An Ecologic Approach to Using Surveillance Data to Obtain Information on the Efficacy of Screening for Prostate Cancer

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Definition of the Problem

- Identification of ecologic associations at the county level between a PSA-related measure of prostate cancer incidence and prostate cancer rates that may reflect the impact of PSA screening

Background

- PSA testing formally approved by the FDA in 1986 for monitoring disease status in patients with prostate cancer
  - Apparently also used for diagnostic purposes
    - Reported correlation of PSA testing with prostate cancer incidence
- PSA testing approved in 1992 for screening purposes on a limited basis

Effect of PSA Testing on Prostate Cancer Rates Observational Studies Based on SEER Data

- Legler 1998: PSA testing rate patterns correlated with prostate cancer incidence rate patterns
- Hankey 1999: Documented decrease in distant stage disease beginning in 1992
- Feuer 1999: Analysis of incidence-based mortality rates suggested that decrease in distant stage disease was contributing factor to decrease in mortality
- Lu-Yao 2002: Analyzed data from Connecticut and Seattle, which had extremes of PSA testing rates, and found no correlation with mortality rates

Effect of PSA Testing on Prostate Cancer Rates

Modeling Studies Using SEER Data Linked to Other Databases

- Etzioni 1999: Modeled PSA screening data for a male cohort aged 65 to 84 and found no association between screening and mortality
- Etzioni 2002: Modeled PSA screening data for a male cohort aged 65 to 84 and estimated the percent of overdiagnosed prostate cancer to be 30

Effect of PSA Testing on Prostate Cancer Rates
International Studies

- Bartsch 2001: Decreased mortality in Tyrol vs. Austria correlated with PSA testing rates
- Oliver 2001: PSA screening and mortality data for 24 industrialized nations were analyzed but possible role of PSA testing on mortality rates could not be established
- Coldman 2003: PSA screening and mortality data from Canada for the time period 1985-99 were analyzed but no association of PSA screening with a decrease in mortality was found

Data Sources

- SEER incidence data for 9 SEER areas
  - San Francisco-Oakland, Connecticut, metropolitan Detroit, Hawaii, Iowa, New Mexico, Seattle-Puget Sound, Utah, metropolitan Atlanta
- NCHS mortality data for 9 SEER areas
- Area socioeconomic status index developed by Gopal Singh at the county level

