James R. Hébert, Sc.D., Professor, Arnold School of Public Health Department of Epidemiology and Biostatistics

Director, South Carolina Statewide Cancer Prevention & Control Program

Diet and Hormone-Sensitive Cancers:

Comparing and Contrasting Breast and Prostate

Overview: The study of diet and cancer represents an area of research that is interesting, controversial, and of great public health relevance. Breast and prostate cancers show a pattern of incidence and mortality in poor countries that is markedly different from what is observed in affluent countries. Using examples from work conducted in the United States and in India and directing attention toward methodologic issues related to study design, dietary and other risk factor assessment, and the pathophysiology of these diseases, we will suggest areas on which to focus effort in order to make progress in the fascinating and often frustrating fields of breast and prostate cancer research.

Preliminary Points:

- Hormone ≈ Steroid Hormone
- Of course, the concept could be interpreted more expansively (e.g., colon has melatonin receptors & IGFBP-3)
- Role of SHBG, availability of hormone
- Receptors may be important
- Also, most cells are subject to signaling, even if receptors aren't identified

ISSUES in Studying Hormone-Sensitive Cancers

- Generally long, but very variable, latency periods
- Complicated, multifactorial processes of disease promotion/ possibly initiation
- What kind of outcome/ information yield do you expect?

ISSUES in Studying Hormone-Sensitive Cancers

- Each site probably represents a number of distinct disease entities (PrCA presents as heterogeneous tumors)
- Virulence (e.g., case fatality) tends to decrease with age, even though incidence increases (usually sharply) – Huge implications for study design and screening

Keep in Mind That:

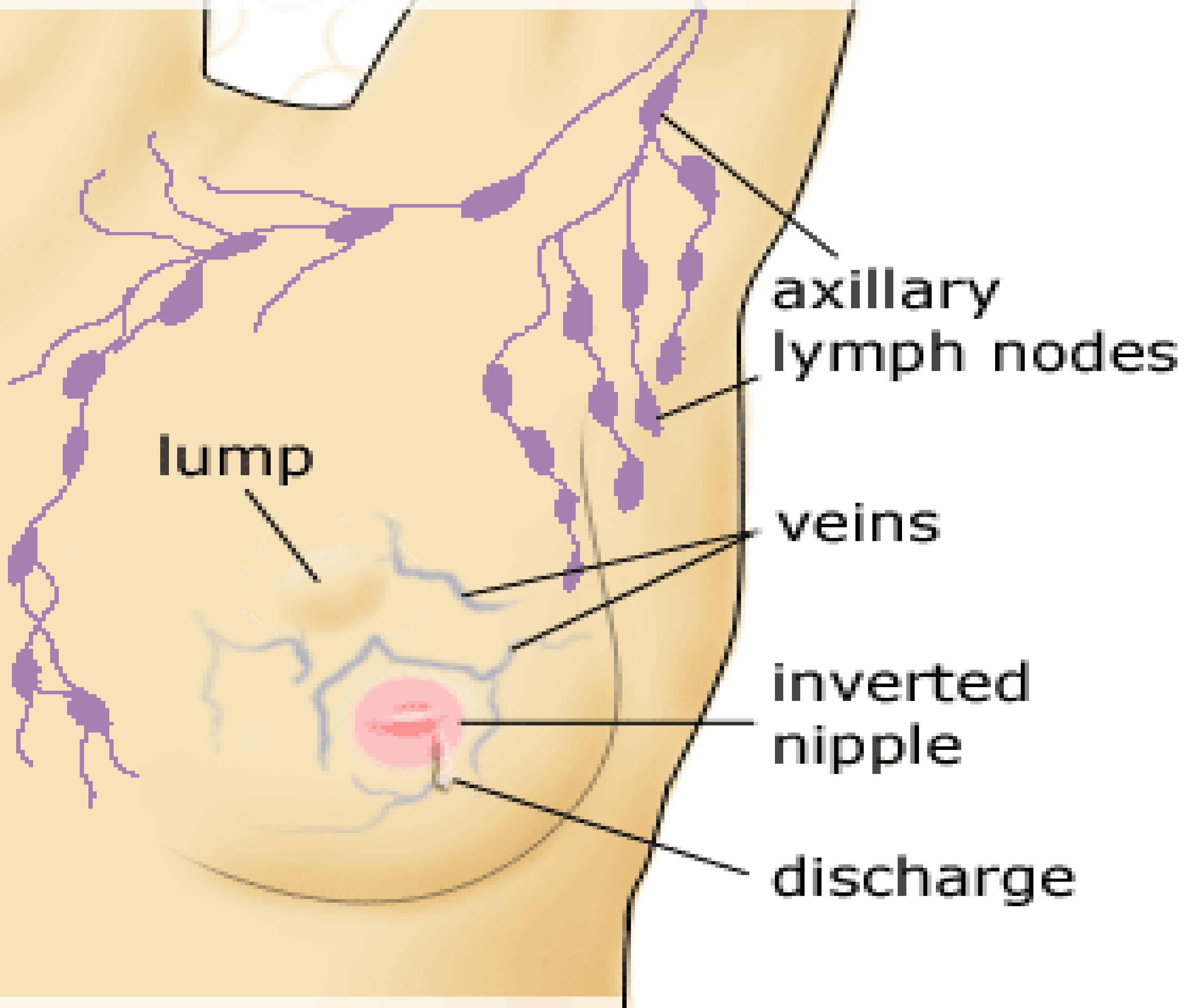
In the absence of hormone, these cancers would be very rare.

