
- All invasive malignancies (a few benign tumors)
- All cases found in a CA resident at diagnosis
- Hospitals collect reports to maintain certification
- Non-hospital labs, death certificates covered
- Reports returned to the place of residence
- Around 99% complete by regular audits using sampling and death certificates

Malignancies according to Annual (Age-Adjusted) New Cases /100,000

- **50+: M Prostate, F Breast**
- **30-49: MF Lung, M/F Colorectum**
- **10-29: MF Melanoma, M Oropharynx, M Bladder, F Ovary, F Endometrium, MF Non-Hodgkin Lymphoma, M Leukemia**
- **5-9: M Stomach, M Larynx, M Testes, F Melanoma, F Thyroid**
- **F Cervix, F Oropharynx, F Leukemia, MF Pancreas, MF Kidney, MF Brain**
- **<5: M Thyroid, M Penis, F Stomach, F Larynx, F Bladder, MF Liver, MF Esophagus, MF Gallbladder, MF Hodgkin Lymphoma, MF Eye**

Selection of malignancies

- Every cancer has a unique set of causes
  - (A few exposures, i.e. smoking, cause a portion of several cancers, but the rate of cancer at all sites is not informative)
- Cancers were selected for assessment:
- In all, thirteen different malignancies
  - The four most common cancers
  - Others possibly caused by chemicals/radiation

Cancers selected

Neoplasm	Major Causes	Descriptive Predictors
Lung	Cigarette smoking	Blue collar occupation
Bladder	Cigarettes, aniline dyes (rare)	White Race
Pancreas	Cigarette smoking	None strong
Oropharynx	Tobacco, Alcohol, Pap.Virus	None strong
Leukemia	Genes, benzene, ? virus	None strong
Breast	Genes, Hormones	Higher education
Colorectal	Genes, Diet, Activity	None strong
Prostate	Genes, Diet	Race, Age, Access to screening
Thyroid	Ionizing radiation (rare)	Access to screening
Brain	Ionizing Radiation (rare)	None strong
Liver	Hepatitis B, C viruses	National origin
NHL	Immune depletion	None strong
Melanoma	Sunlight, light skin	Race, Higher education

Screening Methods

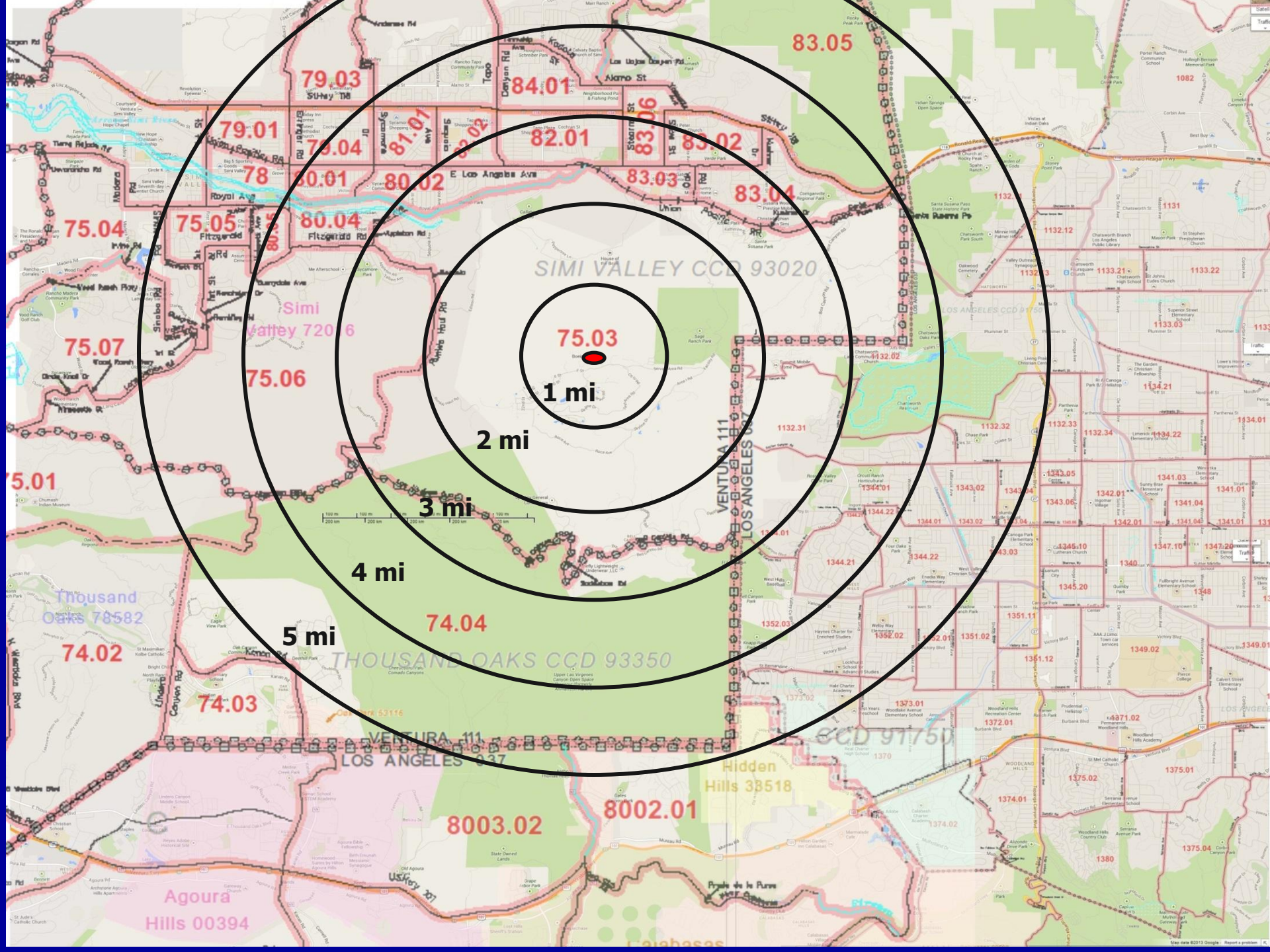
- Genders assessed separately
- Three time periods:
  - 1988-95, 1996-2003, 2004-2010
  - Separate denominators from 3 censuses

- All census tracts within 5 miles of SSFL
  - 1988-95: 22 VEN, 16 LA census tracts
  - 1996-2003 : 29 VEN, 17 LA census tracts
  - 2004-2010: 29 VEN, 17 LA census tracts

- Number of comparisons:
  - 130 period-tracts X 24 gender-cancers= 3120 searches
  - Up to 78 (3 per gender-cancer) “significantly” high-risk tracts by chance

Screening Criteria

- Significantly higher rate than County mean at the 95% confidence level ($p < 0.05$)
- At least a 50% increase in risk ($RR > 1,5$)
- Histological (Causal) homogeneity of excess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To find a result consistent with local cancer causation by disbursed carcinogen

- Consistent risk over calendar time
- High risk for both genders in the same area
- Higher risk proximate to SSRL
- Geographic clustering of high risk areas
- Pattern consistent with dispersion flow
- We screen by a relative risk (RR) of 1.5, but if RR is below 2.0, any observed case would likely have occurred anyway

- No plausible alternative explanation is available

Reasons for Caution in Assessing Impact

- 3 “Significant” excesses each are expected by chance

- No known clear evidence of personal exposure
- Waterborne and airborne dispersion imprecise
- Dosage is unknown

- Exposed workers are likely to reside together
- Census errors: rapid local growth may distort incidence estimates

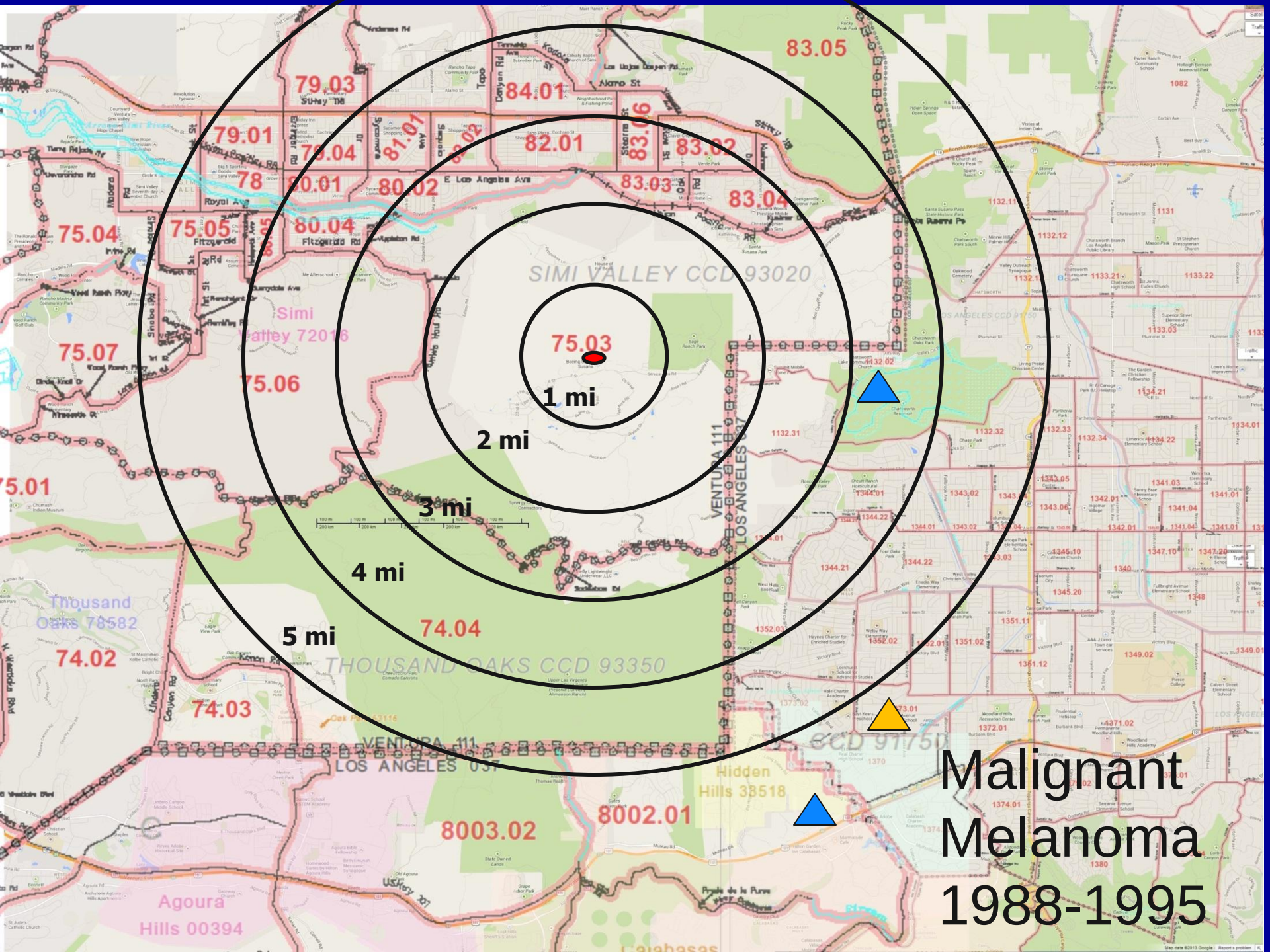
- Evaluation is based on residential address at diagnosis

Summary Screening Findings

Neoplasm	"Significant" tract-periods	In Both genders	In Adjacent tracts	In 2 or more periods
Breast	26 (3 exp)	---	8	6
Melanoma	23 (6 exp)	8	17	7
Colorectal	7 (6 exp)	2	0	0
Lung	4 (6 exp)	0	0	1
Prostate	4 (3 exp)	---	0	0
Thyroid	3 (6 exp)	0	0	0
Brain	3 (6 exp)	0	0	0
NHL	2 (6 exp)	0	0	0
Leukemia	1 (6 exp)	---	---	--
Bladder	1 (6 exp)	---	---	---
Oropharynx	0 (6 exp)	---	---	---
Liver	0 (6 exp)	---	---	---
Pancreas	0 (6 exp)	---	---	---