Area Socioeconomic (SES) Index (Factor Loadings), United States, 1990

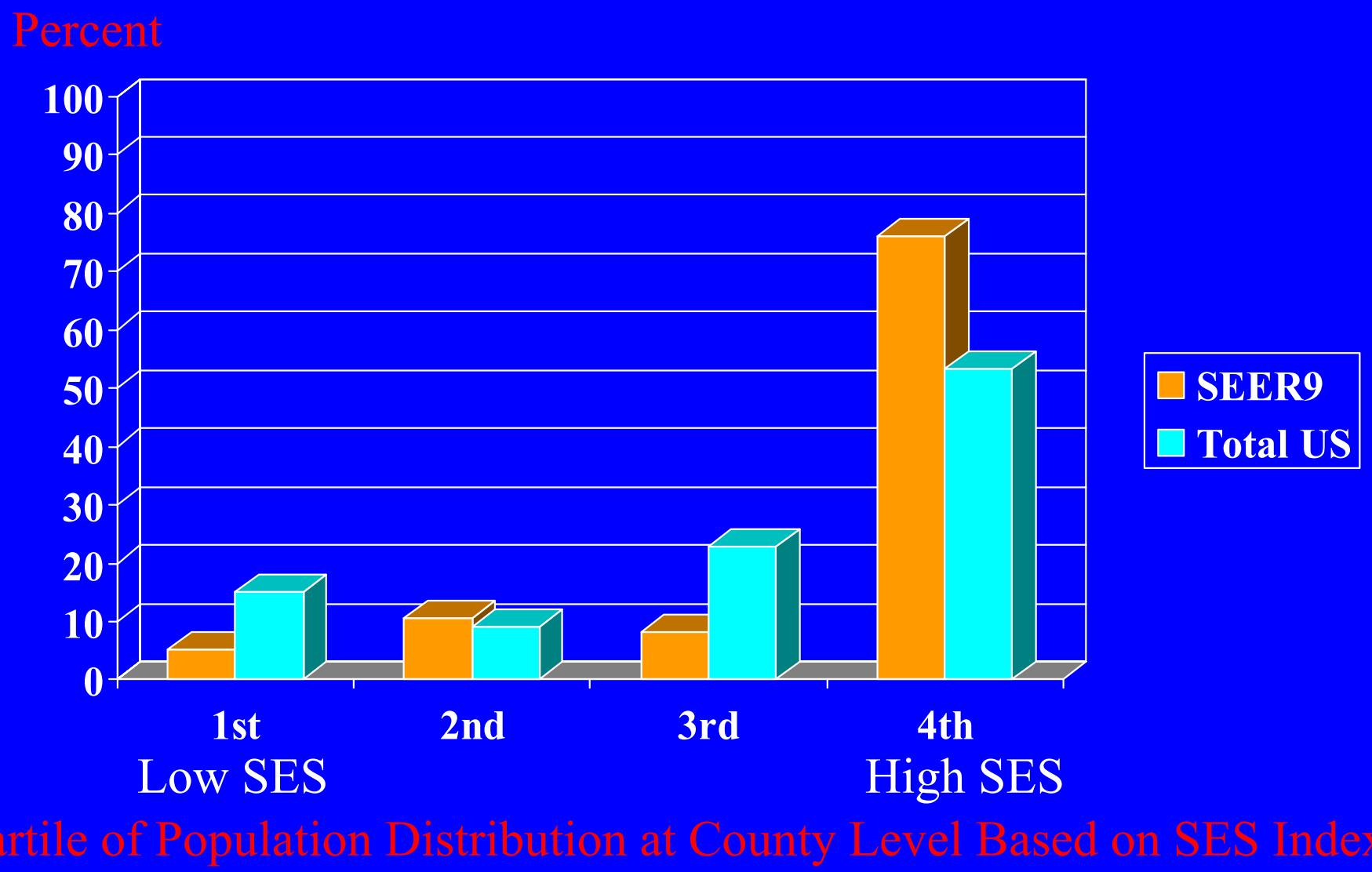
Census Socioeconomic Variable	Census Tract Index	Zip Code Index	County Index
Education			
%Population aged 25+ years with <9 years of education	-0.77	-0.77	-0.83
%Population aged 25+ years with at least a high school diploma	0.87	0.83	0.86
Occupation and Employment			
%Employed persons aged 16+ in white collar occupations	0.83	0.75	0.71
%Civilian labor force population aged 16+ unemployed (unemp. rate)	-0.68	-0.50	-0.57
Income Distribution, Inequality and Wealth			
Median family income ($)	0.87	0.87	0.90
Income disparity	-0.83	-0.72	-0.84
Median home value ($)	0.66	0.70	0.70
Median gross rent ($)	0.74	0.74	0.80
Poverty and Welfare Assistance			
%Families below poverty level	-0.81	-0.76	-0.87
Housing Tenure and Quality			
%Households without a telephone	-0.77	-0.66	-0.80
%Occupied housing units lacking complete plumbing facilities	-0.50	-0.51	-0.65
Proportion of total variance explained by factor	*0.58*	*0.52*	*0.61*
Cronbach's alpha (reliability coefficient)	*0.94*	*0.92*	*0.94*

Source: Singh GK, Miller BA, Hankey BF, et al. J Natl Cancer Inst; 2002:94:904-925.

Geographic Areas

- How defined?
  - Counties in each registry classified into 1 of 20 groupings based on the percentiles of SES index at the county level for the total US
  - Percentiles used to identify the 20 areas were 5, 10, 15, 20, ------, 95

Population distribution for white males 50-79 years old at county level based on quartiles of SES index



Statistics And Methods

- PSA-related incidence rates by geographic area
- Outcome measures
  - Focus is on events that occurred subsequent to screening, and in the age groups most affected by screening (ages 50-79)
    - Distant stage incidence rates by geographic area
    - Incidence-based mortality rates by geographic area
- Linear regression

PSA-Related Incidence Rate
Surrogate for Screening?

- Annual rate for 1996-2000
- Patient selection
  - White males, 50-79 years old at diagnosis
- Numerator is those cancers not clinically apparent, i.e., not palpable or visible by imaging, and incidentally detected by a needle biopsy for reasons such as an elevated PSA
  - From SEER clinical extension code for prostate cancer
- Calculated for each of 20 geographic areas

Outcome Measures
Incidence of distant stage disease

- Patient selection
  - White males, 50-79 years old at diagnosis
- Annual rate for 1992-2000
  - Decrease in distant stage disease began in 1992 for all SEER areas combined
  - Calculated for each of 20 geographic areas

Outcome Measures

Incidence-based Mortality (IBM) Rate

i = age group at death (population variable)

r = calendar year of death (population variable)

s = geographic area (population variable)

t = age at diagnosis

u = year of diagnosis

v = stage at diagnosis

X_{irs} = number of deaths in age group i for calendar year r in geographic area s