How do we know?

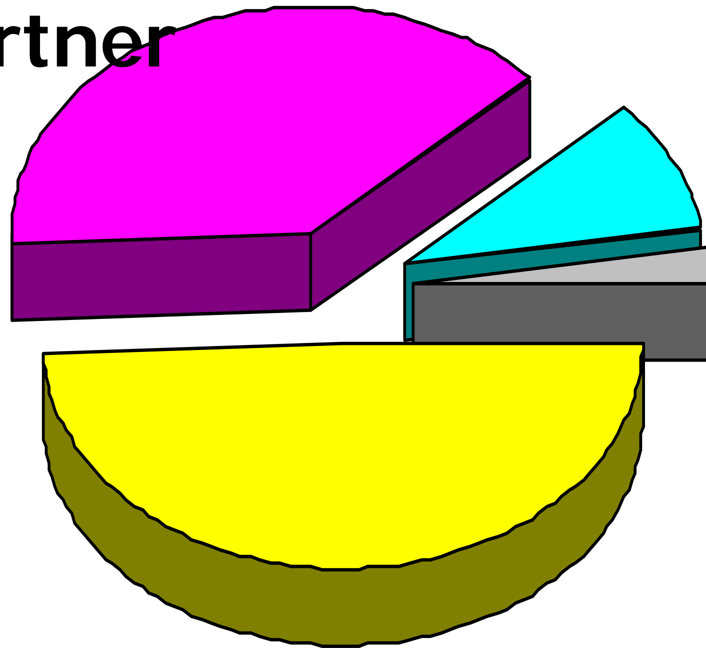
- Studies of women without ovaries
- Studies of male BrCA
- Observations that PrCA does not exist in eunuchs

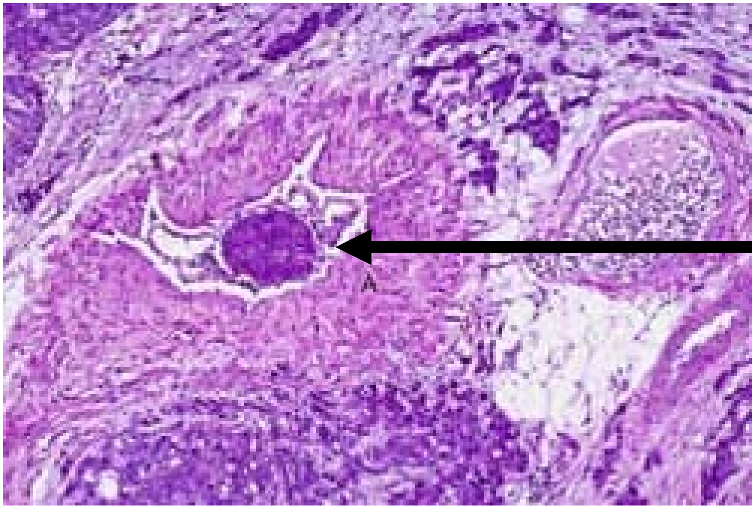
Breast Cancer

- Is the most studied and well-funded of any cancer site
- Pre- and post-menopausal cancer are different diseases
- Racial differences exist; how fundamental are they?
- Estrogen and Progesterone receptivity (i.e., SH signaling) is critically important
- Grade is important, even after accounting for TNM stage