Legend

Period	Males	Females	Both
1988-1995			
1996-2003			
2004-2010			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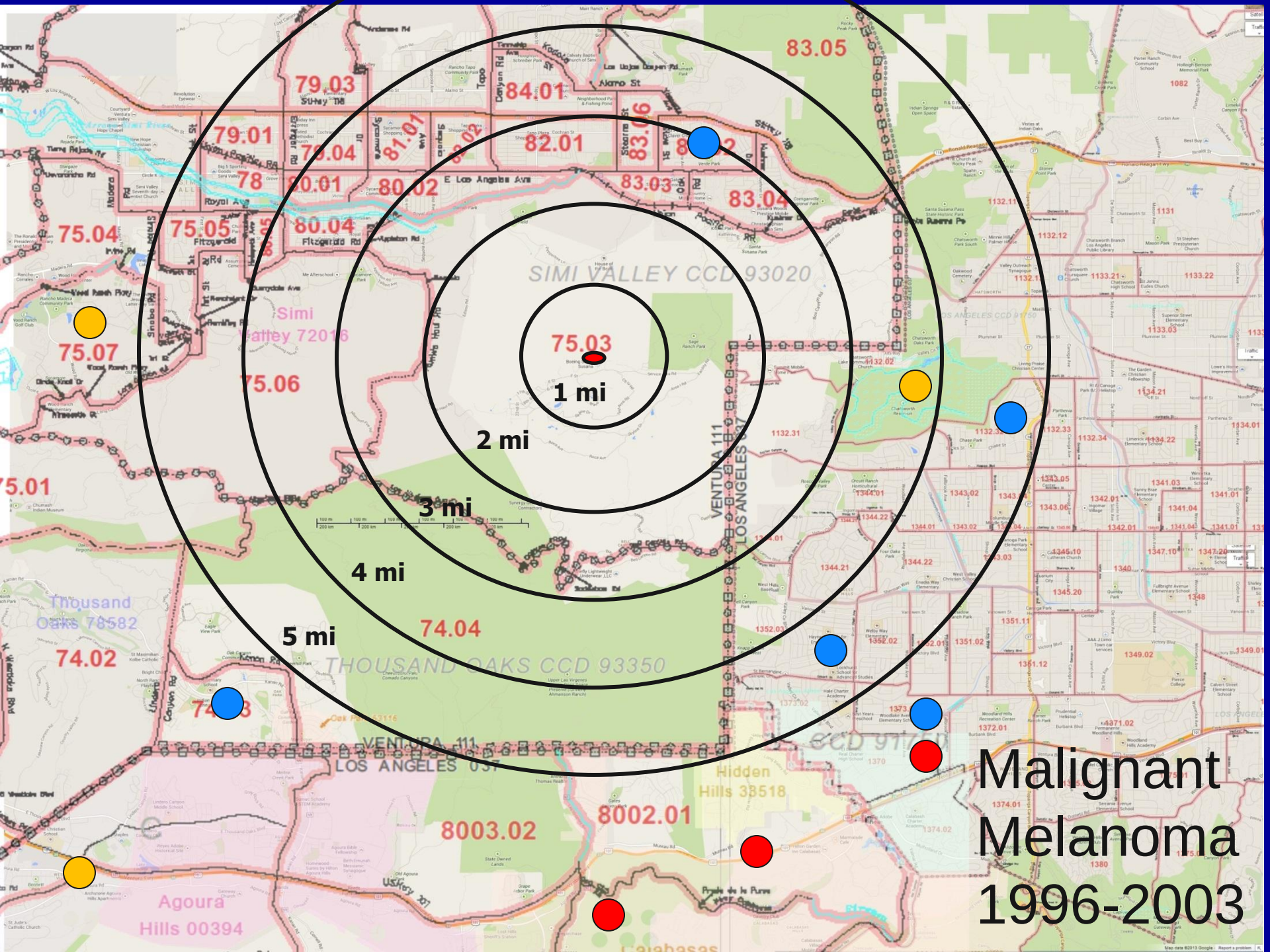
Malignant Melanoma 1988-1995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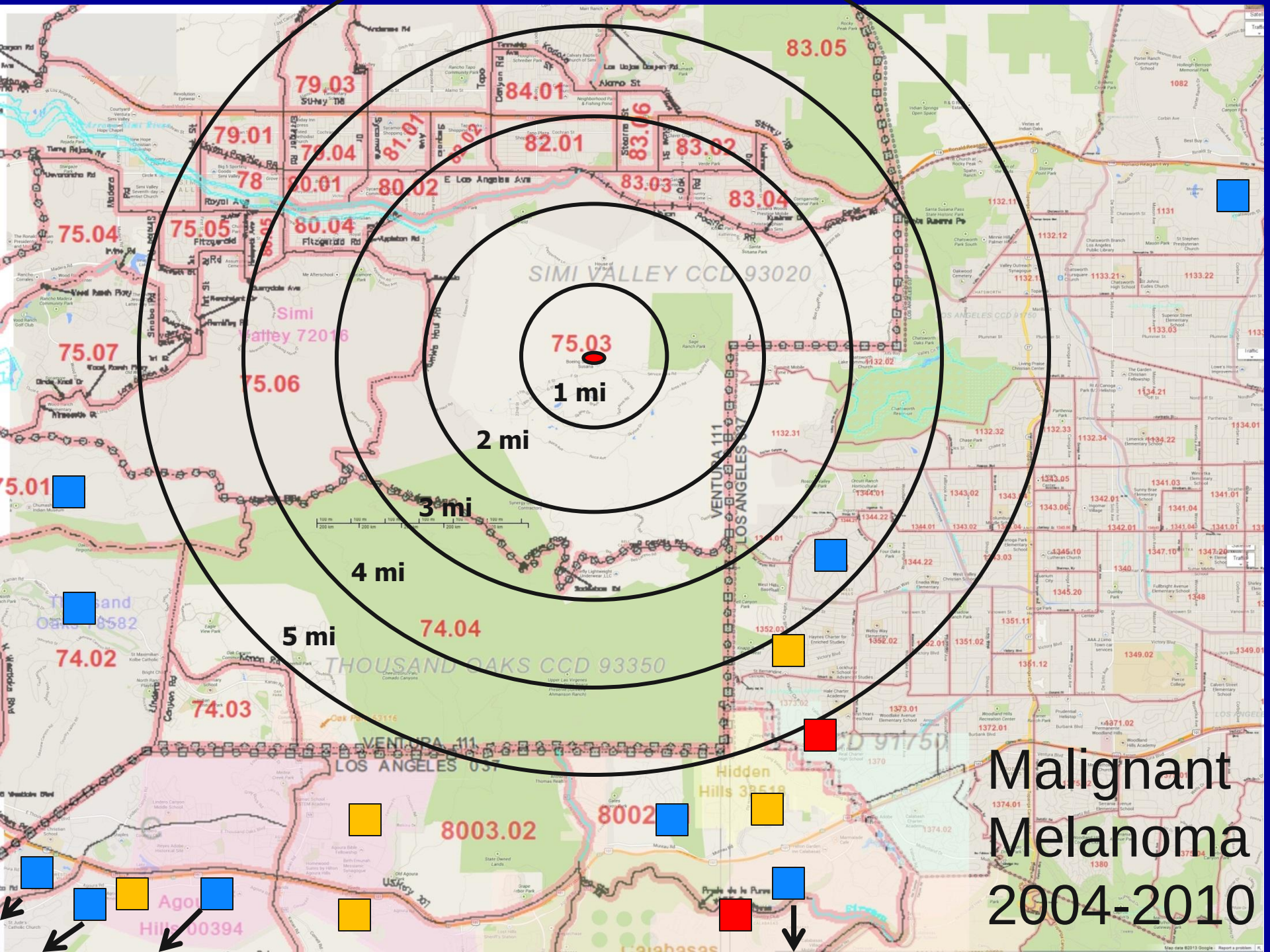
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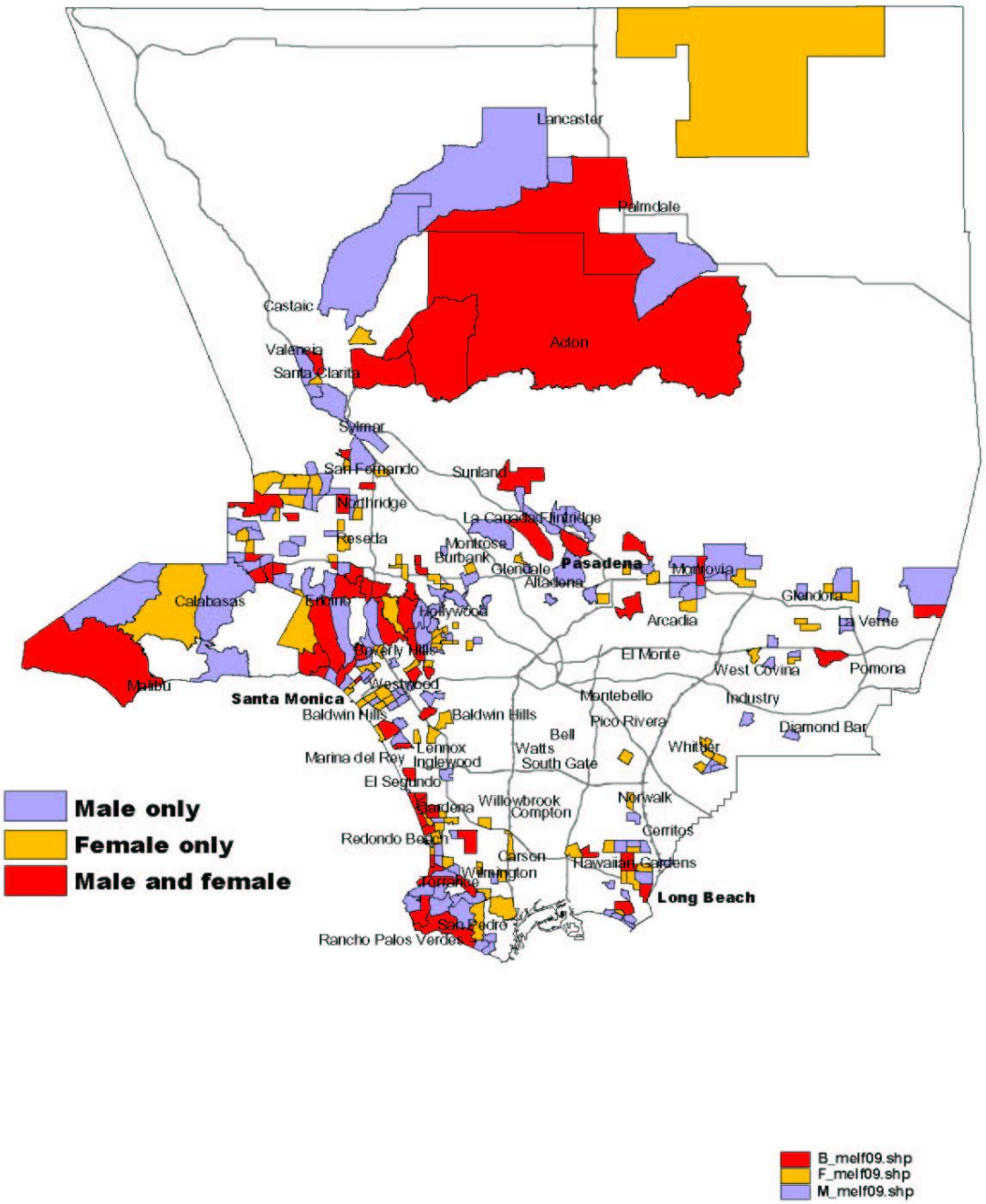
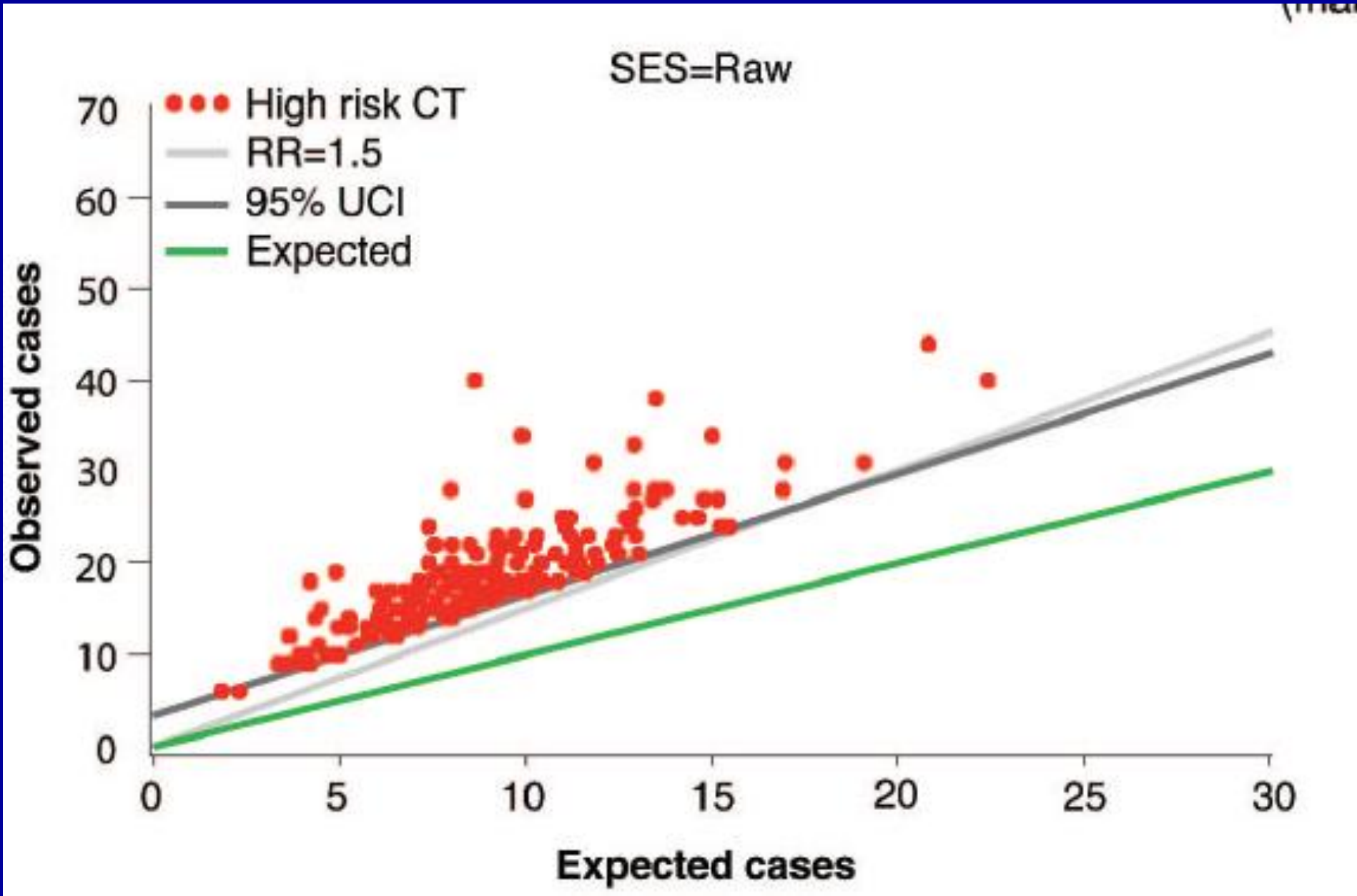
Malignant
Melanoma
2004-2010