N_{irs} = population in age group i for calendar year r in geographic area s

W_i = weight for age group i based on standard population (2000 Standard)

$$IBM_{rstuv} = \sum_i w_i \frac{X_{irstuv}}{N_{irs}}$$

Outcome Measures

IBM Rates And Patient Selection

Prostate Cancer IBM Rate

IBM (s) i=50-79 r=1988-2000 t= 50-79 u=1988-2000 v=all stages

S = 1 to 20

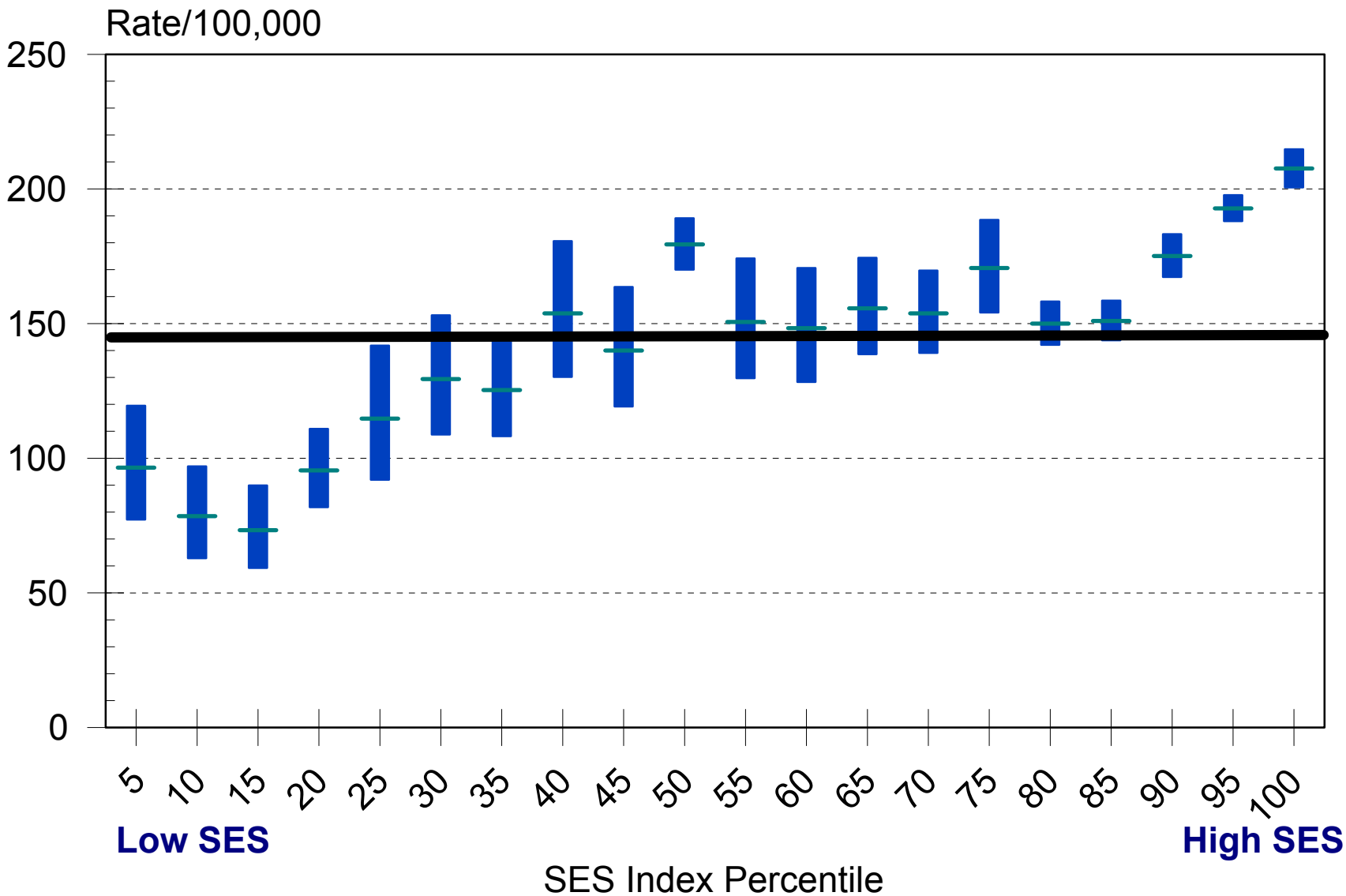
Distant Stage Prostate Cancer IBM Rate

IBM (s) i=50-79 r=1988-2000 t= 50-79 u=1988-2000 v=distant stage

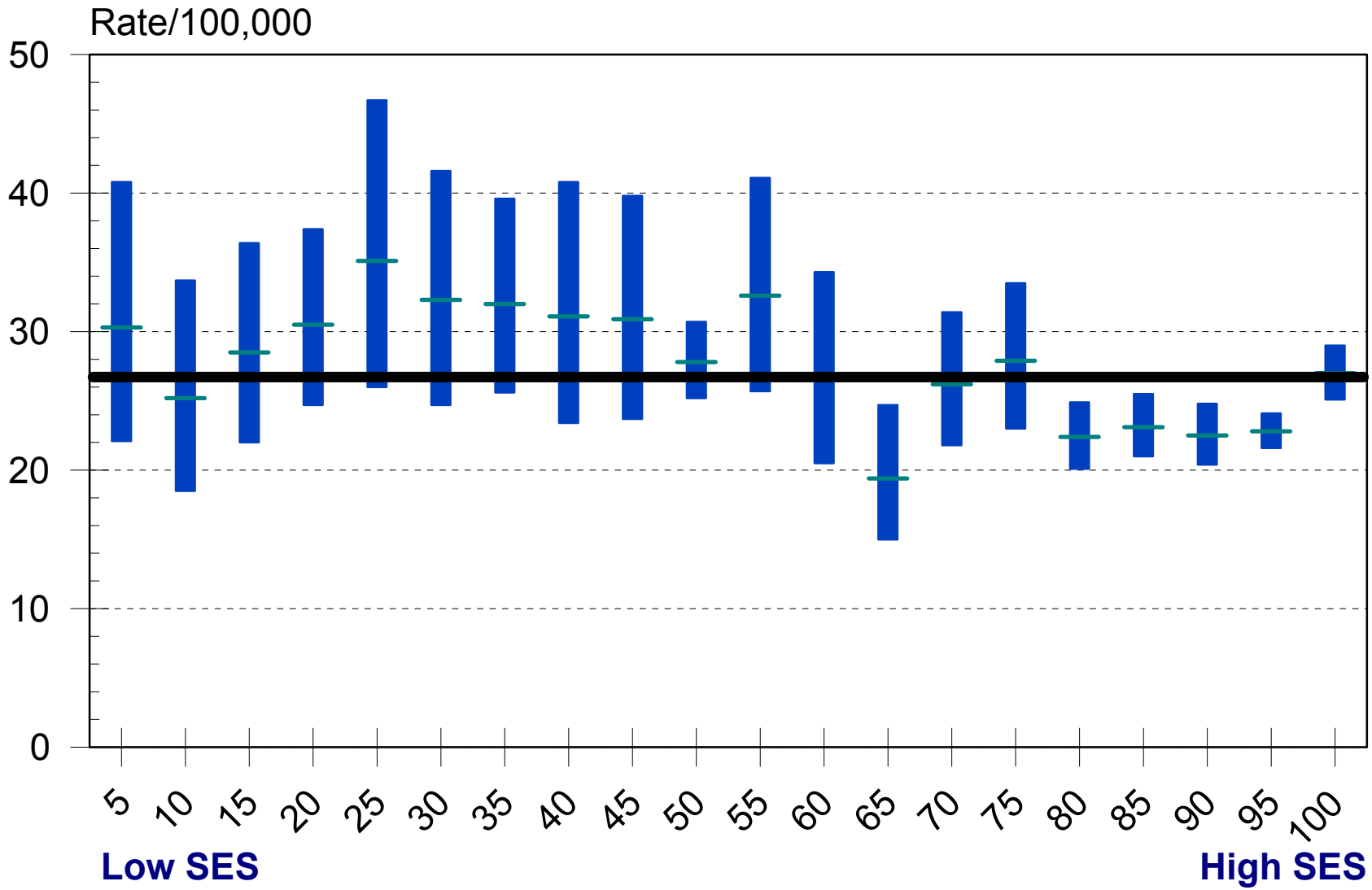
S = 1 to 20

Note: Rates include deaths associated with the diagnosis of a first prostate cancer