Symptoms of Breast Cancer
axillary lymph nodes
lump
veins
inverted nipple
discharge

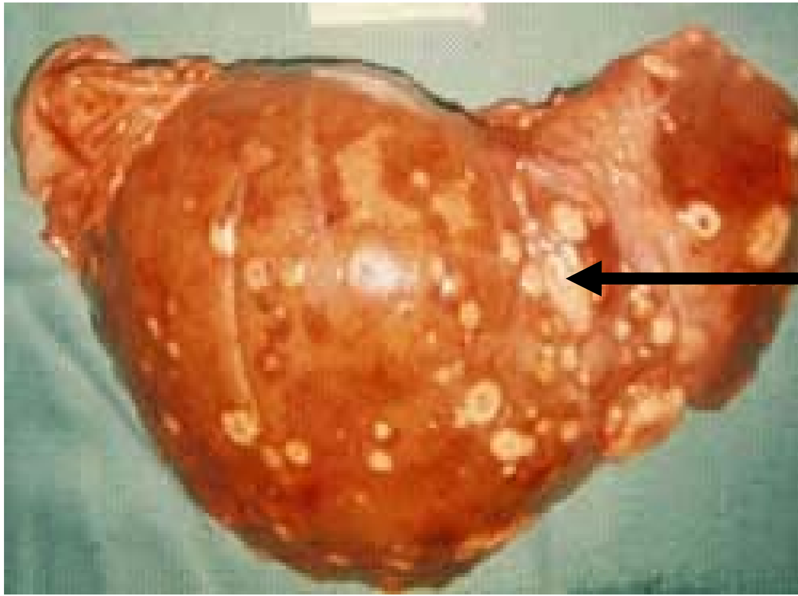
BrCA Detection; USA





The artery (A) in this breast contains a tumor embolus of breast cancer. This is an indication of high risk for distant metastatic disease.

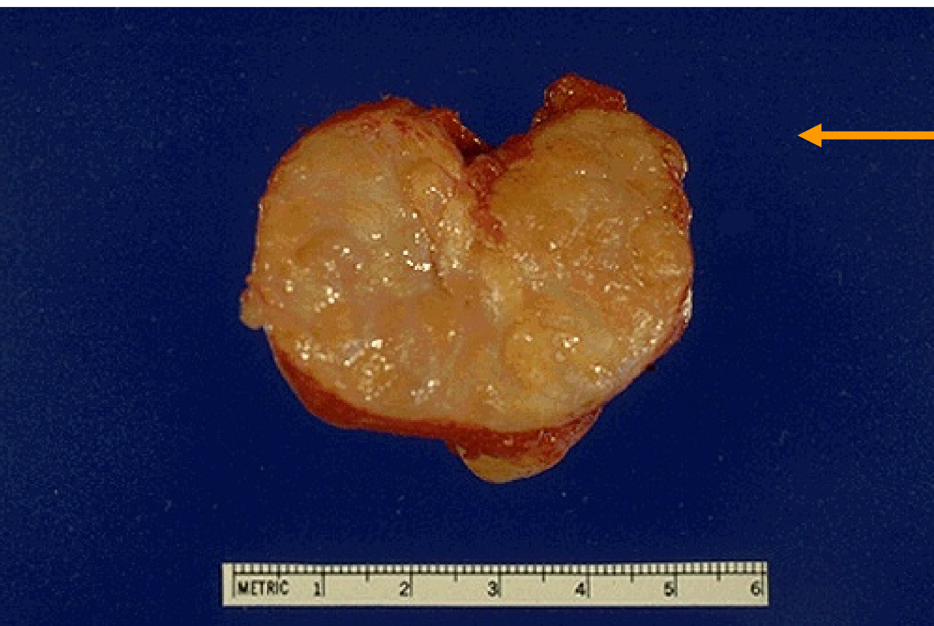
Vertebrae sliced at autopsy of a breast cancer patient. The gray-white areas represent metastases.



The liver of this breast cancer patient shows numerous foci of metastases.