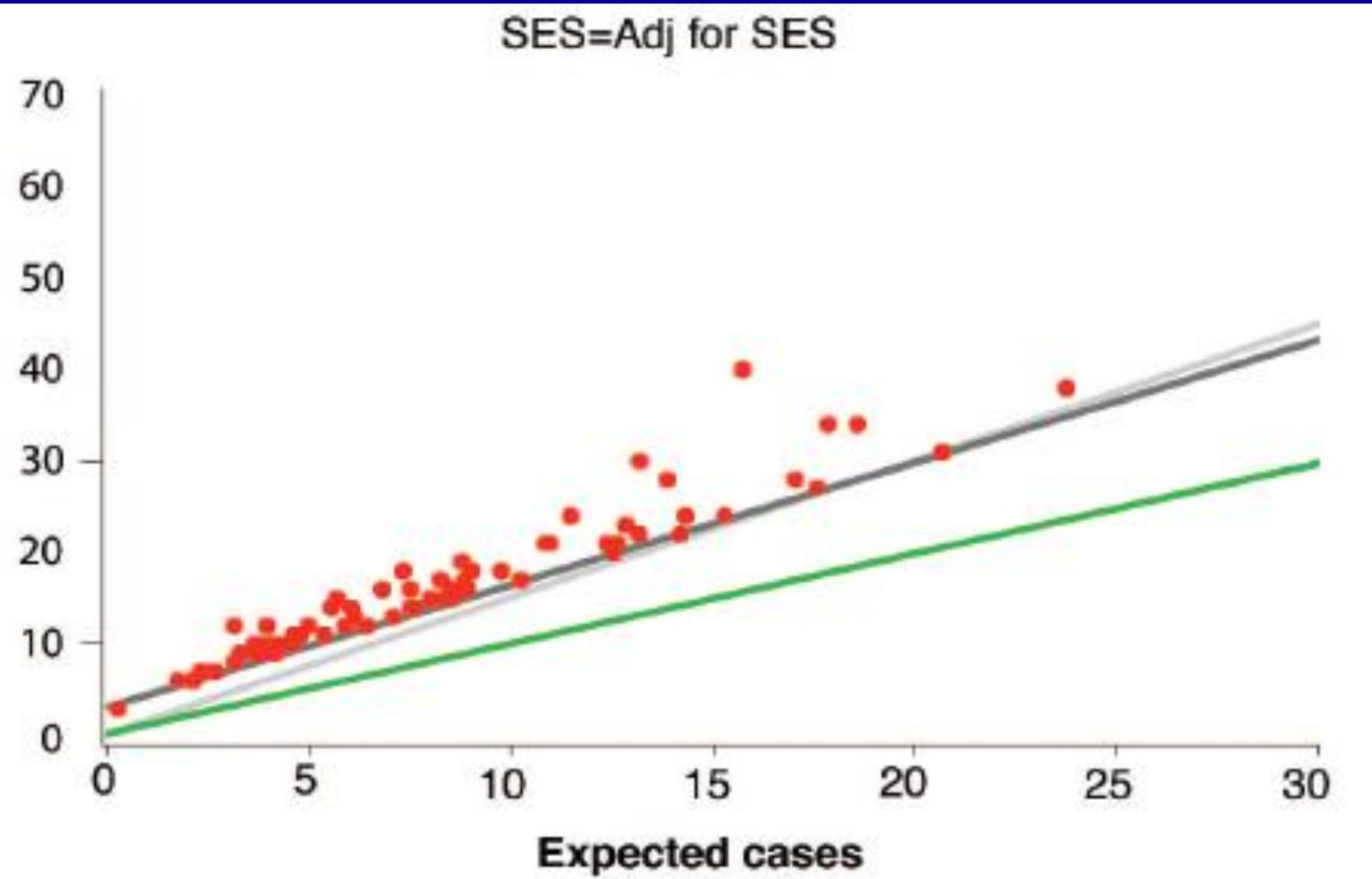
Malignant Melanoma



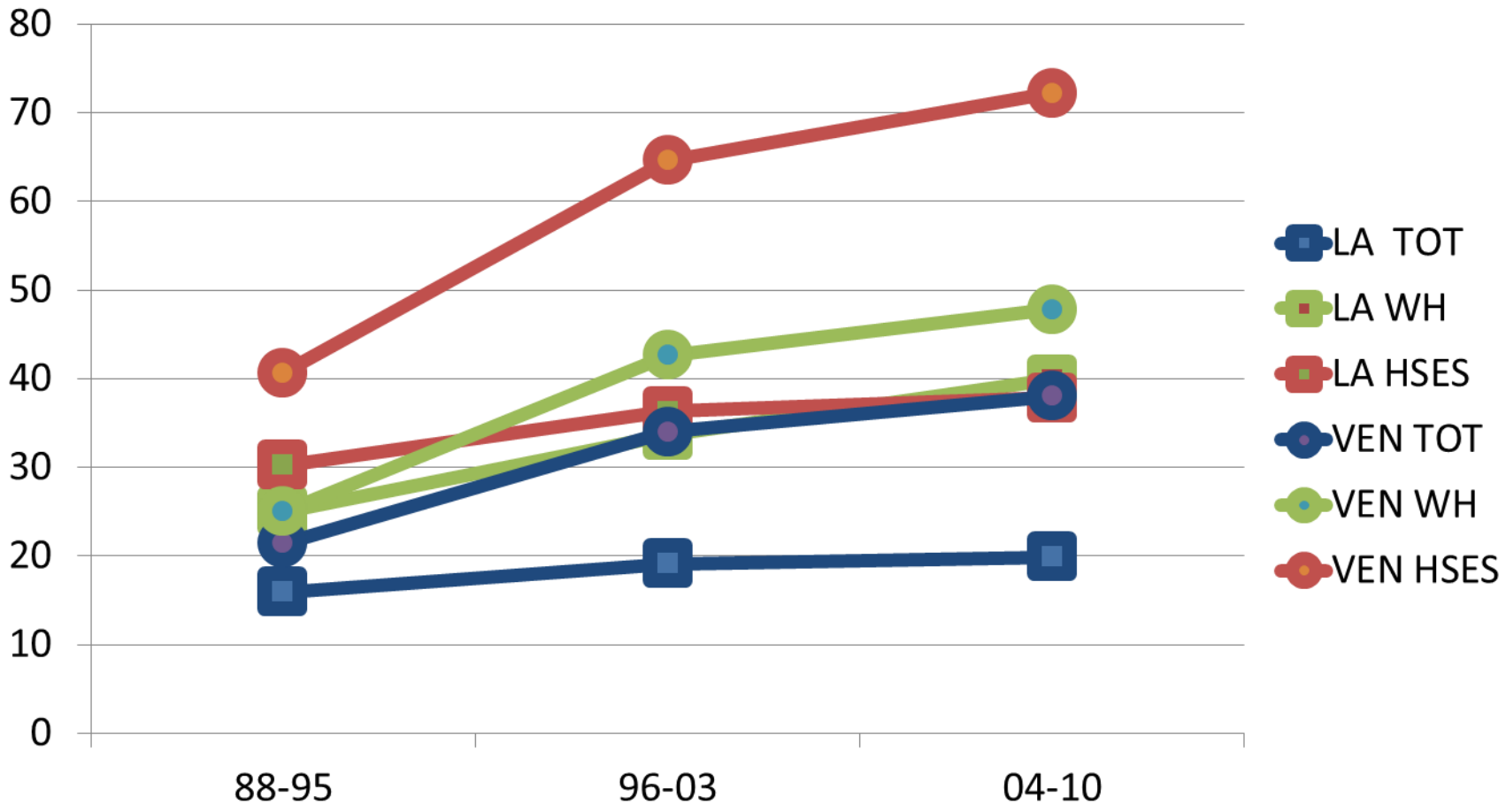
Malignant Melanoma



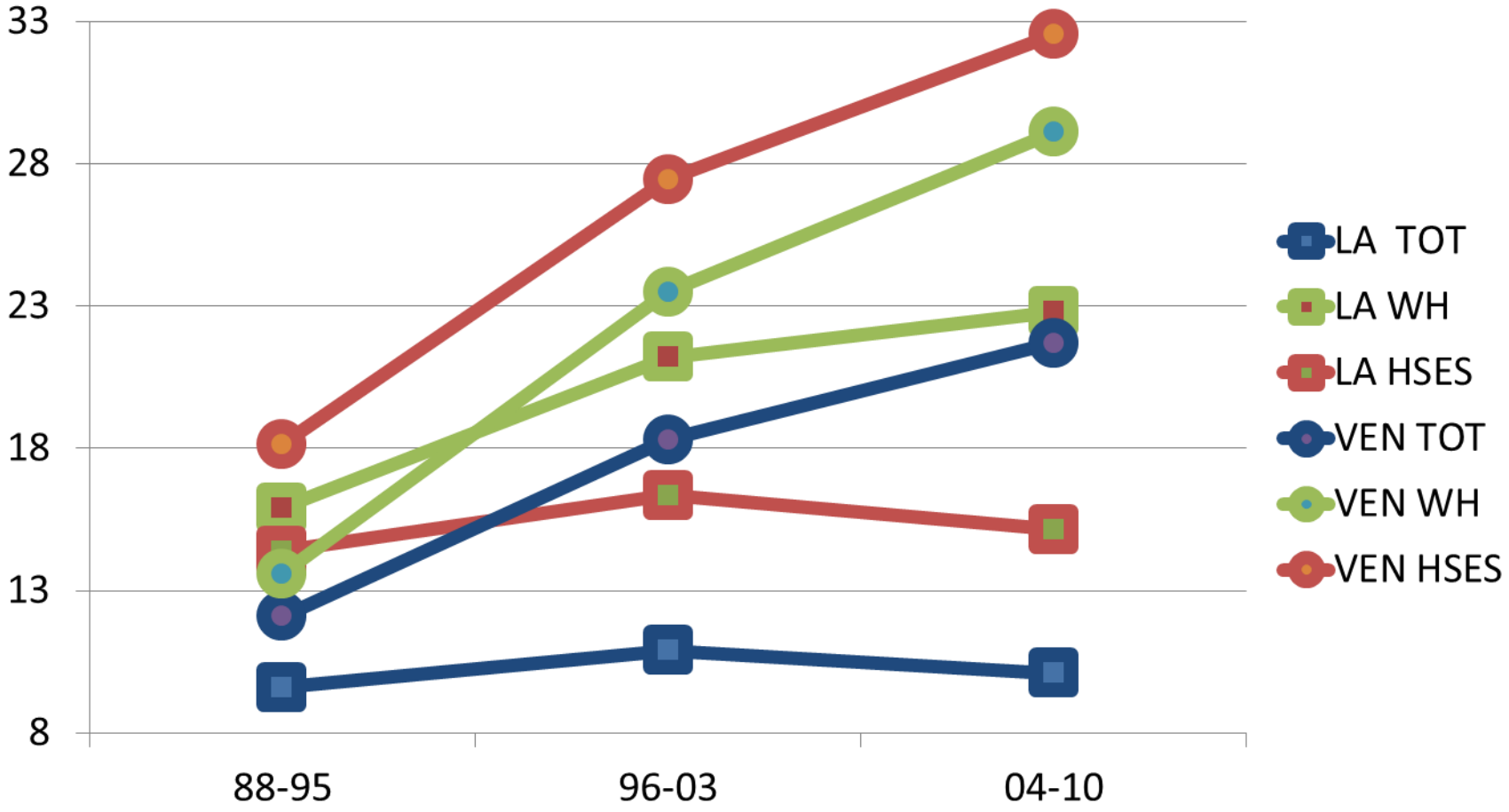
Malignant Melanoma-Adjusted for SES

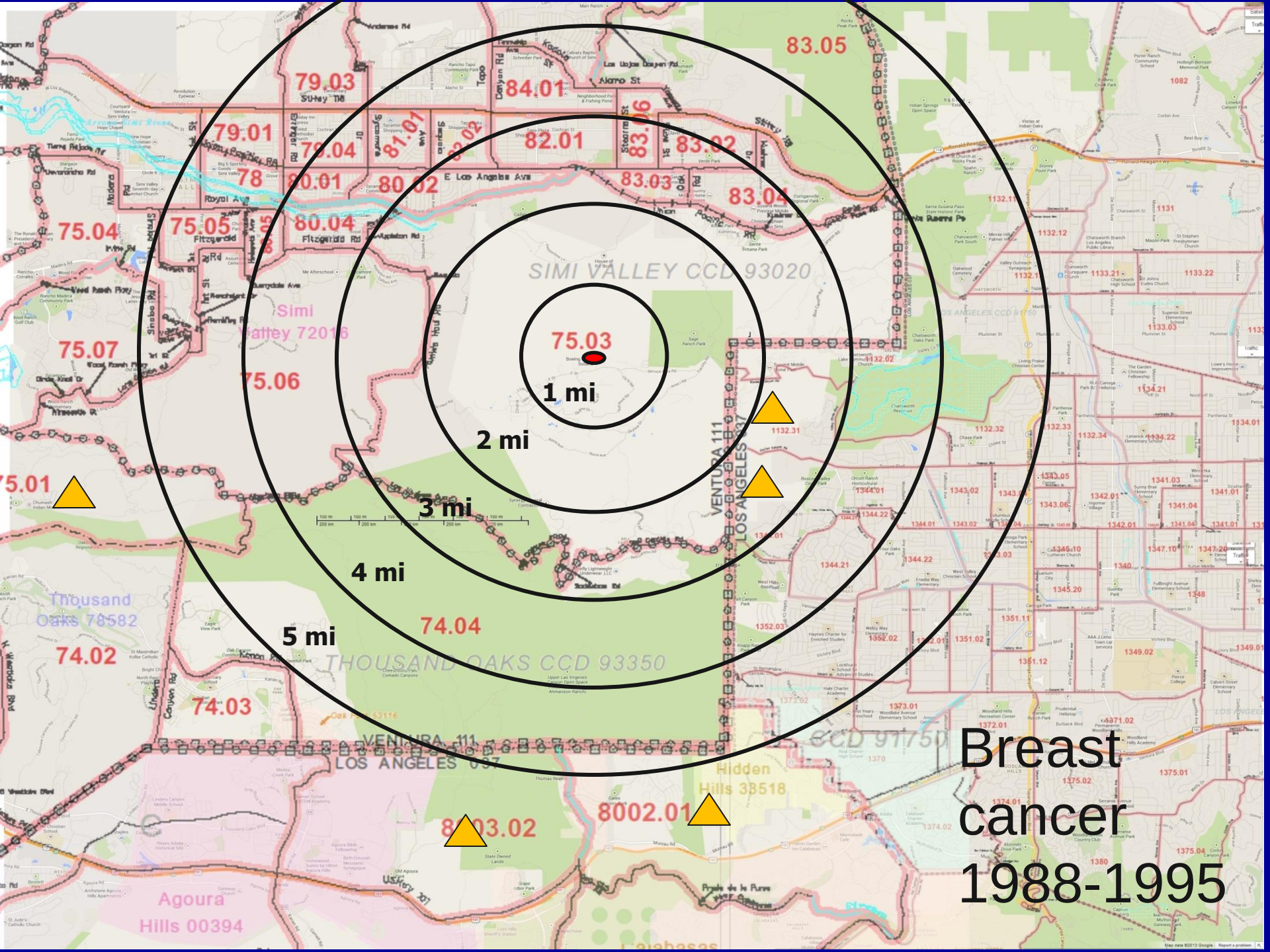


MALE MELANOMA



FEMALE MELANOMA

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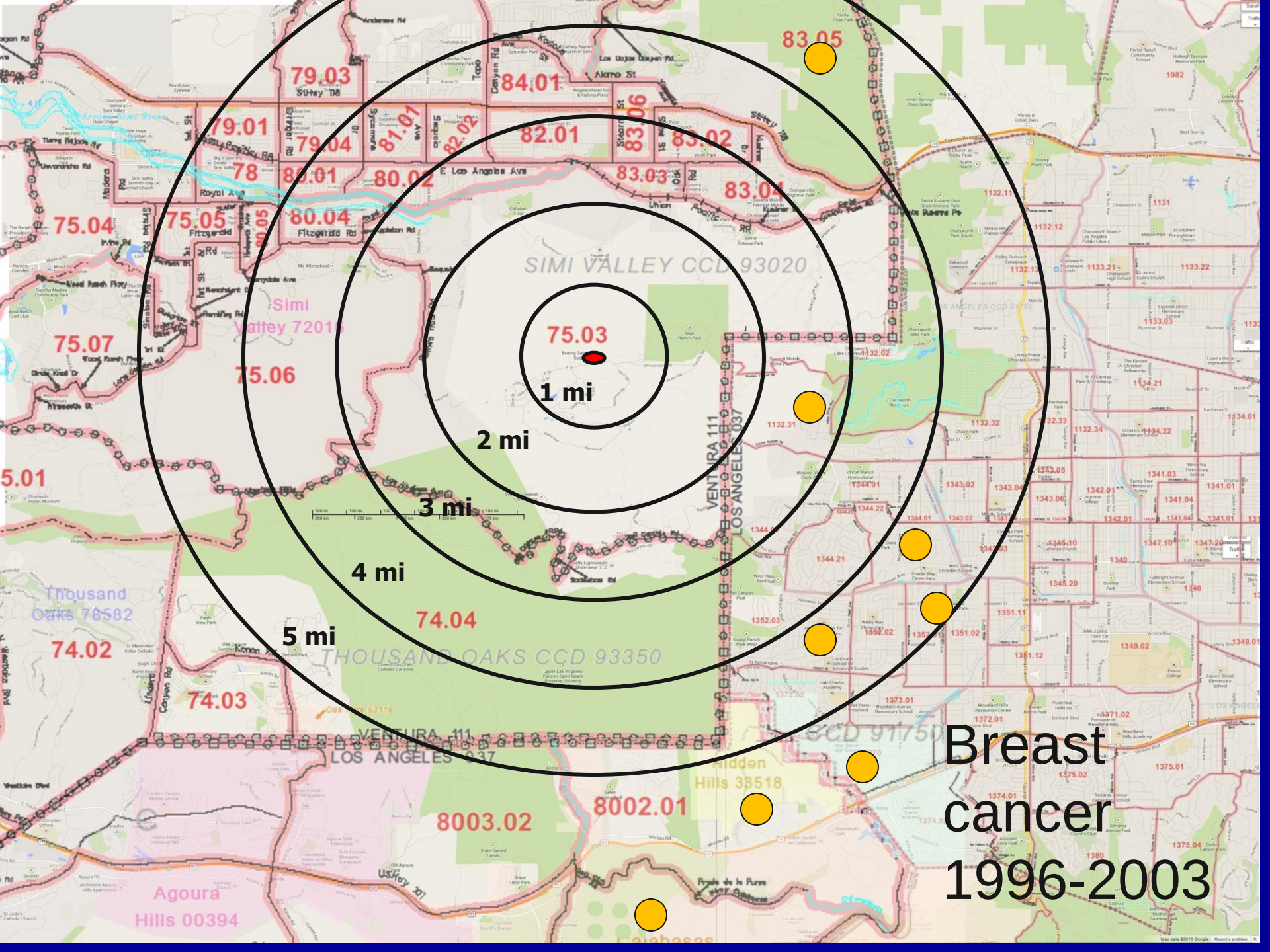