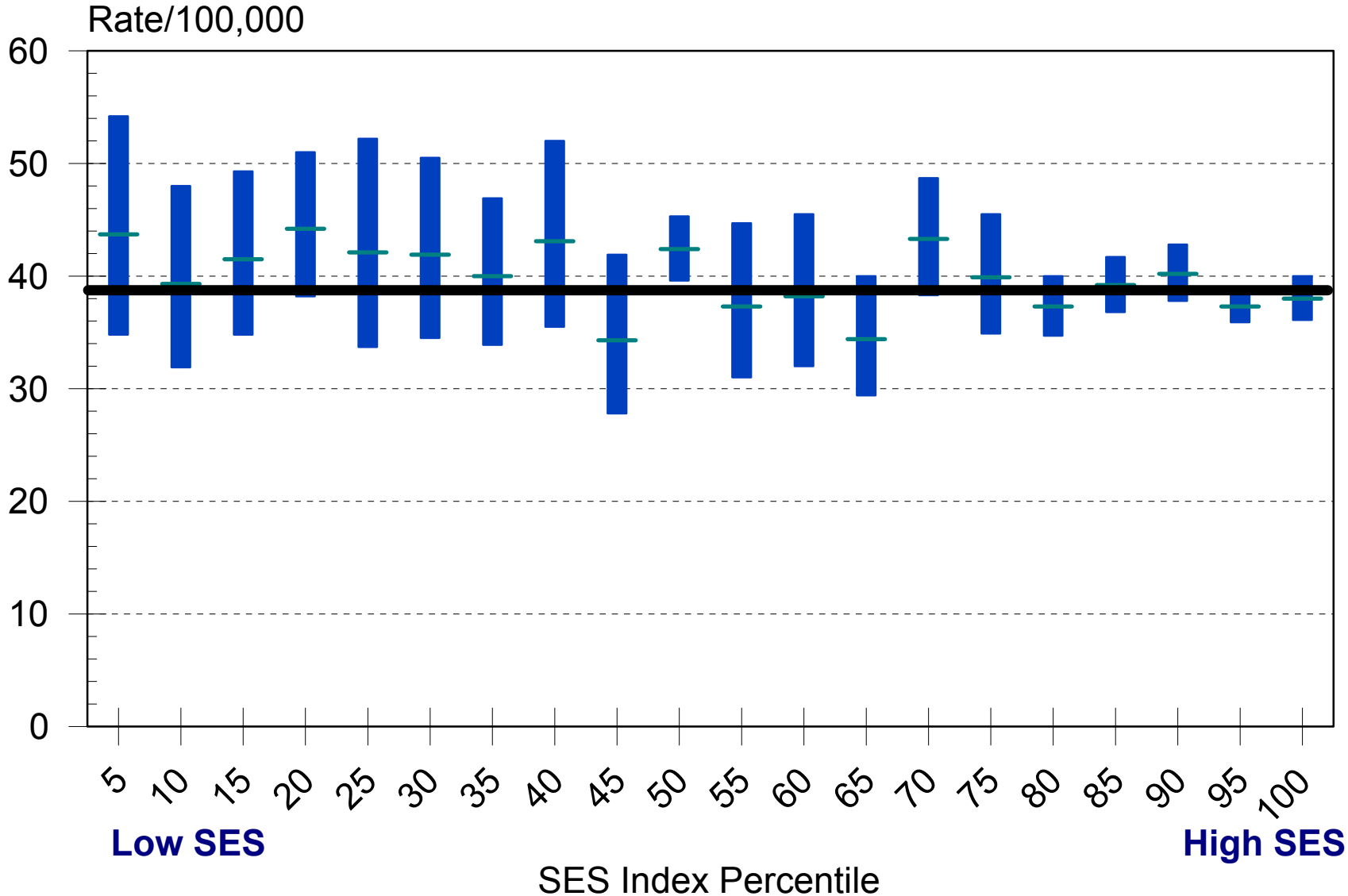
Annual incidence of psa-detected prostate cancer (including 95% confidence limits) for 1996-2000; whites, ages 50-79, by geographic areas based on percentiles of SES index; SEER9.



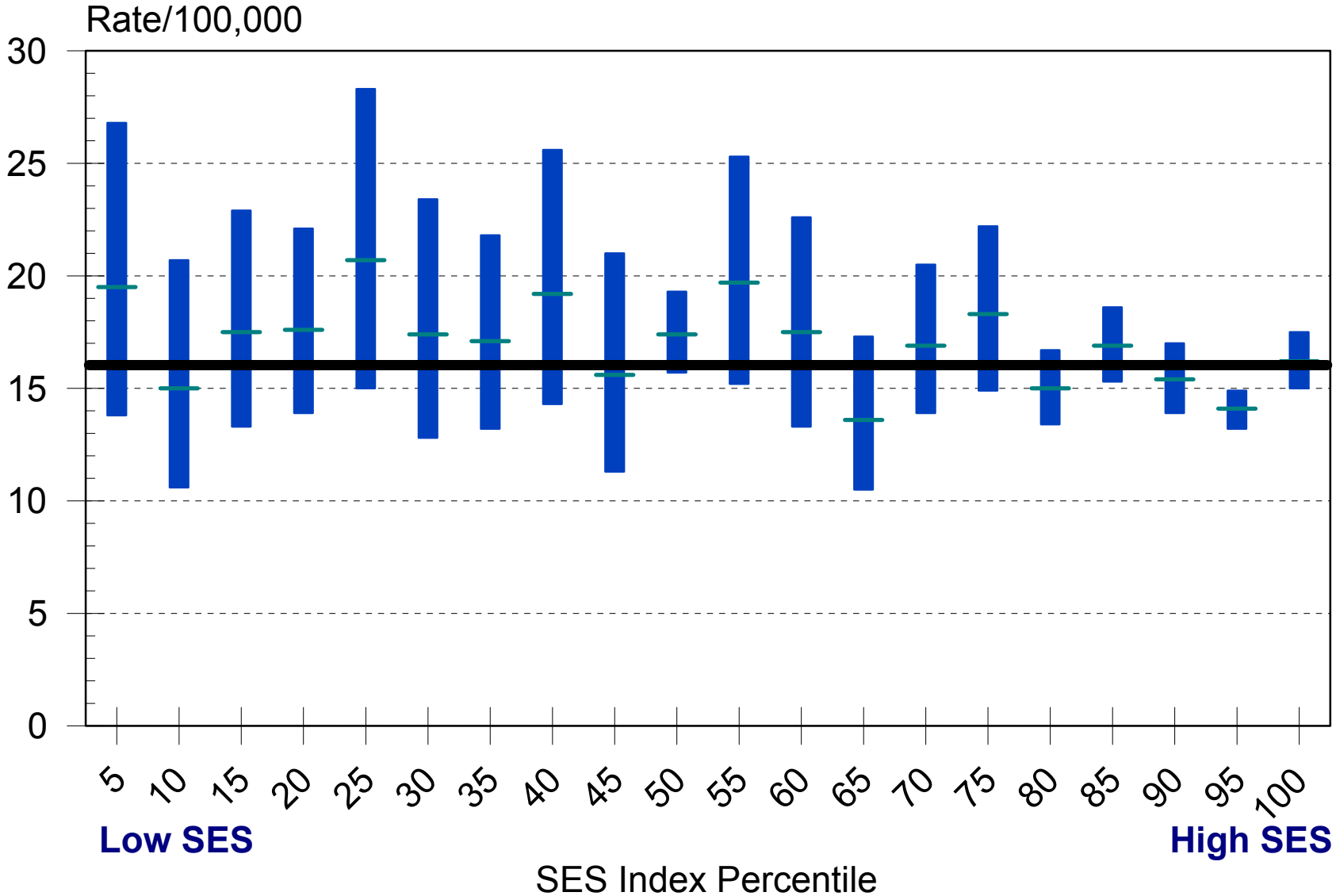
Annual prostate cancer incidence rate for distant stage disease (including 95% confidence limits) for 1992-2000; whites, ages 50-79 at diagnosis, by geographic area based on percentiles of SES index: SEER9.