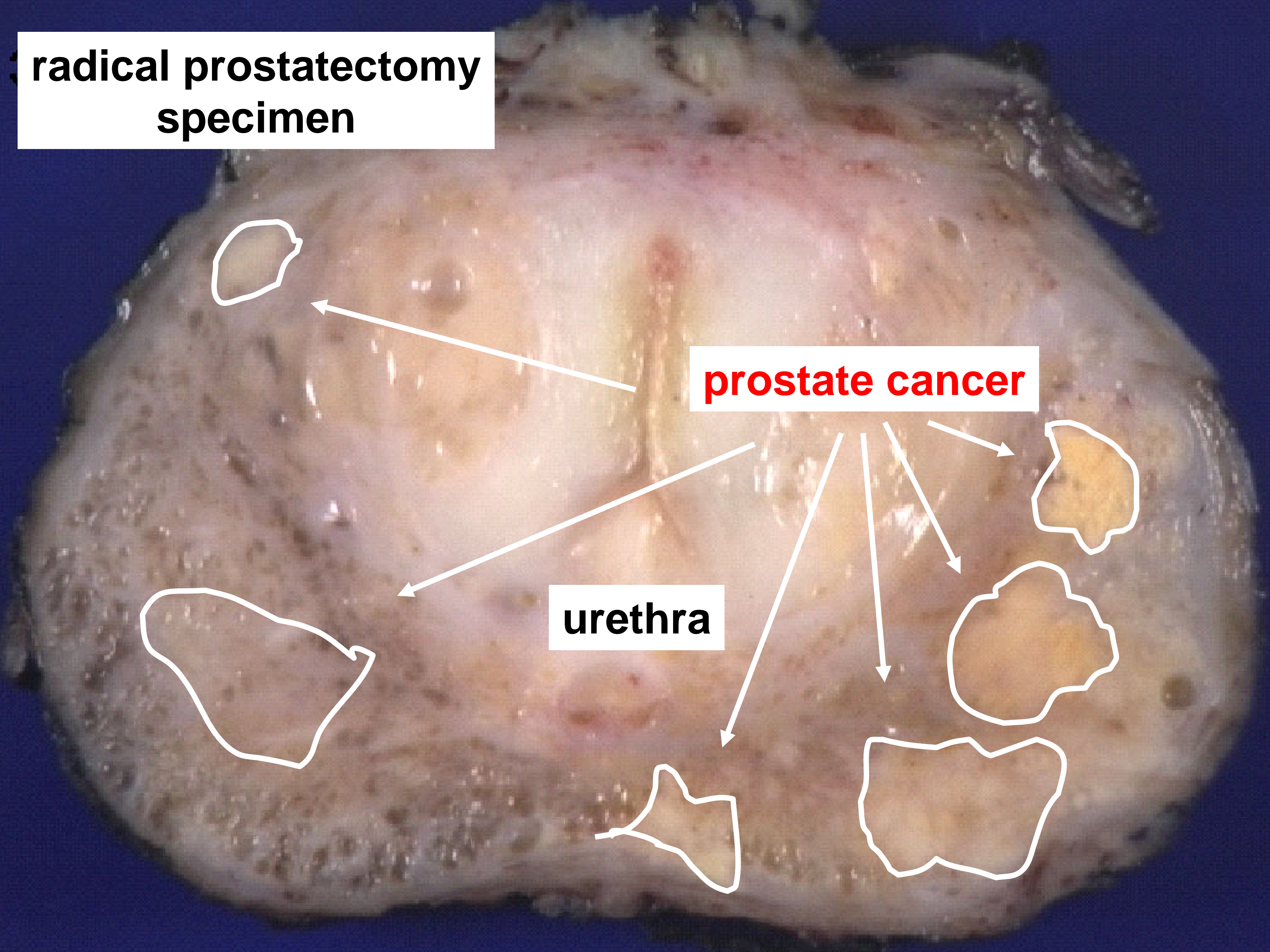
Prostate Cancer

- Is more common than BrCA, in the West
- Virulence is inversely related to age
- Tension exists between over-treating indolent disease and under-treating virulent disease
- Androgen receptivity is generally ignored; all PrCAs are androgen receptor positive
- Grade is considered >>important than stage
- As with BrCA, racial differences exist; how fundamental are they?