Breast cancer 1988-1995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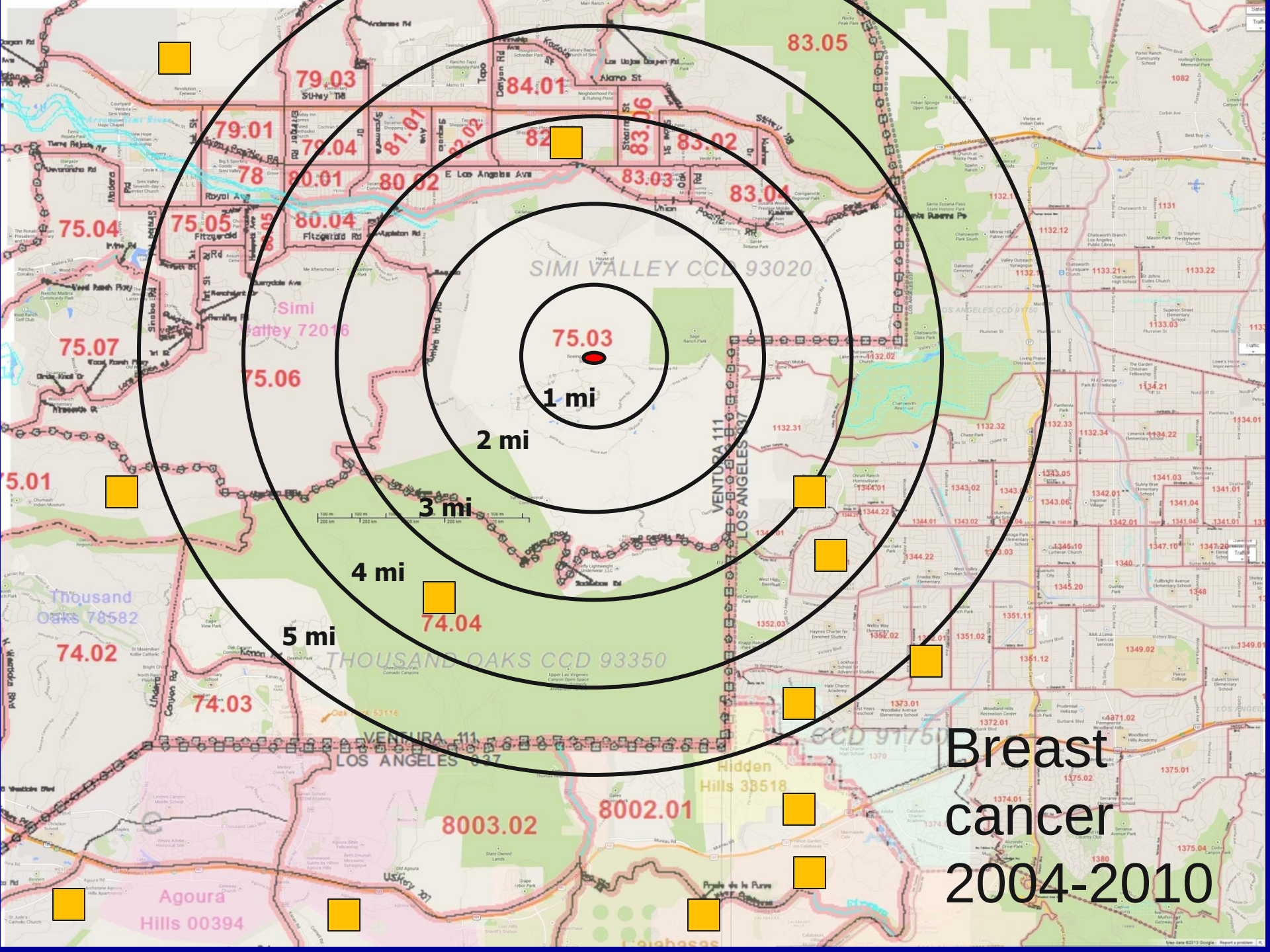
Breast cancer 1996-2003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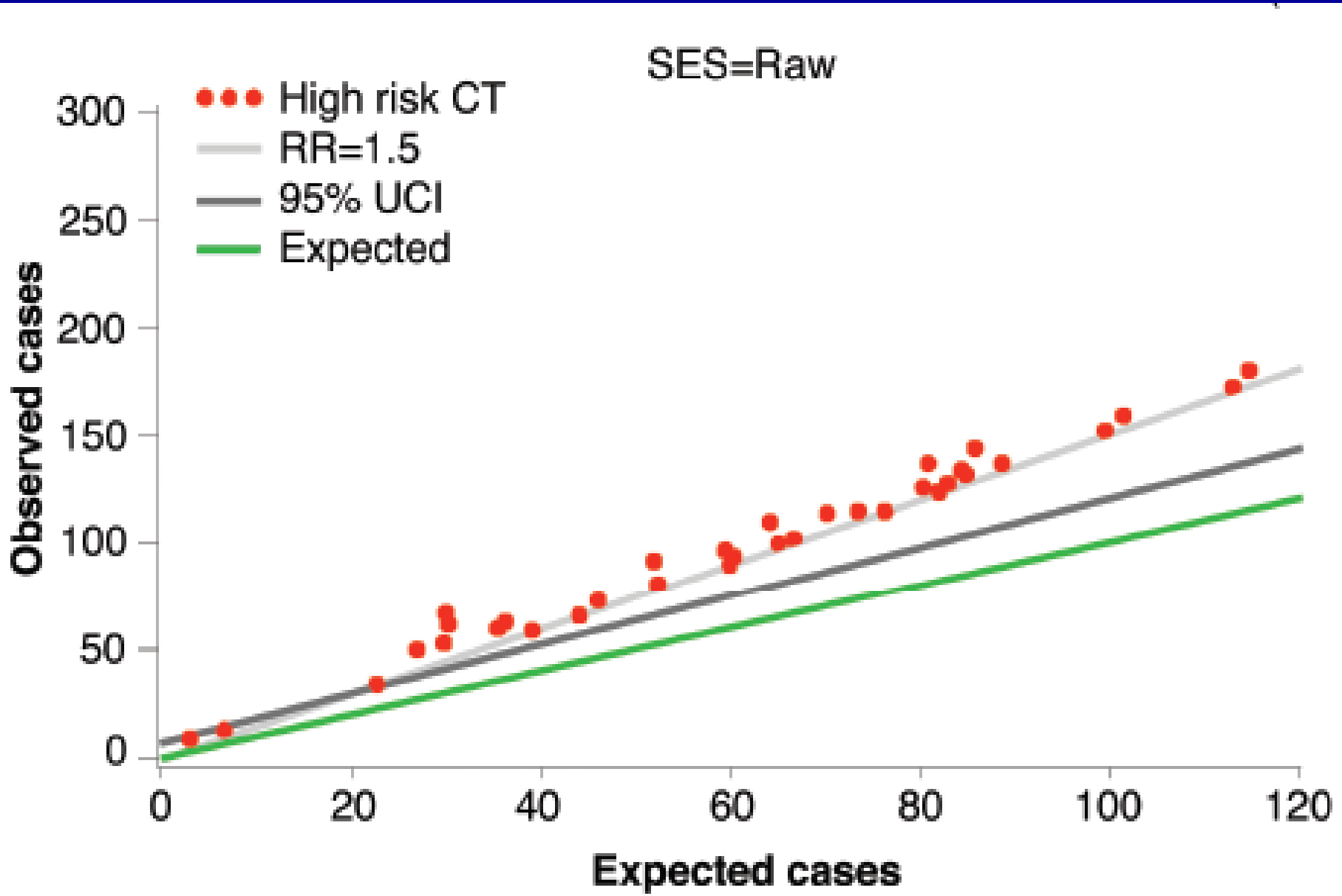
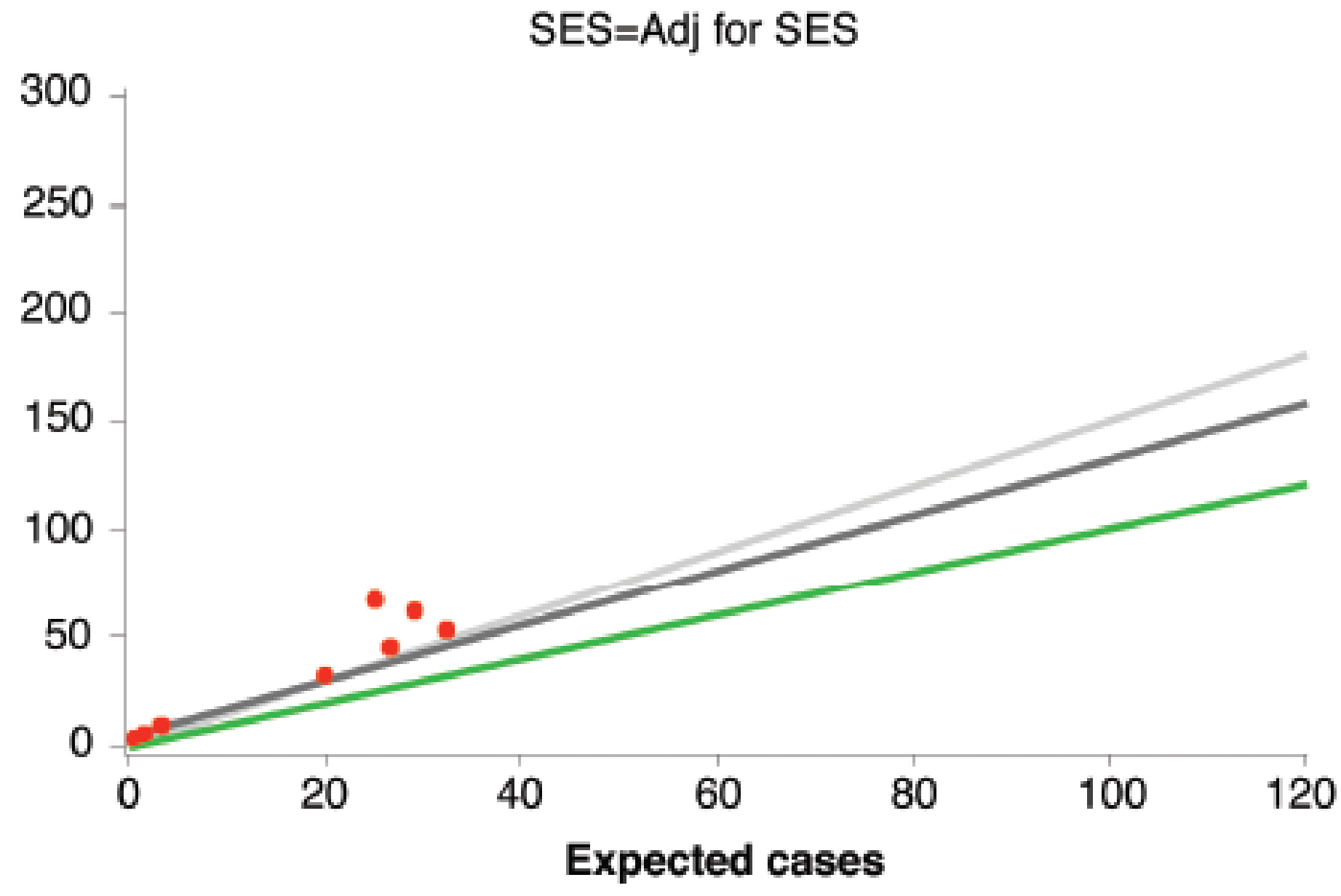
Breast cancer 2004-2010