Annual incidence-based prostate cancer mortality rate (including 95% confidence limits) for 1988-2000; whites, 1988-2000 diagnoses, ages 50-79 at diagnosis, ages 50-79 at death, by geographic area based on percentiles of SES index: SEER9.



Annual incidence-based distant stage prostate cancer mortality rate (including 95% confidence limits) for 1988-2000; whites, 1988-2000 diagnoses, ages 50-79 at diagnosis, ages 50-79 at death, by geographic area based on percentiles of SES index: SEER9.

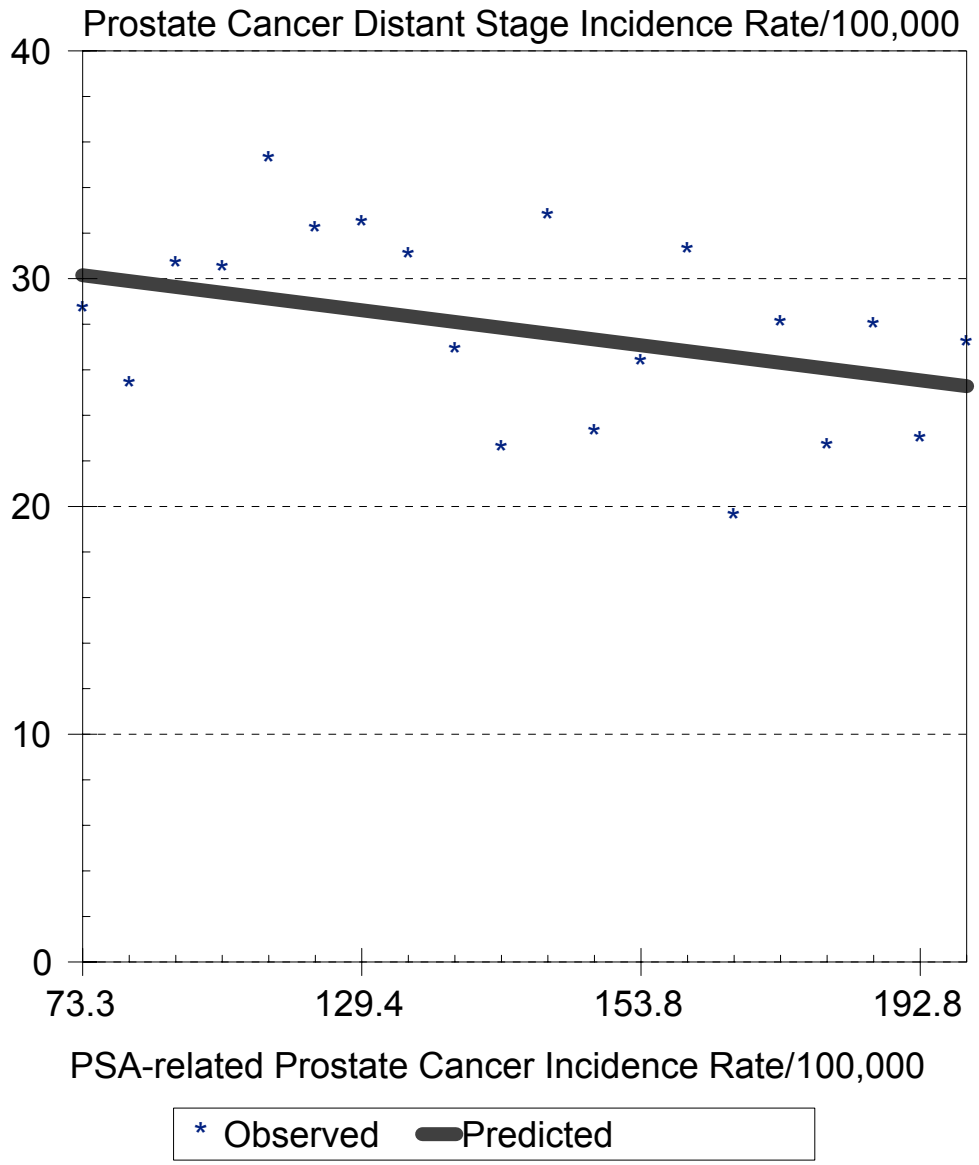


Hypothesis to Be Tested

- There should be a negative correlation between the PSA-related incidence rate and the various outcome measures which focus on the potential impact on distant stage disease and mortality that occurred after the introduction of PSA testing

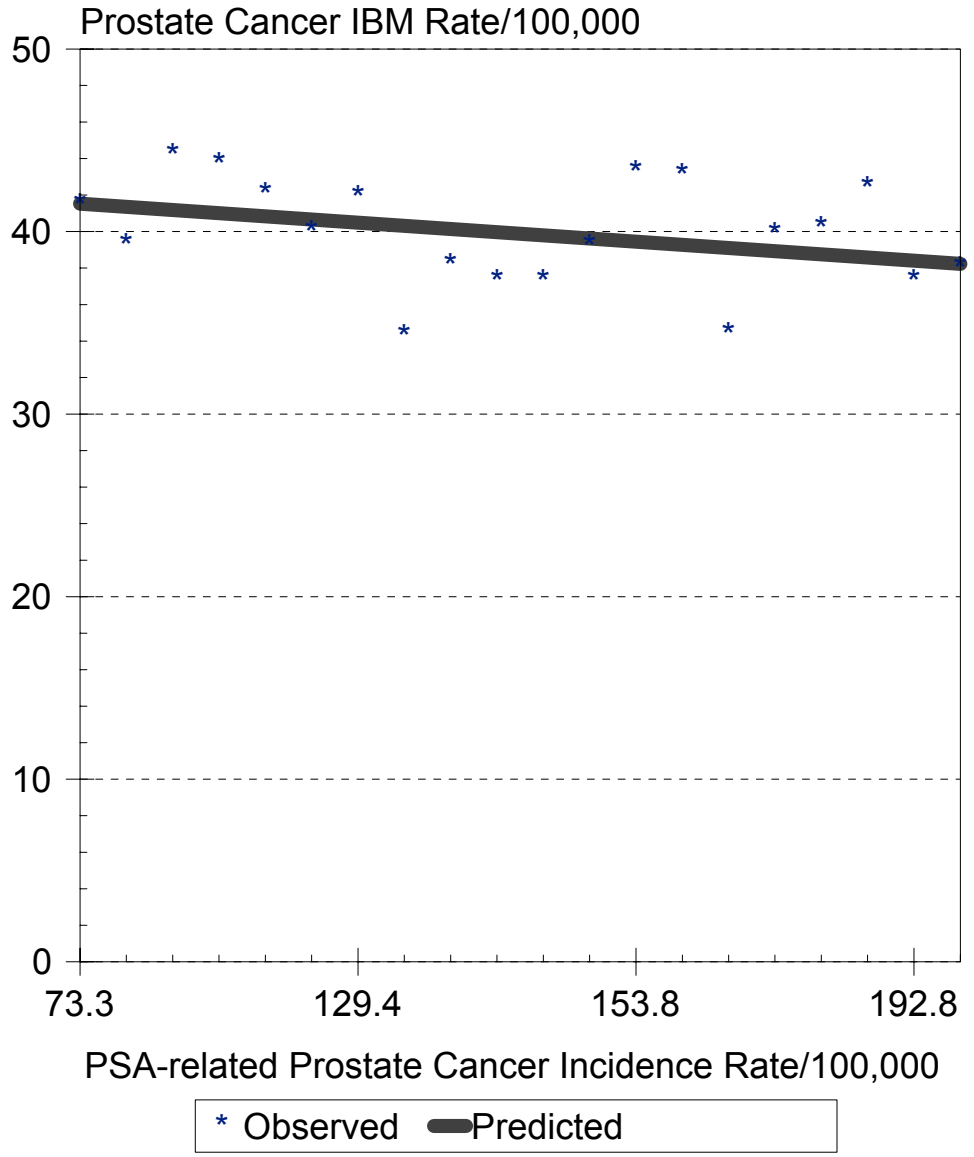
Linear Regression of Prostate Cancer Distant Stage Incidence on PSA-related Incidence