A normal prostate gland is about 3 to 4 cm in diameter. This prostate is enlarged due to benign prostatic hypertrophy (BPH) / hyperplasia.

These sections through a prostate removed via radical prostatectomy reveal irregular yellowish nodules, mostly in the posterior portion (seen here superiorly). These proved to be adenocarcinoma, which may coexist with hyperplasia. Note lack of glandular enlargement. Also note that the tumors are not morphologically very distinct.


radical prostatectomy specimen
prostate cancer
urethra

SPECIMEN DIAGRAM

CASE#:

NAME:

D1-5 Distal

R L

6 8 3mm 7 9

10 12 9mm 11 13

R L 14 16 15 17

18 20 19 21

R L 22 24 23 25

R L 26 28 27 29

30 32 31 33

R L

orange Blue Blade green

Color Code

34 - 35

Bladder Margin

R L C 36

Seminal Vesicles

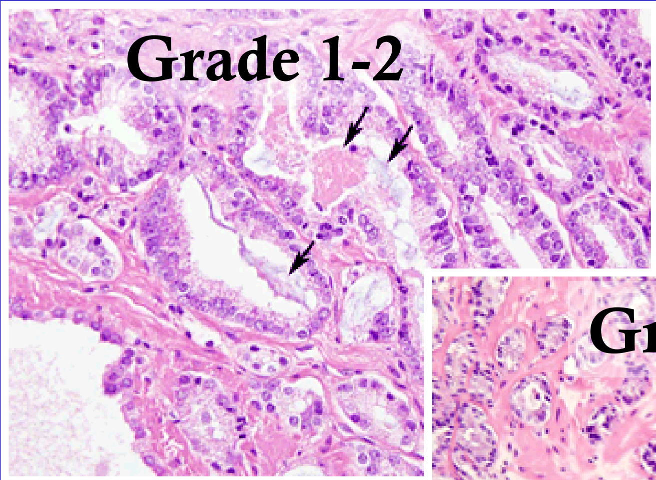
= Adenocarcinoma

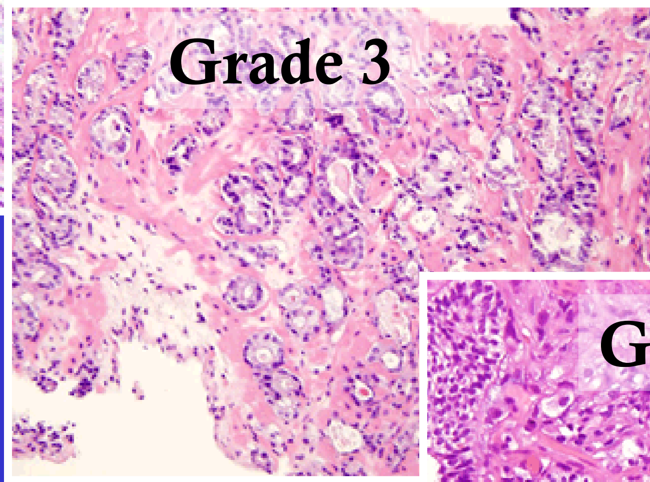
+ : positive margin

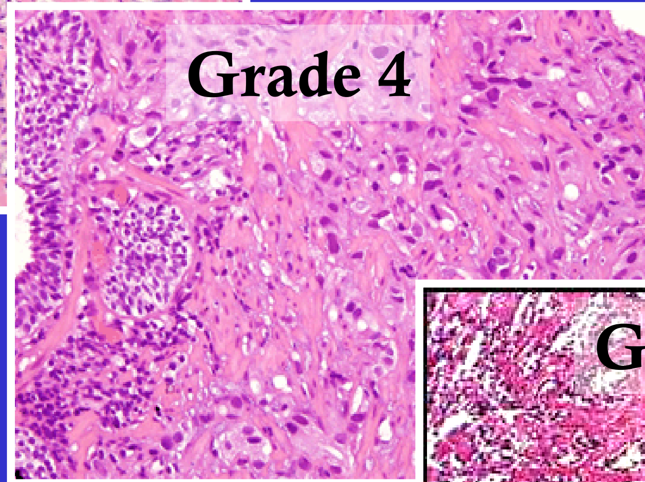
DRAWN BY: Paul [illegible] MD

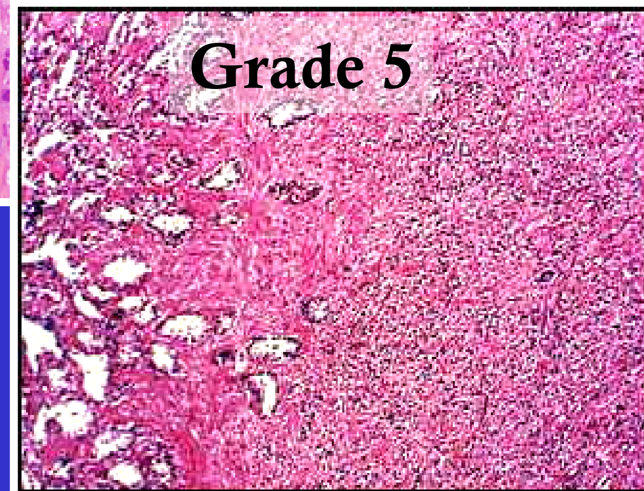
DATE: 2/11/05

The Gleason Score







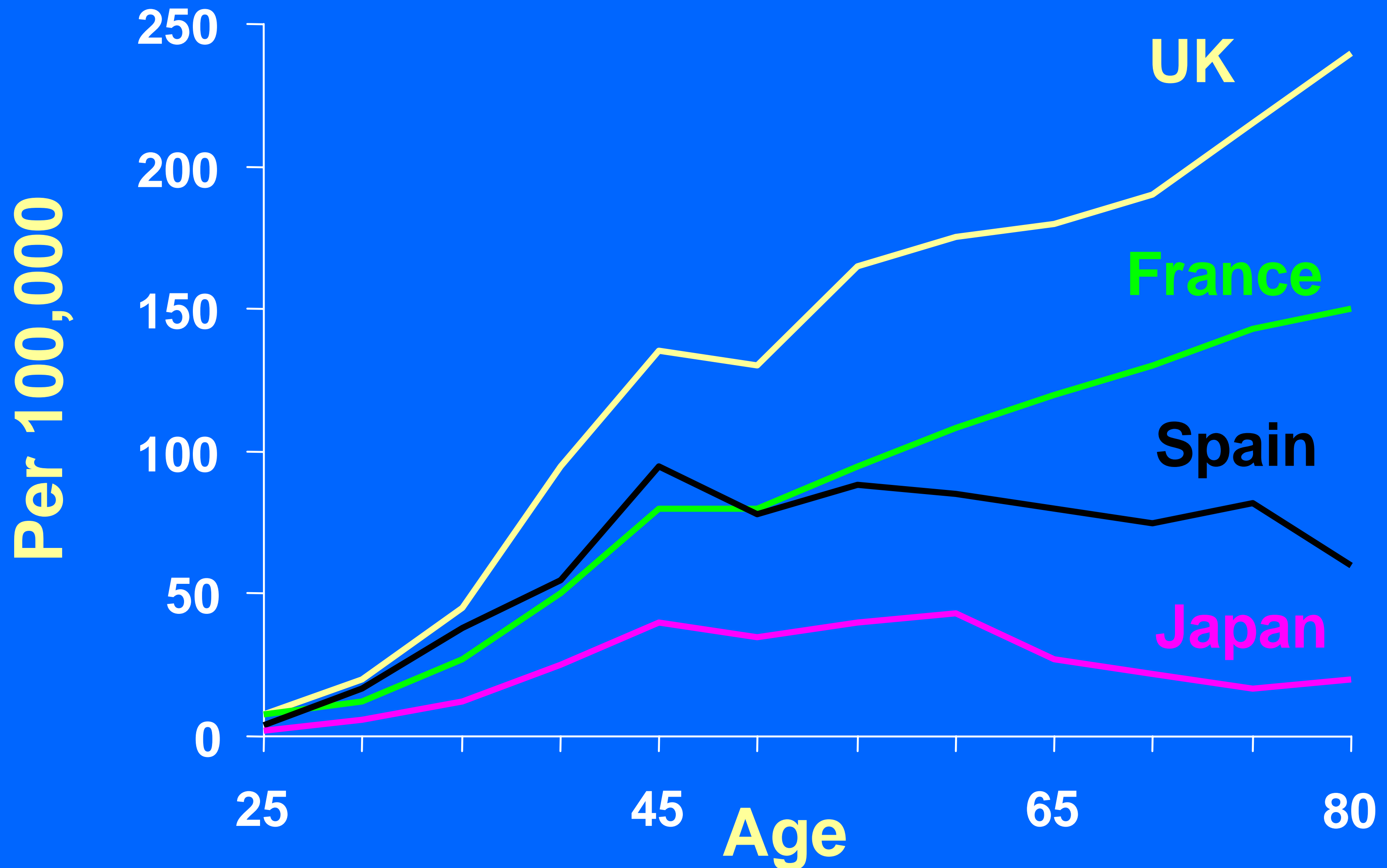