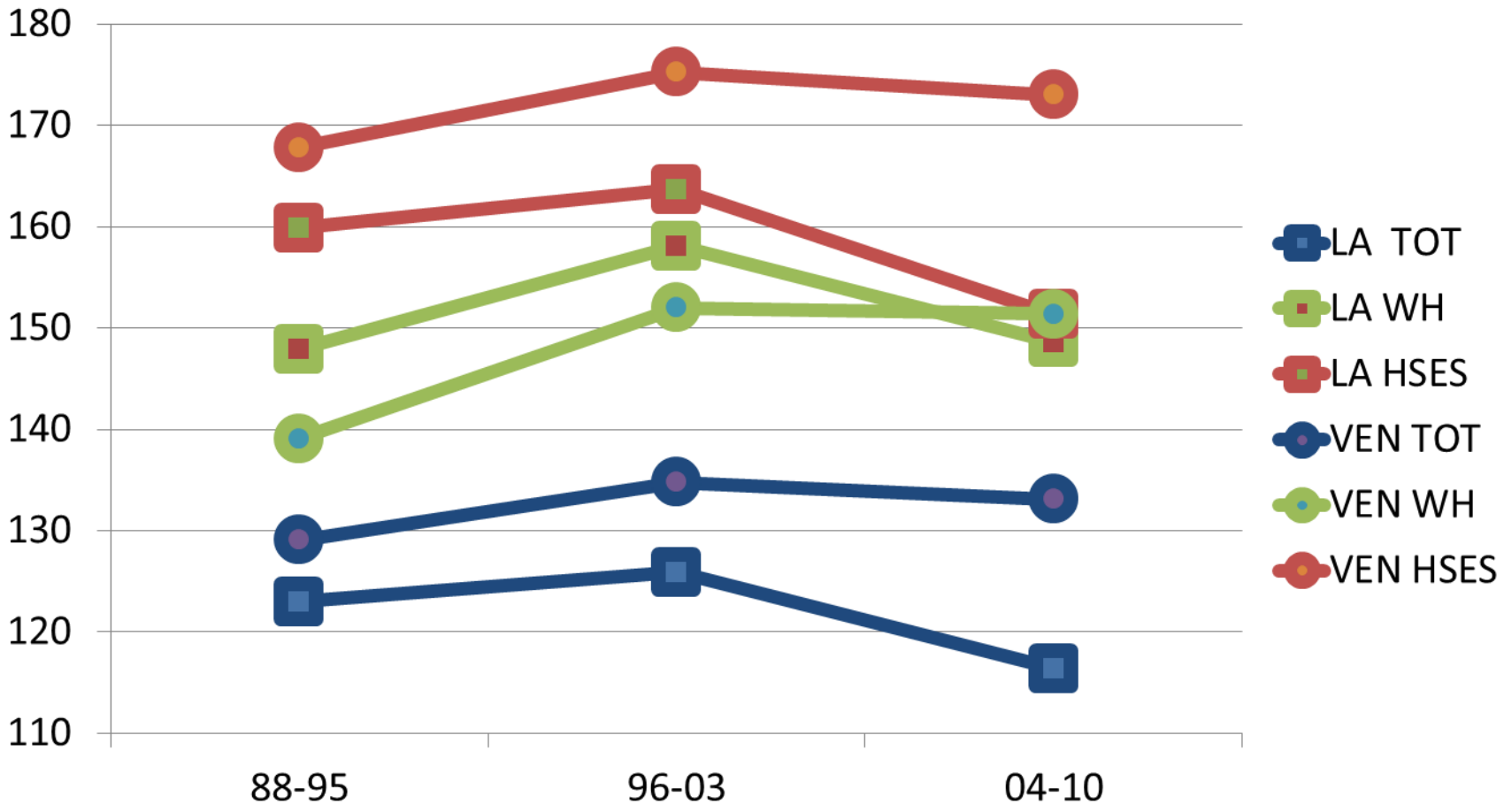
Female Breast Cancer

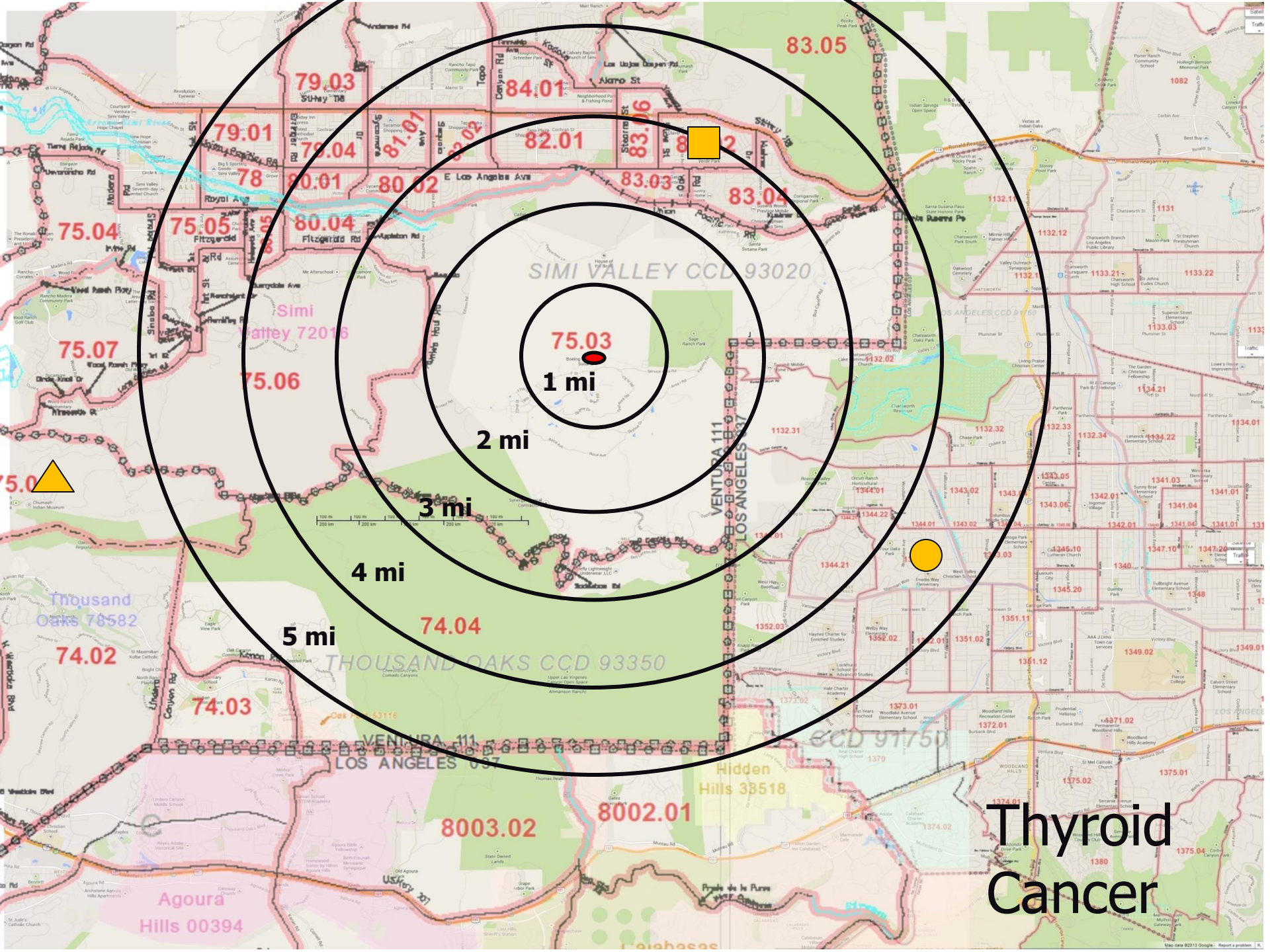


Female Breast Cancer



FEMALE BREAST




Thyroid Cancer
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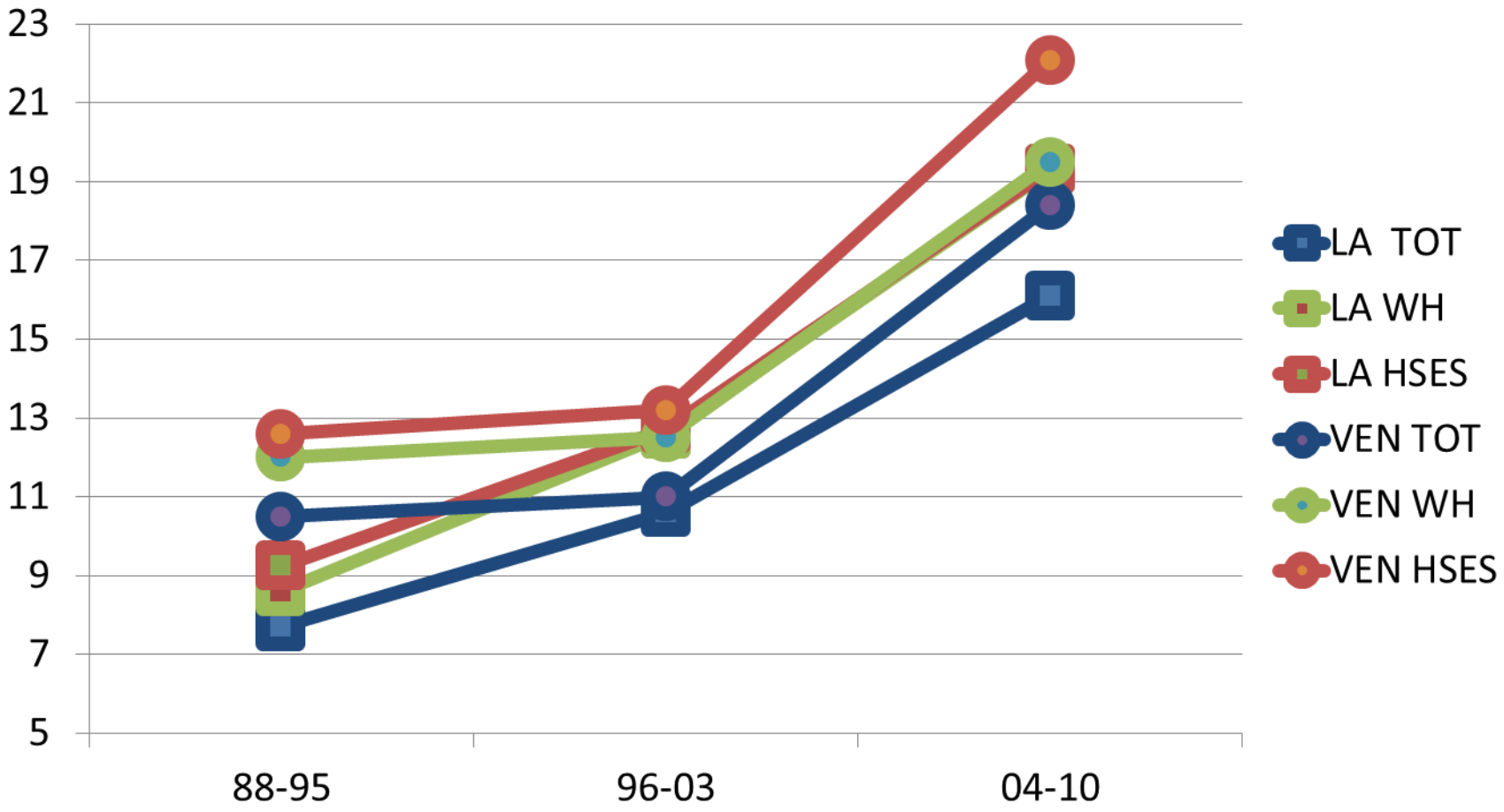
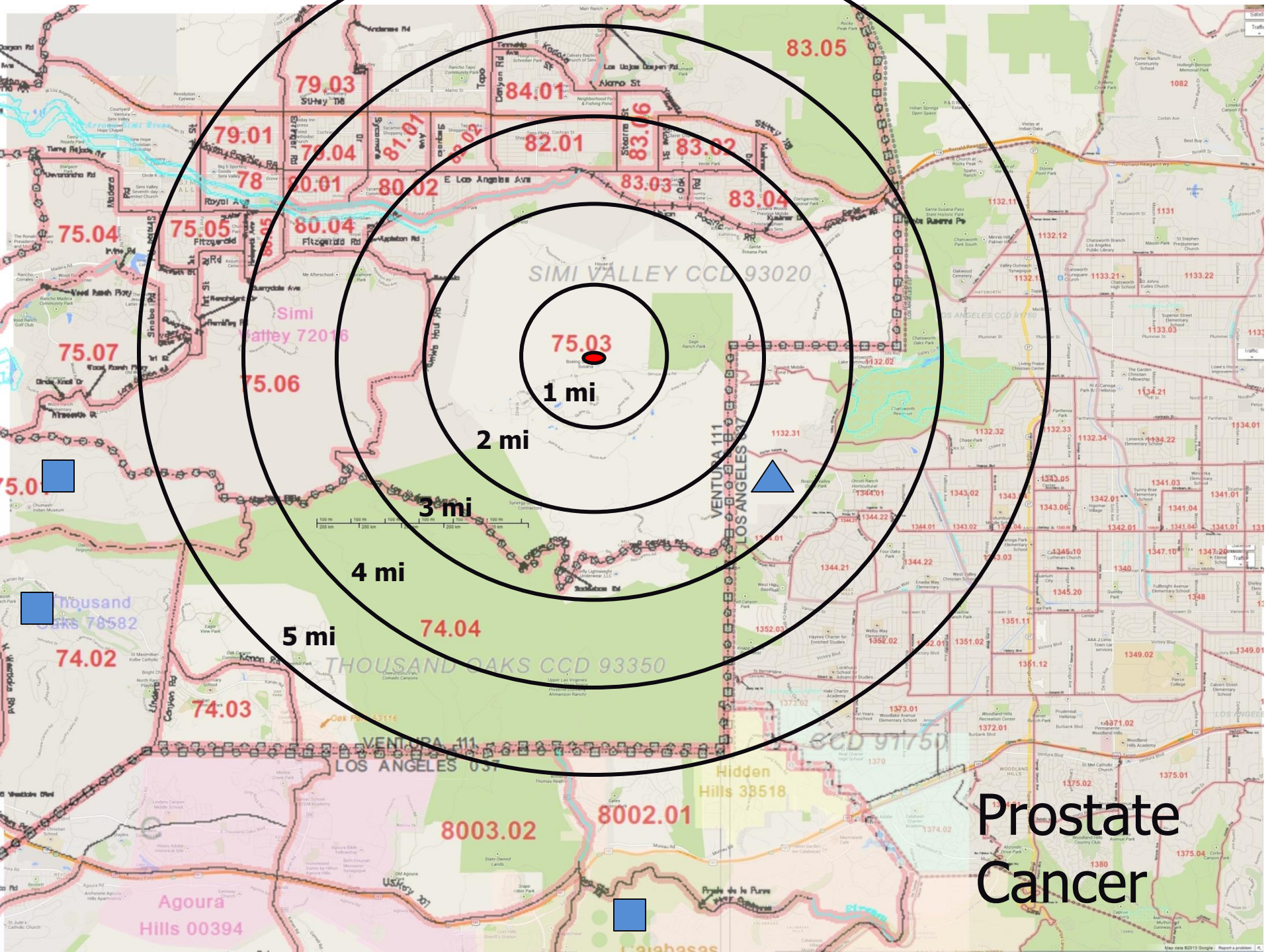
FEMALE THYROID




Prostate Cancer
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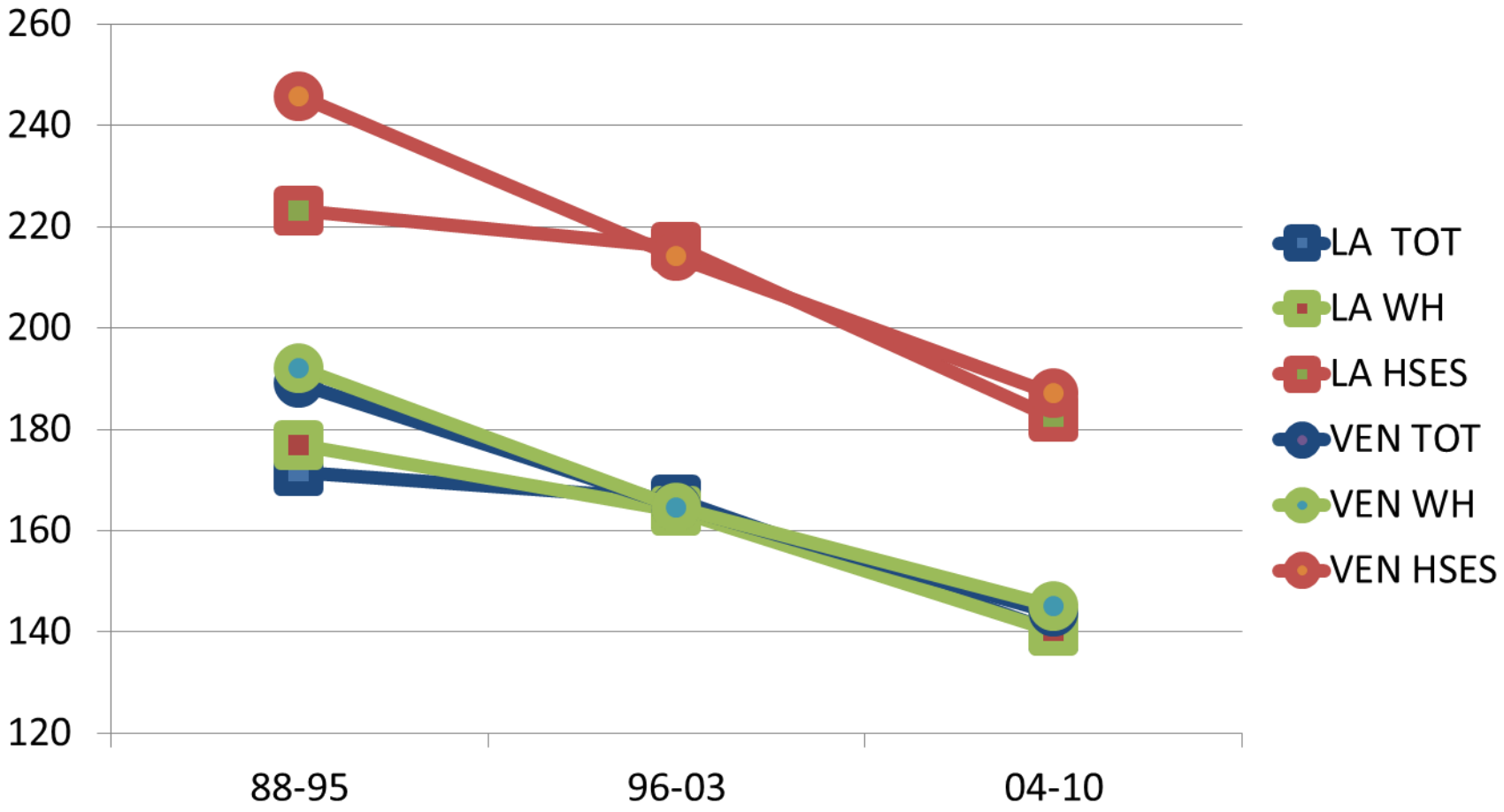
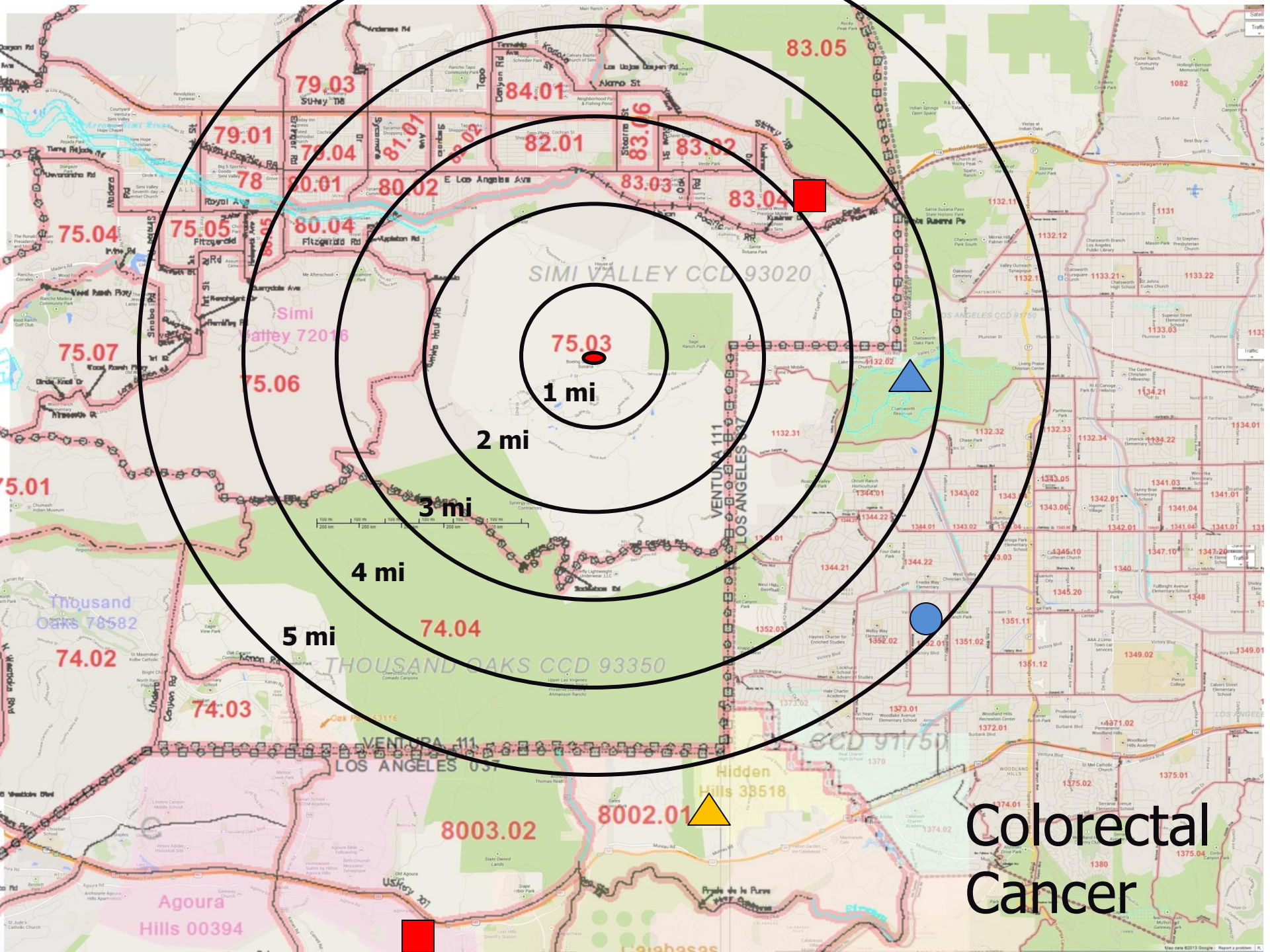
MALE PROSTATE




Colorectal Cancer
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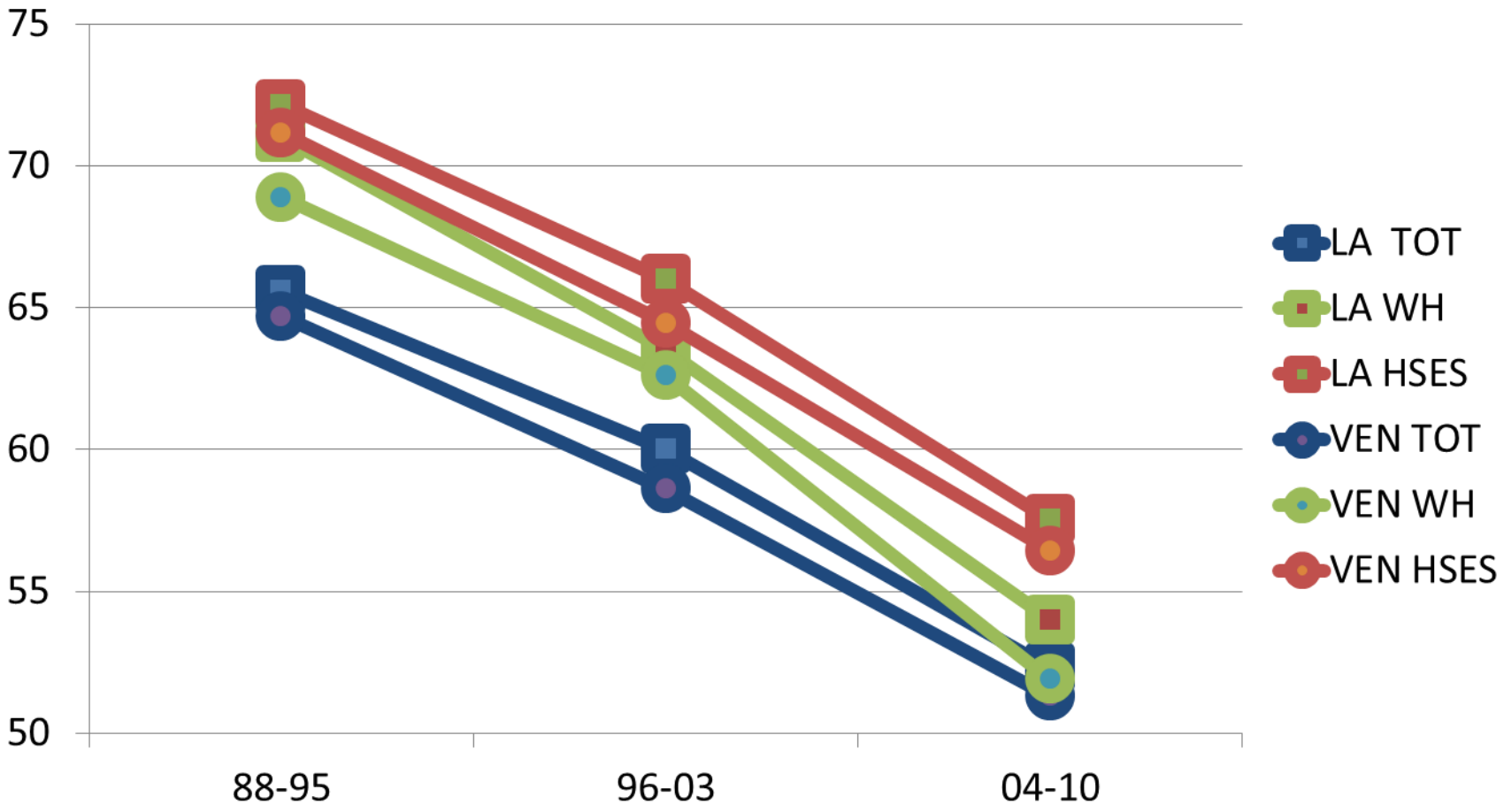
MALE COLORECTAL