White Males, Aged 50-79, SEER 9 Data, r=-0.373, p=0.1057



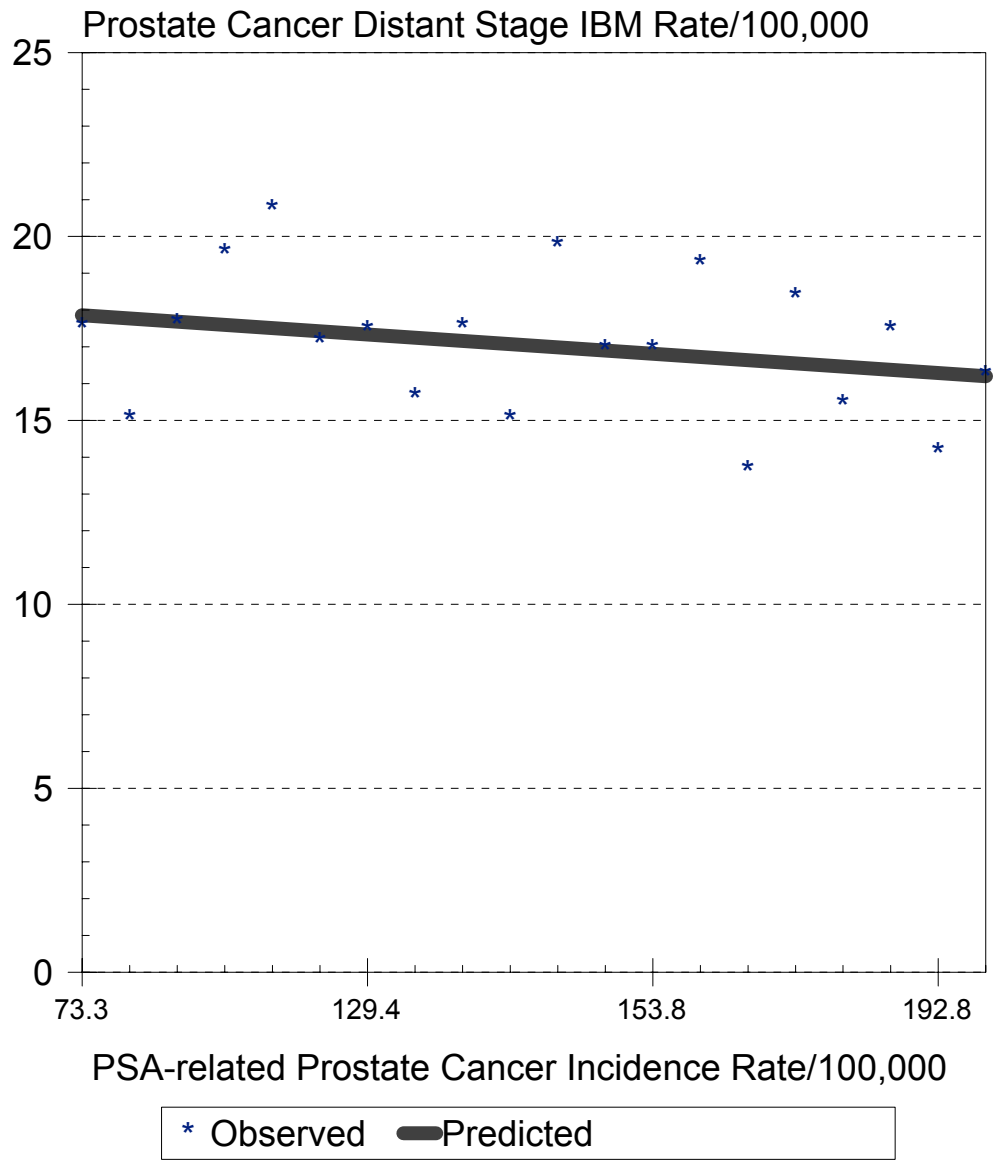
Linear Regression of Prostate Cancer Incidence-based Mortality (IBM) on PSA-related Incidence

White Males, Aged 50-79, SEER 9 Data, r=-0.363, p=0.1157



Linear Regression of Prostate Cancer Distant Stage Incidence-based Mortality (IBM) on PSA-related Incidence

White Males, Aged 50-79, SEER 9 Data, r=-0.281, p=0.2306



Summary

- PSA-related incidence rates were positively associated with SES as expected and appear to reflect differences in PSA screening rates
- PSA-related incidence rates were negatively correlated with each of the three outcome measures as expected but correlation coefficients were not significantly different from zero.
- There are clearly limitations associated with ecologic studies like this and one of them appears to be low statistical power to detect an effect of PSA screening given the observed variability in PSA-related incidence.
- Estimates of over diagnosis have been as high as 30%. If that is the case, one would expect most of the over diagnosis to be associated with PSA-related incidence which comprises approximately 30% of Prostate cancer incidence for the time period 1996-2000.
- Roughly 40-45 % of PSA-related cases were treated by a prostetectomy.