Progression of grade corresponds with increasing abnormality of architecture

PrCA Screening / Early Detection is Very Different than for BrCA

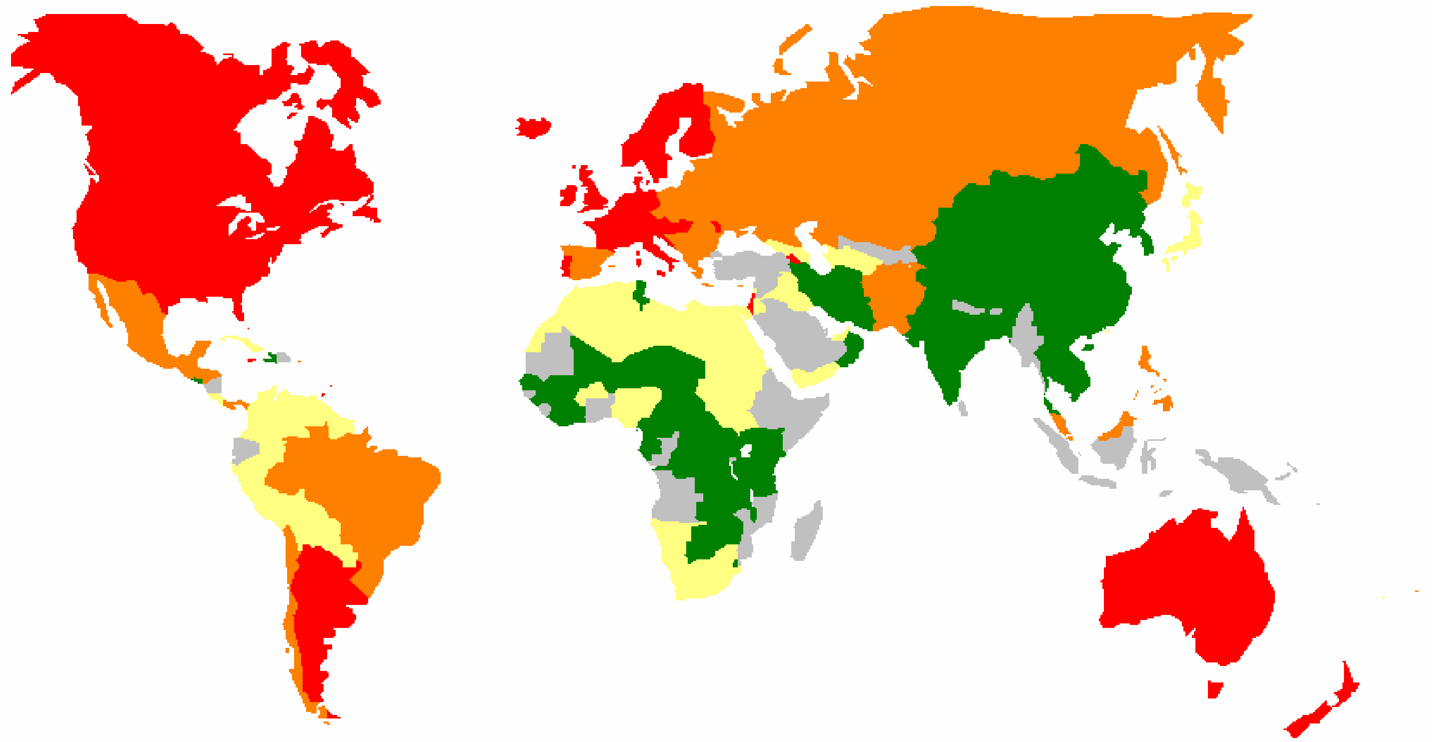
- The lesions are occult; by the time of symptom appearance the disease is in late stage
- No screening device (mainly DRE & PSA), or a combination of ≥ 2, have both sensitivity & specificity > 50%
- The disease is usually pretty indolent
- There are subsets of men for whom either of the previous may not be true
- But we do not know them in advance