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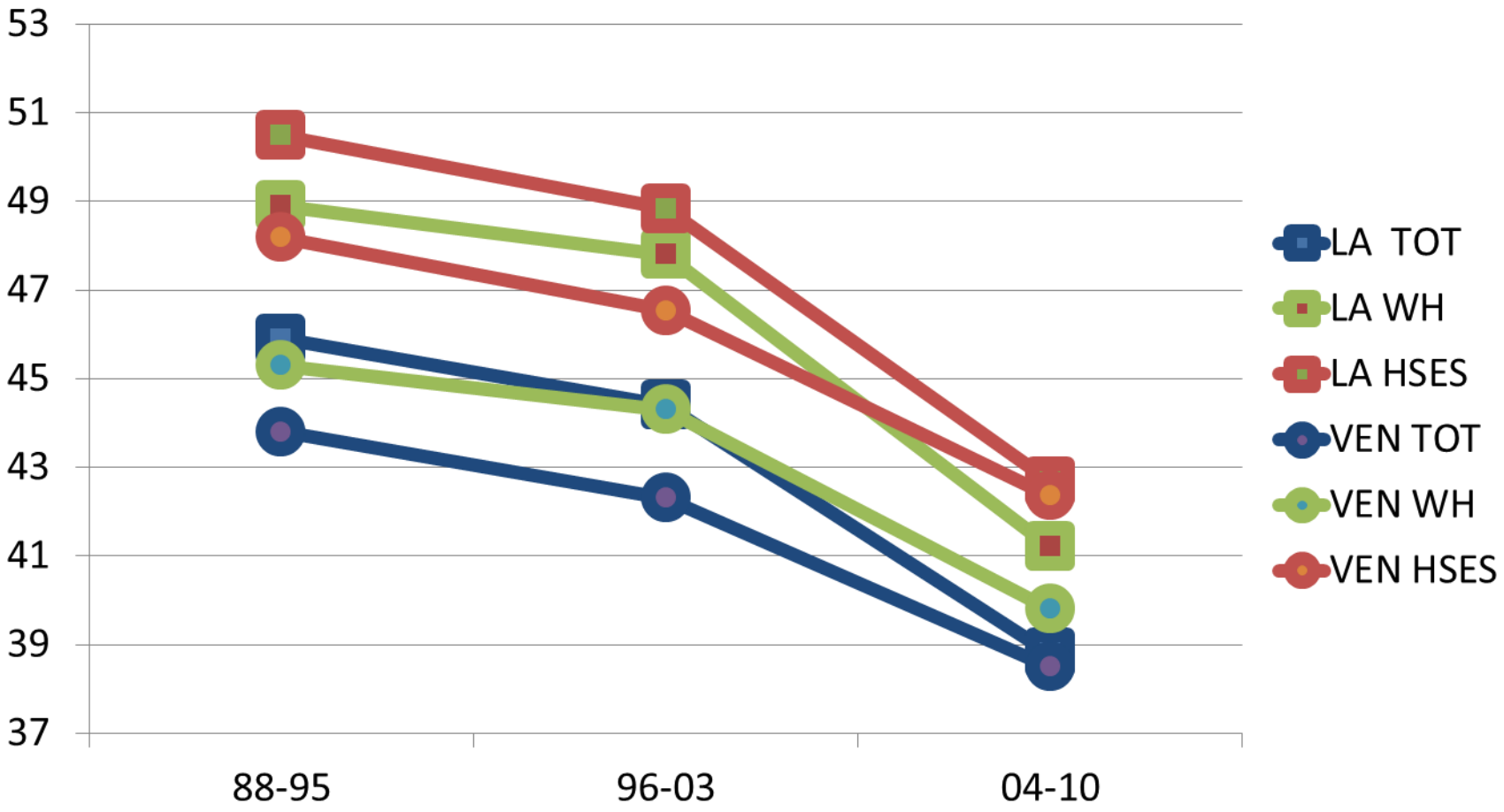

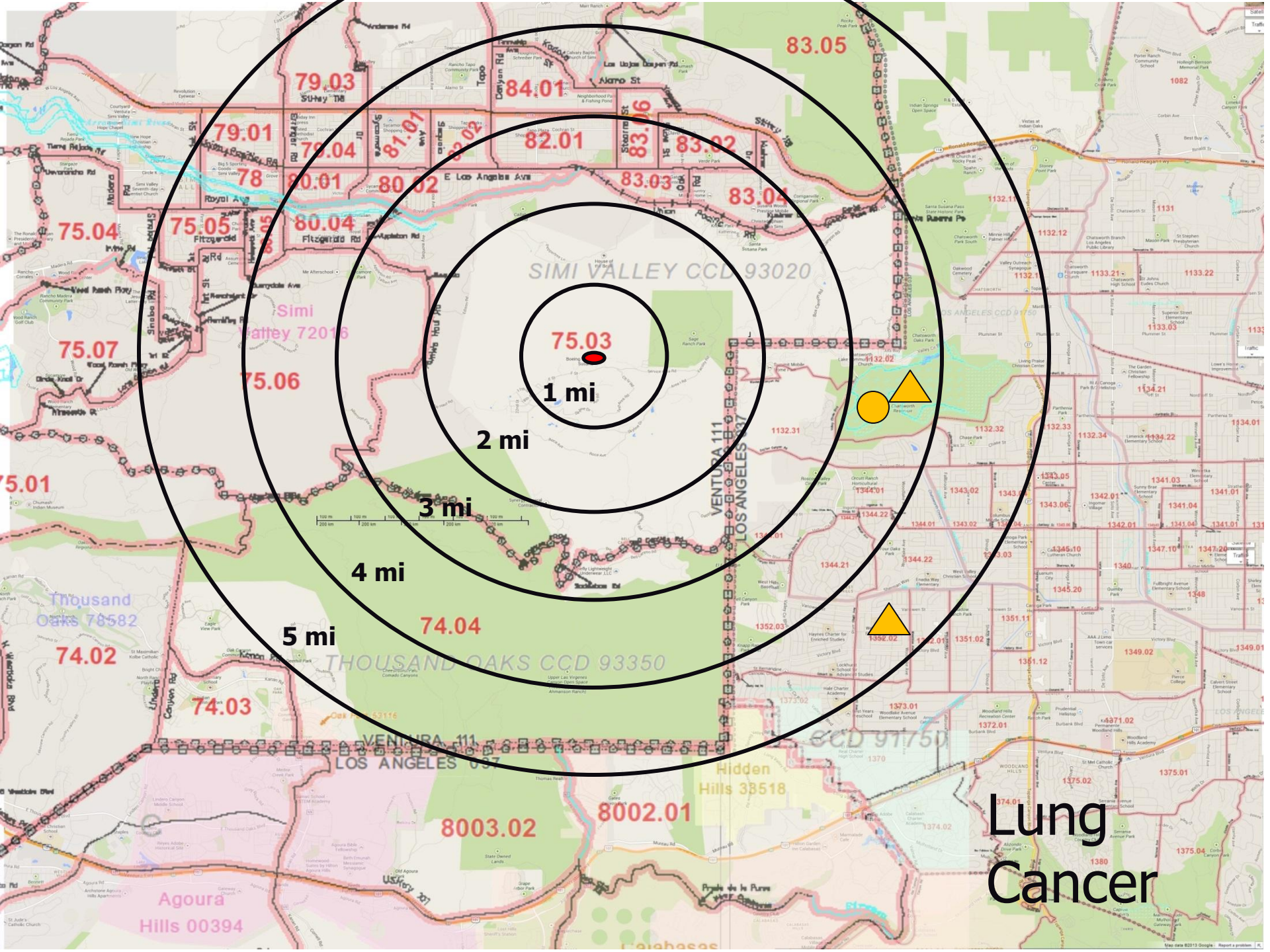
Lung Cancer
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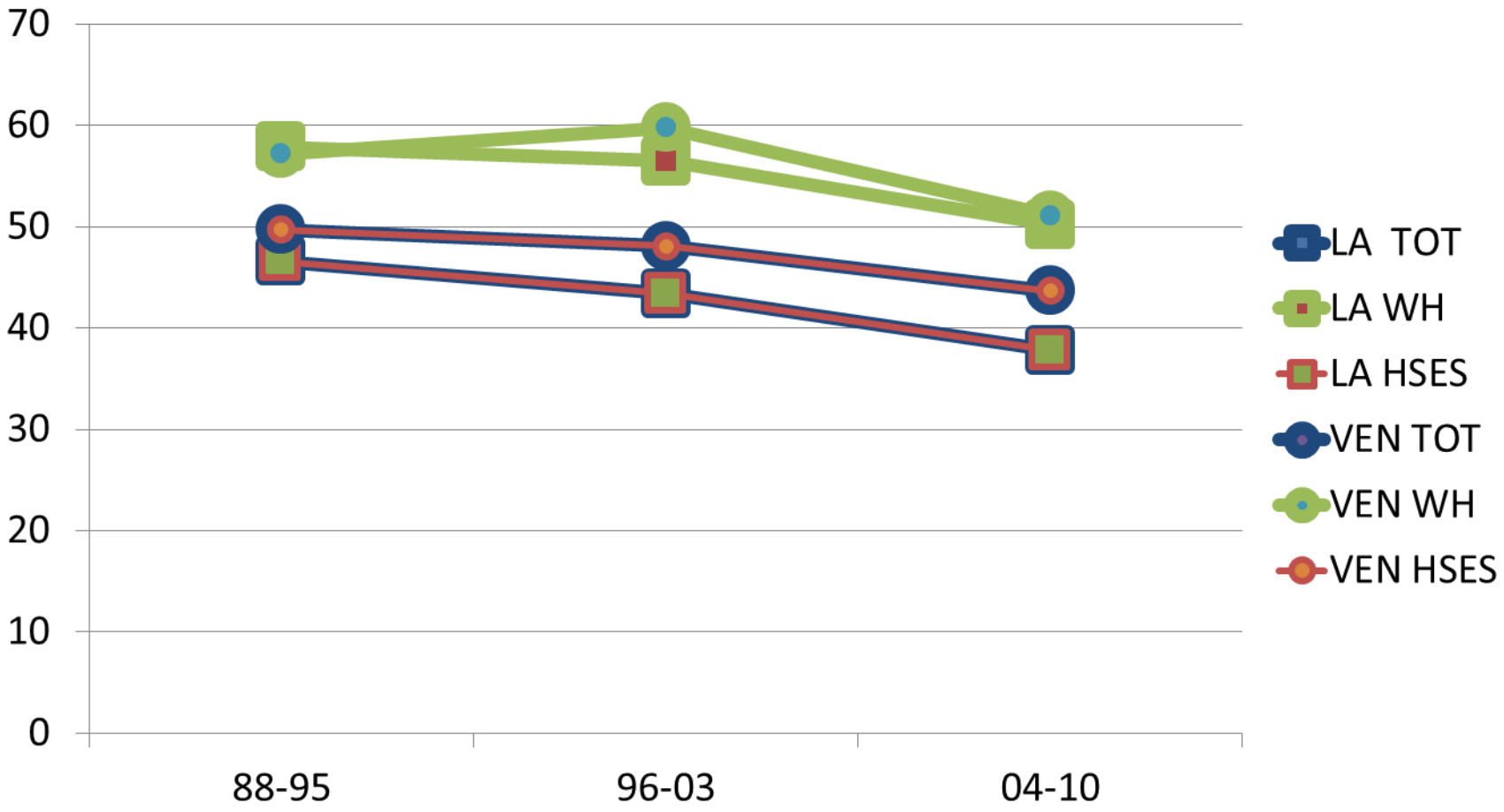
FEMALE LUNG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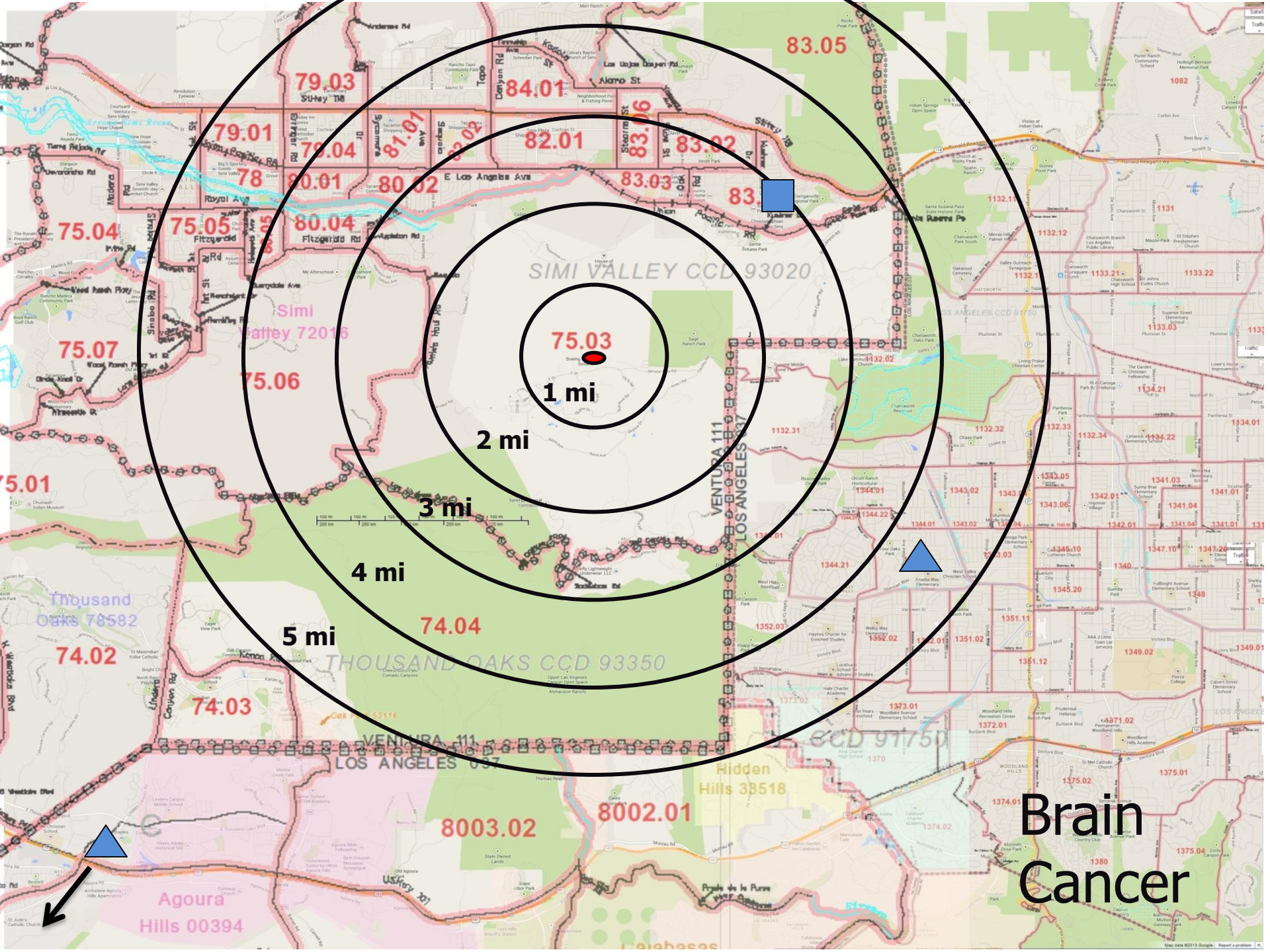
Likely effects of Lifestyle

Some clustering of risk is expected

- Breast and Malignant Melanoma
  - Known strong risk of race and high income/education
- Prostate and Thyroid cancers
  - Known to often not progress; commonly found by asymptomatic screening (PSA, ultrasound) with high access to care (high income/education)
- Lung and Colorectal cancers
  - Strongly determined by habitual factors:
    - Smoking for lung, diet/physical inactivity for colorectal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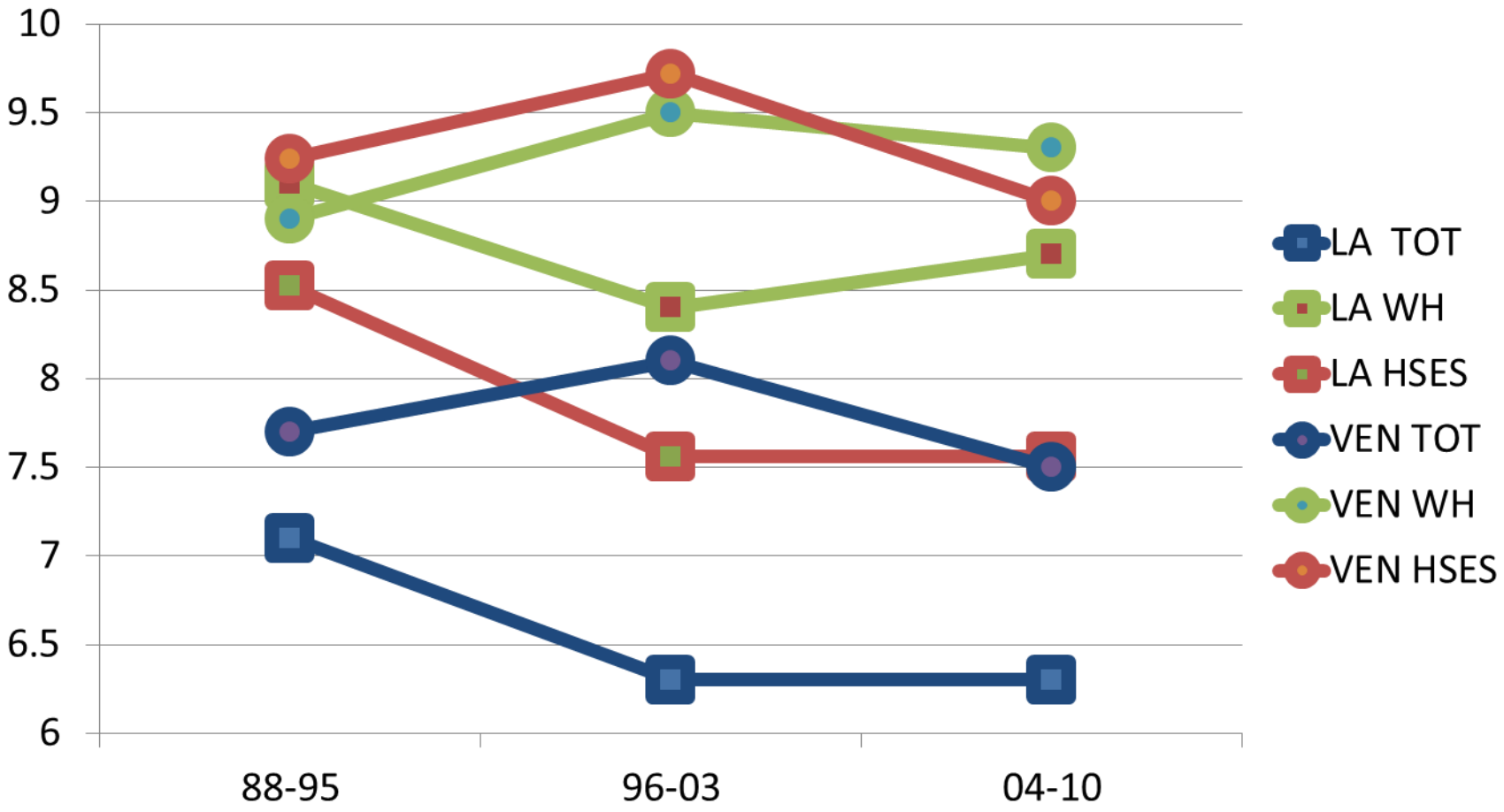
MALE BRAIN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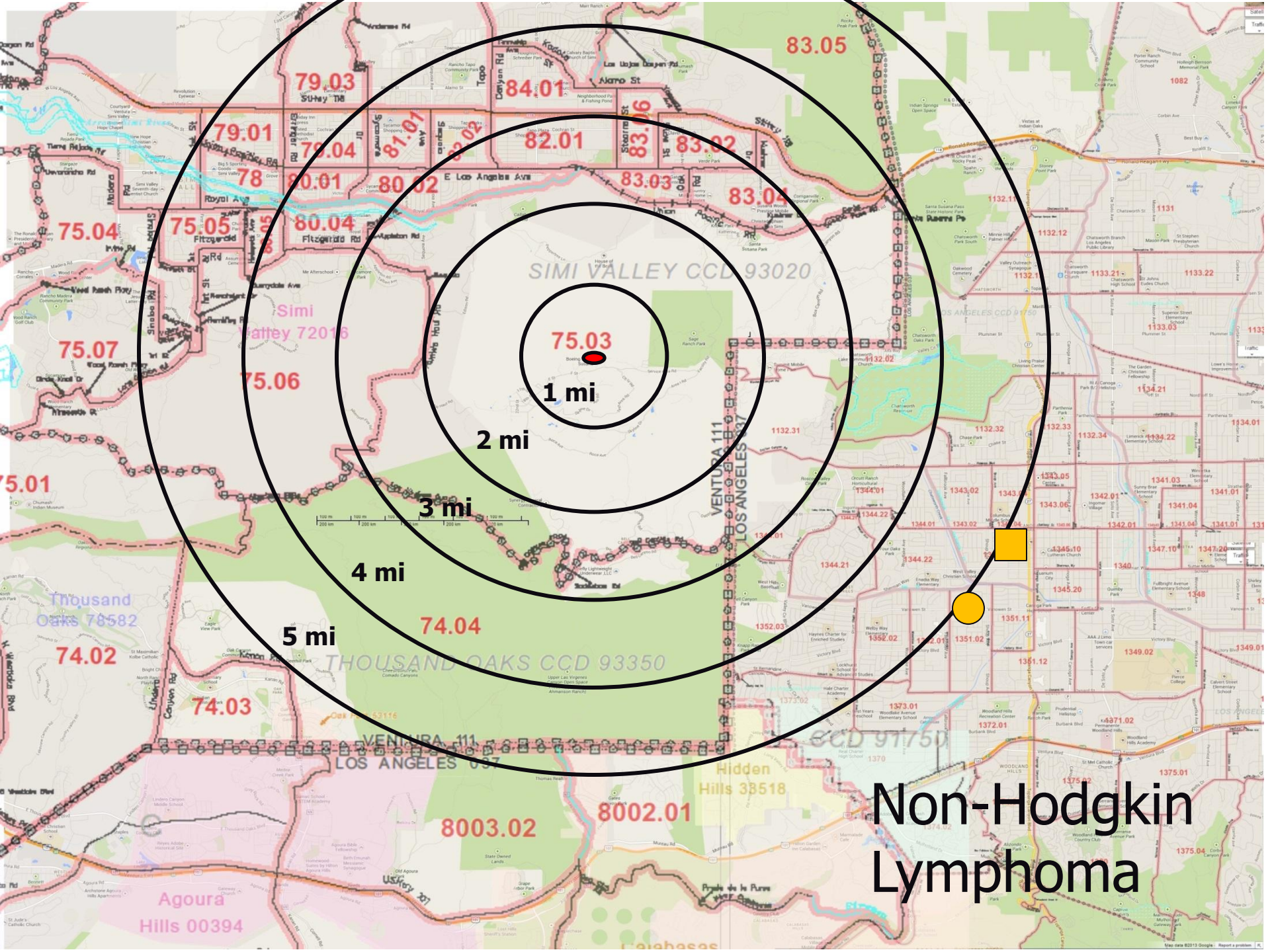
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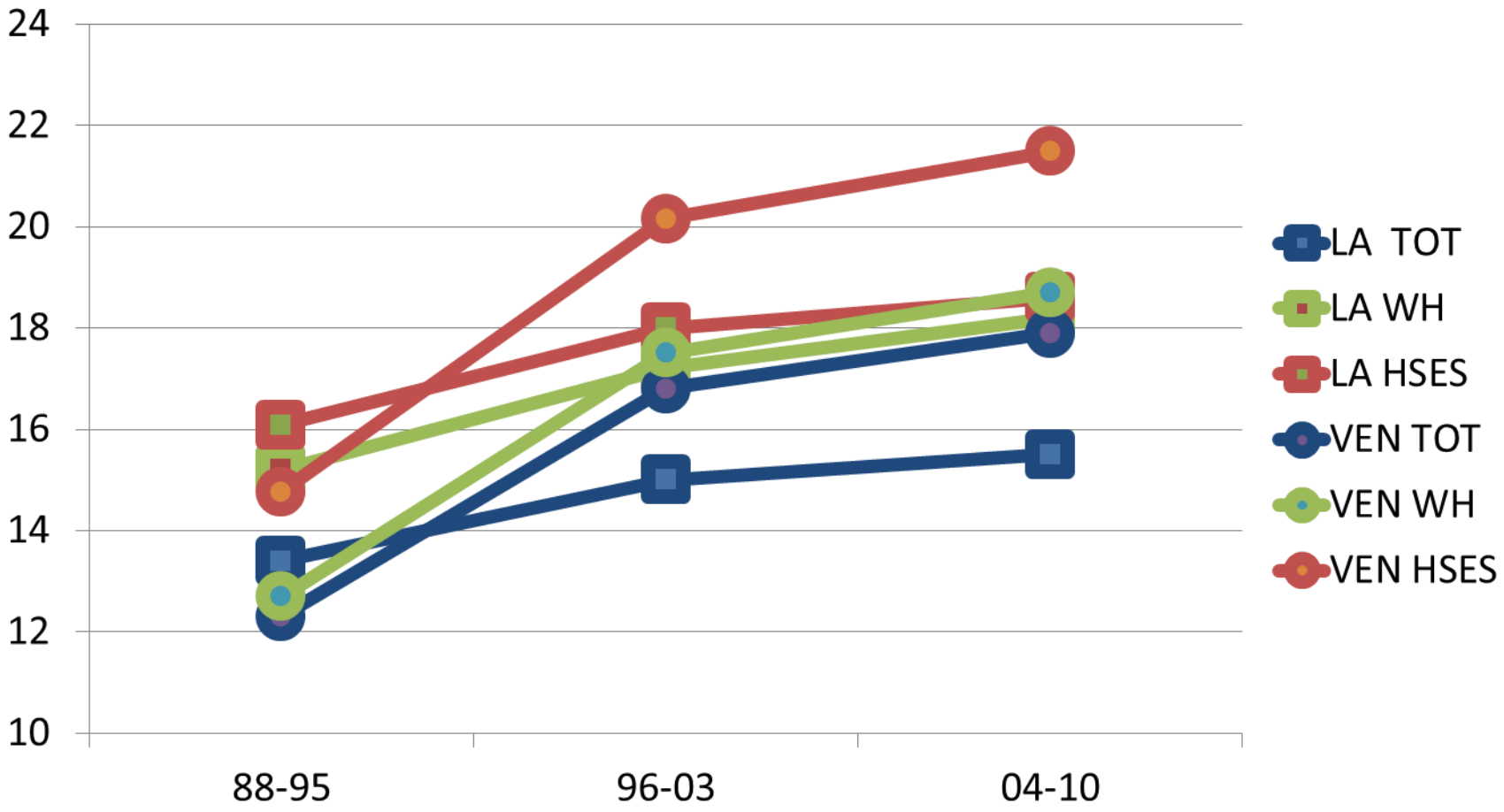
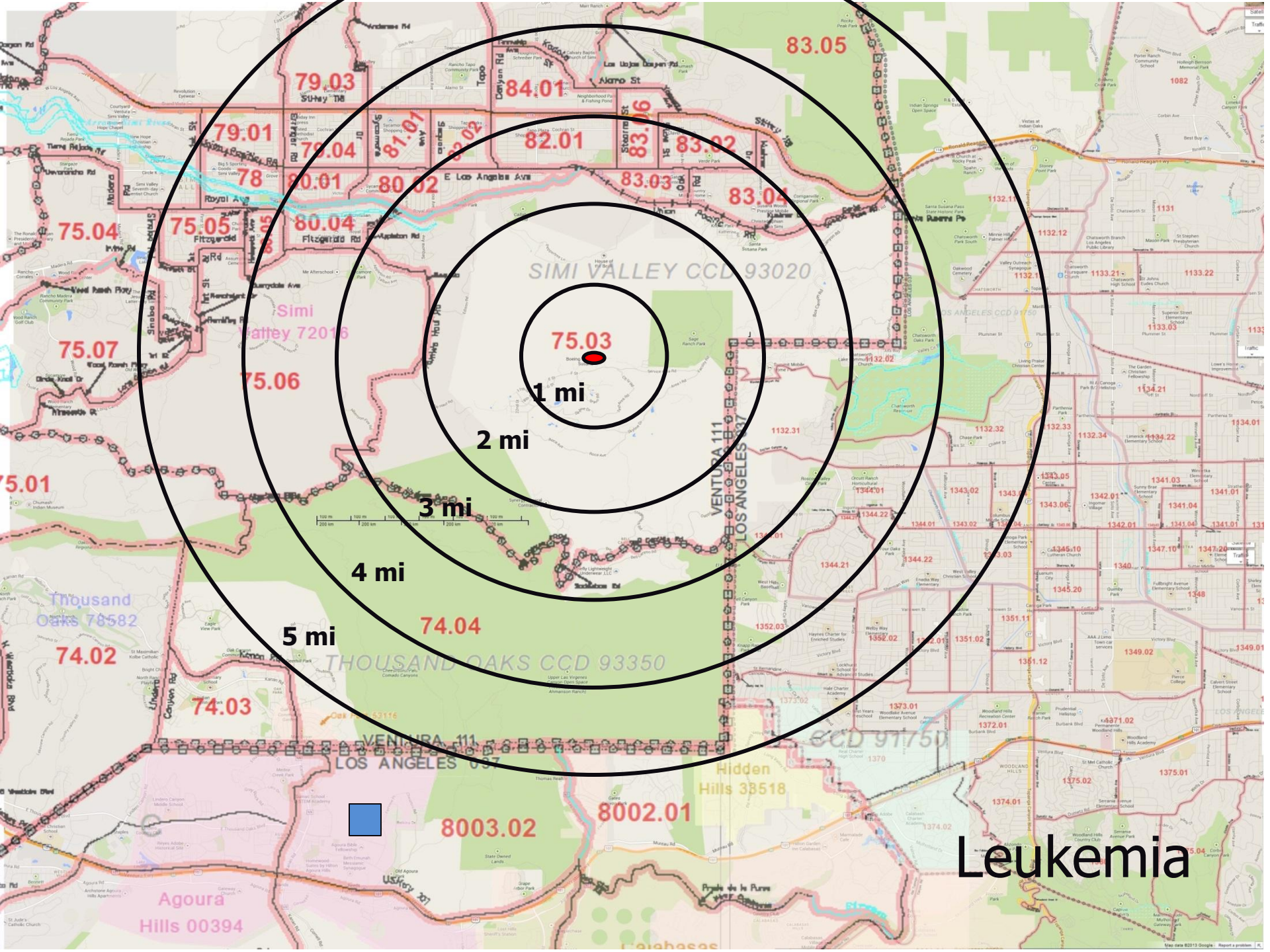
FEMALE NON-HODGKIN'S LYMPHOMA

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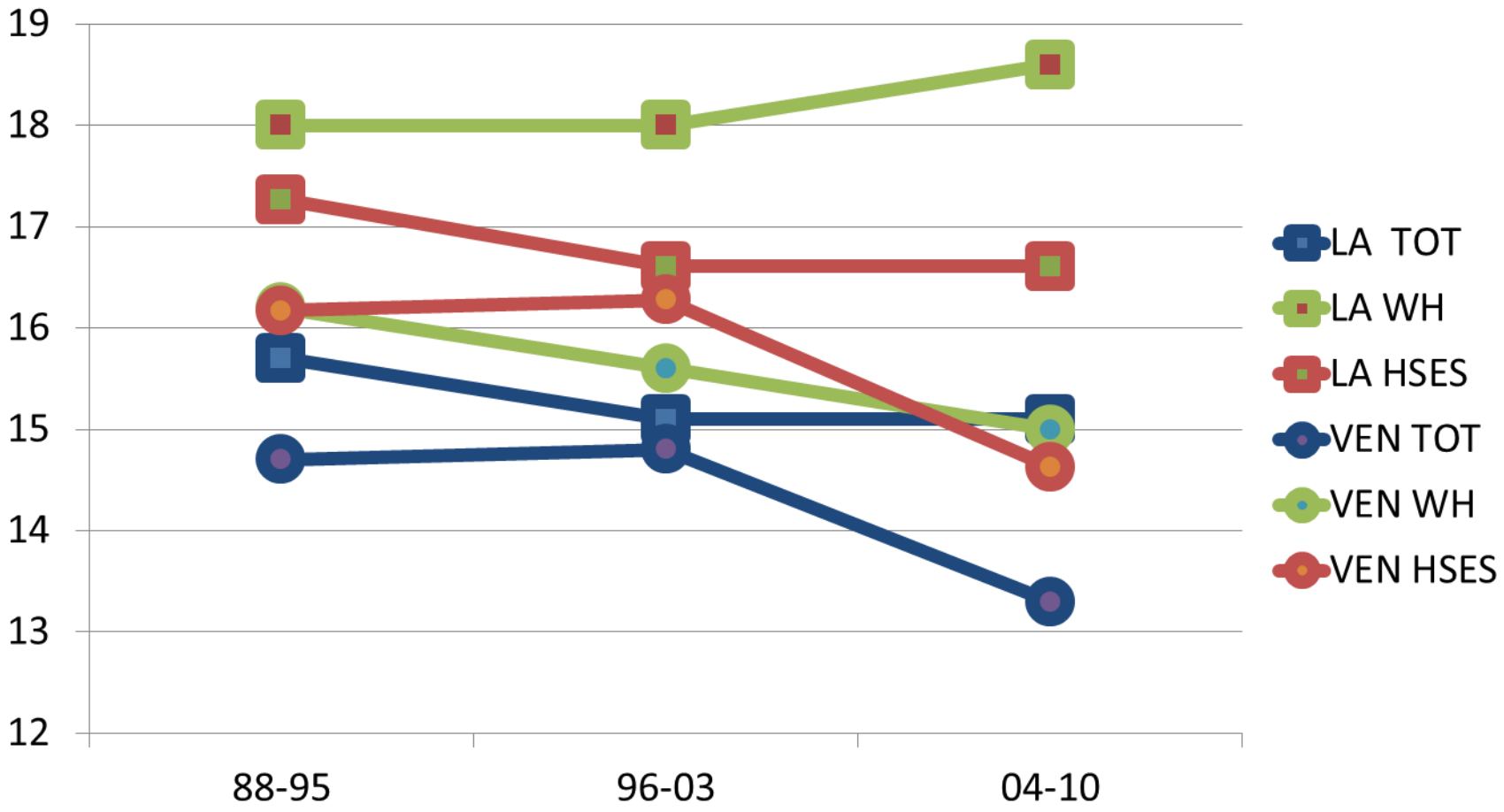
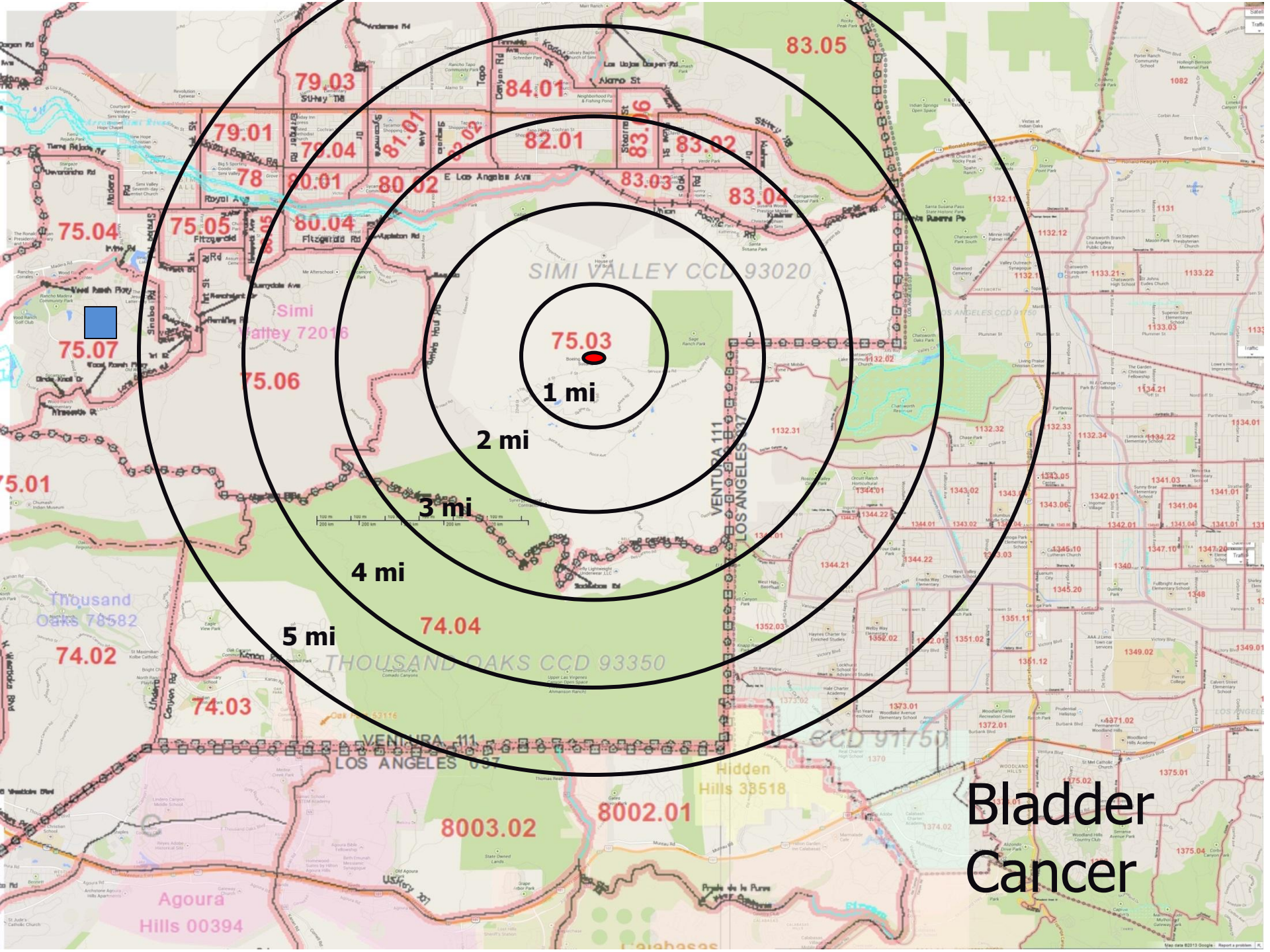
E Los Angeles Ave

MALE LEUKEMIA



These cancer rubrics oversimplify causal heterogeneity

- Brain: several excess cases are benign, slow-growing tumors with different causes
- Non-Hodgkin lymphoma excess includes at least five different malignancies known to have different causes
- Leukemia excess also is made up of three common and several uncommon varieties
- In each of these, the “high-risk” tracts identified were no more numerous than was expected by chance, and included cases of diverse , most having no known environmental causation


Bladder Cancer
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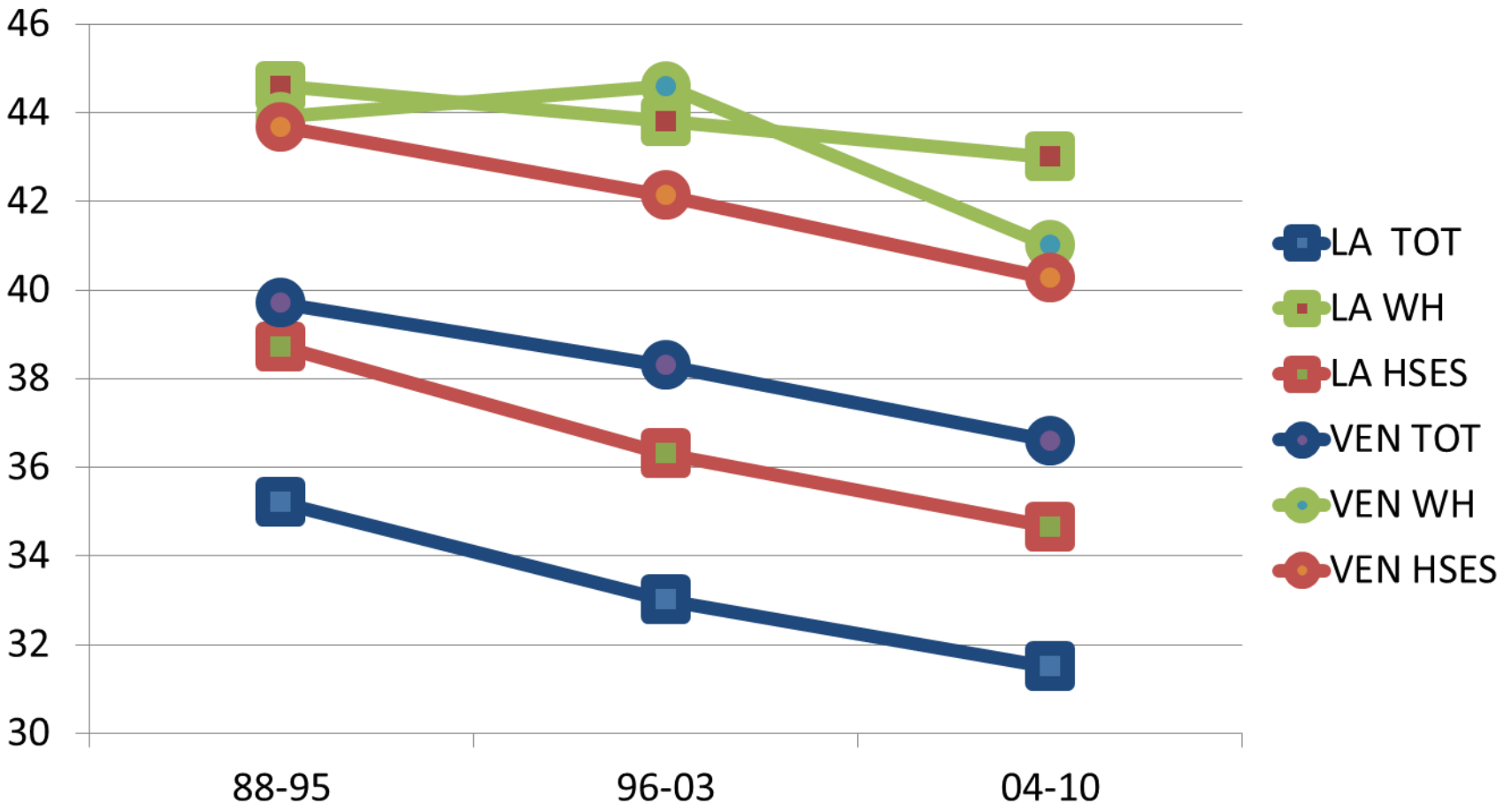
VENTURA 111
LOS ANGELES 037
E Los Angeles Ave
Alamo St
Fitzgerald Rd
Royal Ave

MALE BLADDER



Excess of bladder cancer in one tract in 2004-2010

- Extreme finding: RR >4
- Case tumors had the same common histology
- Most residences scattered, but several are within one mile
- The most prevalent cause of bladder cancer is smoking
- Environmental causes are industrial, waterborne arsenic
- Diagnoses were not clustered in time
- The tract is more than 5 miles to the west of SSFL
- Residential community: no known exposure, specifically no high arsenic in tap water, no local industry, no increase in kidney cancer (another arsenic outcome)

- 66% of the cases were >75 at diagnosis, and all but one of those was over 85.
- Census may have undercounted seniors

Neoplasm	"Significant" tract-periods	Observed/ Expected number per tract	Interpretation	Estimated number of CA tracts with that many or more cases
NHL	2 (3 exp. by chance)	8/2.5 12/5.3	No clustering of high-risk tracts No evidence of proximity to SSFL Mixture of cell types, no trend	50-100
Brain	3 (3 exp. by chance)	6/0.9 8/2.3 11/3.5	No clustering of high-risk tracts No consistent proximity to SSFL Mixture of cell types, no trend	10-50
Leukemia	1 (3 exp. by chance)	7/1.3	No clustering of high risk tracts No evidence of proximity to SSFL Mixture of cell types, no trend	10
Bladder	1 (3 exp. by chance)	11/2.5	No clustering of high risk tracts No evidence of proximity to SSFL No evidence of carcinogens Preponderance of elderly cases ? Smoking, census error	1-2

Conclusion

- It is not possible to completely rule out any offsite carcinogenic effects from SSFL

- No evidence of measureable offsite cancer causation occurring as a result of emissions from the SSFL was found.

- Further, no evidence of any cancer causation by any environmental factor was found.

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USC
SCHOOL OF
MEDICINE

Dear Mrs. Rowe: March 27, 2018

You have asked me to summarize my presentation to the staff of the Childrens' Hospital of Los Angeles regarding the recent leukemia experience in those regions of Los Angeles County adjacent to Ventura County and less than 5-6 miles from the Santa Susana Field Laboratory (SSFL).

As you know, SSFL has been in operation since 1948 and covered an area of nearly 3000 acres. During the 70's and 80's it was extensively used for the testing of rocket engines and rocket fuel by North American Aviation, Rocketdyne, NASA, DOE, and Boeing. The activities were not fully disclosed to the public, and many have presumed, with some reason that the materials used were probably not meticulously cleaned up, and the companies have not been especially forthcoming in the past. These materials included solvents, such as TCE, Hydrazine fuel, heavy metals, perchlorate, PCB's, PAH's, Dioxins, Furans, and nuclear research produced radionuclides such as Cesium 137 and Strontium 90. Many of these compounds are possible or probable carcinogens, and a study of Rocketdyne conducted by investigators from UCLA concluded that some lung cancers among the workers were probably due to radiation exposure on the job.

For these legitimate reasons, there have been concerns among the residents of nearby areas since at least the 1970's that they and their children have been endangered by proximity to the SSFL location. However, attempts by the California Toxics agency and the EPA to identify dangerous levels of carcinogens and ionizing radiation in areas near to the site have not documented dangerous levels in any recent surveys. According to the EPA after their radiological survey results, they stated in their May 2012 newsletter: "Site access is restricted and therefore, the public is not exposed to this contamination." However, most would agree that in this case the empirical evidence of cancer incidence among nearby residents would be a better guide to the magnitude of the problem. Unfortunately, there is no way to measure levels of cumulative exposure to carcinogens on a personal basis. People move in and move out, unaffected families cannot always be expected to be as cooperative as affected families, and the levels of education and income among nearby residents are quite different from those of all residents of the two Counties. Studies of individuals are quite expensive and require extended periods to complete.

For these reasons, the studies that have been done are not of individuals, but of populations, and have been of the "quick and dirty" kind, in which the cases occurring among blocks of nearby residents have been compared to overall county rates. Such studies have their own problems. In addition to the above, counts of residents needed to estimate rates of incidence are only made every decade, and with particular reference to children, the inter-census extrapolations cannot be assumed to be accurate.

None of the four studies conducted in the past were able to find evidence of a link between SSFL and "offsite" cancer occurrence, but these studies tended to make arbitrary assumptions about the uniformity of exposure to large groups, and paid insufficient attention to the differences between local residents and the population at

large. For these reasons I was requested by the State agencies to analyze the adult cancer occurrence by neighborhood (census tract), calendar period, gender and anatomic site. I examined 13 kinds of cancer in each gender in 130 different census tract-periods from 1988 to 2009 and found no evidence of a relationship between "offsite" residence and cancer incidence.

None of these studies considered childhood cases. I was recently asked by the State, by CHLA, and by some groups of local residents (understandably, residents are not in perfect agreement about the best course of action) to re-examine offsite risk, this time with attention to childhood (0-14) cancer and leukemia in particular. My colleagues and I have done so, again looking at each census tract within an area slightly greater than 5 miles from SSFL. At that farthest distance, carcinogens from on site would be unlikely to be present in doses that could produce extra cases, much less clustered cases. We looked at four periods, including the more recent one of 2010-2015.

You have asked that I describe our findings with respect to that period and in particular to the "offsite" census tracts in Los Angeles County, including West Hills. Overall we found no trend over time in the frequency of childhood cancer or of leukemia (ALL and AML), no consistent excess by census tract. Those census tracts within 3 or 5 miles of the site in either County saw no more cases than those more distant. No more than two cases of leukemia occurred in any one census tract, and even that number occurred only twice among the 60 tracts with such cases. As indicated above, calculation of local incidence is not feasible on account of the unreliability of the population counts, so we looked at the percent of all cancers diagnosed represented by childhood cancer (since the large number of adult cancer types has ensured that the total number closely reflects the population in California), and in each period these were consistent with the overall percentage.

With respect to leukemia occurring in areas of Los Angeles County adjacent to the Ventura County border and therefore relatively near SSFL, we counted cases in 15 census tracts and found 5 cases of acute leukemia. Based on an estimate of the combined population of those tracts, and the five years at risk, one should have expected two cases, so there were more observed than expected. However, before we conclude that the 3 unexpected cases were a result of exposure to the relatively distant (in dosage terms) SSFL site, we must calculate the probability that such an outcome would result by chance. That takes the form of estimating how many of the many groups of 15 tract combinations in either County would be likely to see this many or more cases of childhood cancer by chance. There are roughly 3000 census tracts in the two Counties, and even if they were divided such than no census tract was in more than one 15-tract set, there would be 200 sets. Using the Poisson statistical method of estimation, we calculated that 5.2% of all the units under surveillance would see 5 or more cases, given as indicated that the expected number was 2. Thus even under the unrealistic assumption that if no tract were to be in more than one 15-tract set, there would be about 10 such sets with 5 or more cases during 2010-2015 in the two Counties, and the true number appearing by chance would be substantially larger. We conclude therefore that the extra 3 cases can be explained reasonably on the basis of chance alone and that we have been unable to find evidence of local childhood cancers caused by SSFL. As you well know, we have to carefully say that we cannot rule out such causation, and can only say that we have been unable to find support for it.

I hope this explanation is satisfactory. If you have further questions, don't hesitate to ask.

Thomas Mack MD, MPH.

Dear Dr.x

You have asked me to summarize the recent leukemia experience in those regions of Los Angeles County adjacent to Ventura County and less than 5-6 miles from the Santa Susana Field Laboratory (SSFL).

As you know, SSFL has been in operation since 1948 and covered an area of nearly 3000 acres. During the 70's and 80's it was extensively used for the testing of rocket engines and rocket fuel by North American Aviation, Rocketdyne, NASA, DOE, and Boeing., The activities were not fully disclosed to the public, and many have presumed, with some reason that he materials used were probably not meticulously cleaned up, and the companies have not been especially forthcoming in the past. These materials included solvents, such as TCE, Hydrazine fuel, heavy metals, perchlorate, PCB's, PAH's, Dioxins, Furans, and Radionuclides such as Cesium 137 and Strontium 90. Many of these compounds are possible or probable carcinogens, and a study of Rocketdyne conducted by investigators from UCLA concluded that some lung cancers among the workers were probably due to radiation exposure on the job. At least part of the location has been designated a Superfund site.

For these legitimate reasons, there have been concerns among the residents of nearby areas since at least 1970 that they and their children have been endangered by proximity to the SSFL location. However, attempts by the California Toxics agency and the EPA to identify dangerous levels of carcinogens, and ionizing radiation in areas near to the site have never documented dangerous levels, and even those levels found on the site itself have not been excessive.

However, most would agree that in this case the empirical evidence of cancer incidence among nearby residents would be a better guide to the magnitude of the problem. Unfortunately, there is no way to measure levels of cumulative exposure to carcinogens on a personal basis. People move in and move out, unaffected families cannot always be expected to be as cooperative as affected families, and the levels of education and income among nearby residents are quite different from those of all residents of the two Counties. Studies of individuals are quite expensive and require extended periods to complete.

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I hope that this meets your need, and naturally I will be happy to answer any further questions.