International Breast Cancer Incidence 1968-1972

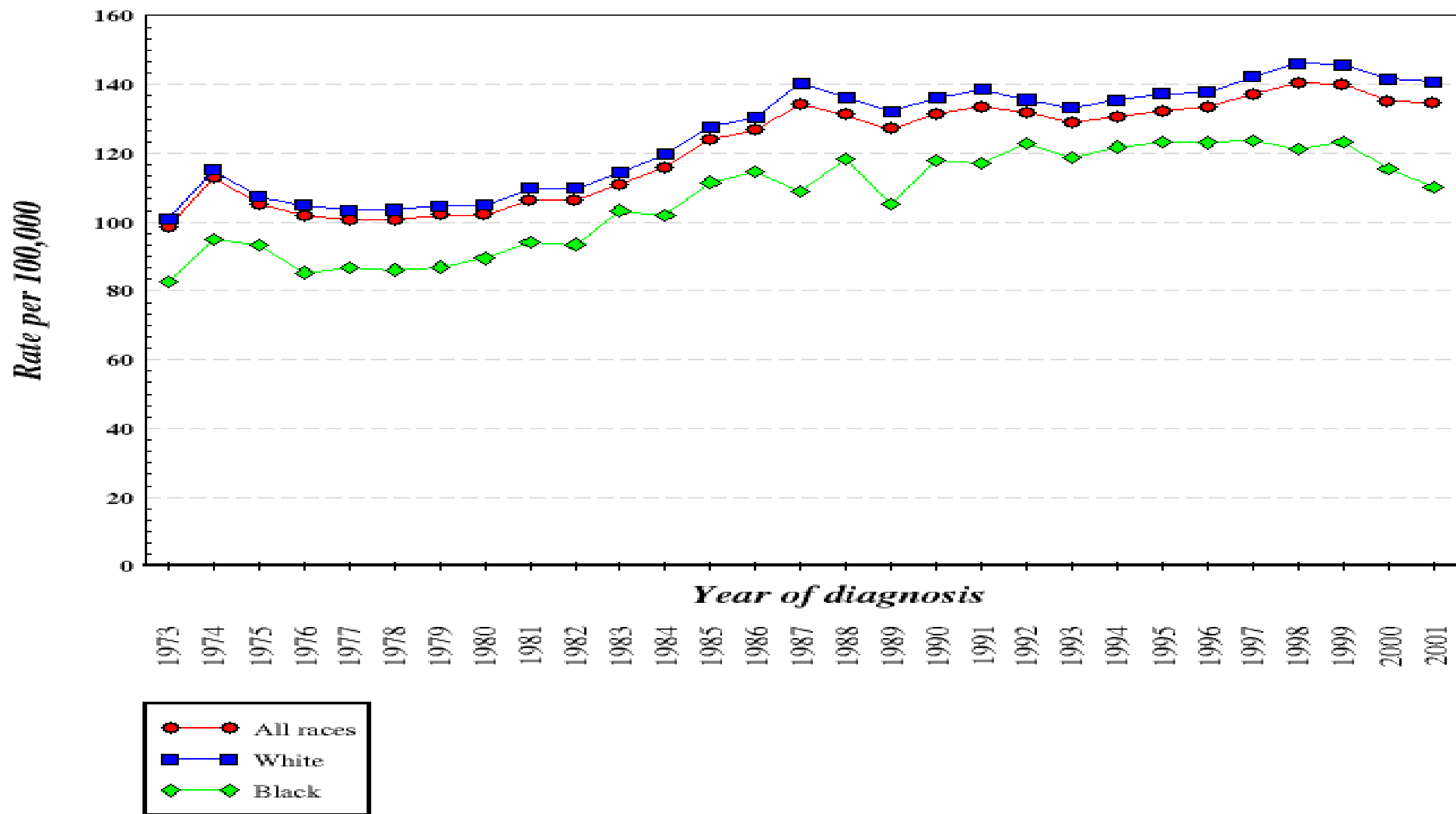


De Waard, F. JNCI 1979

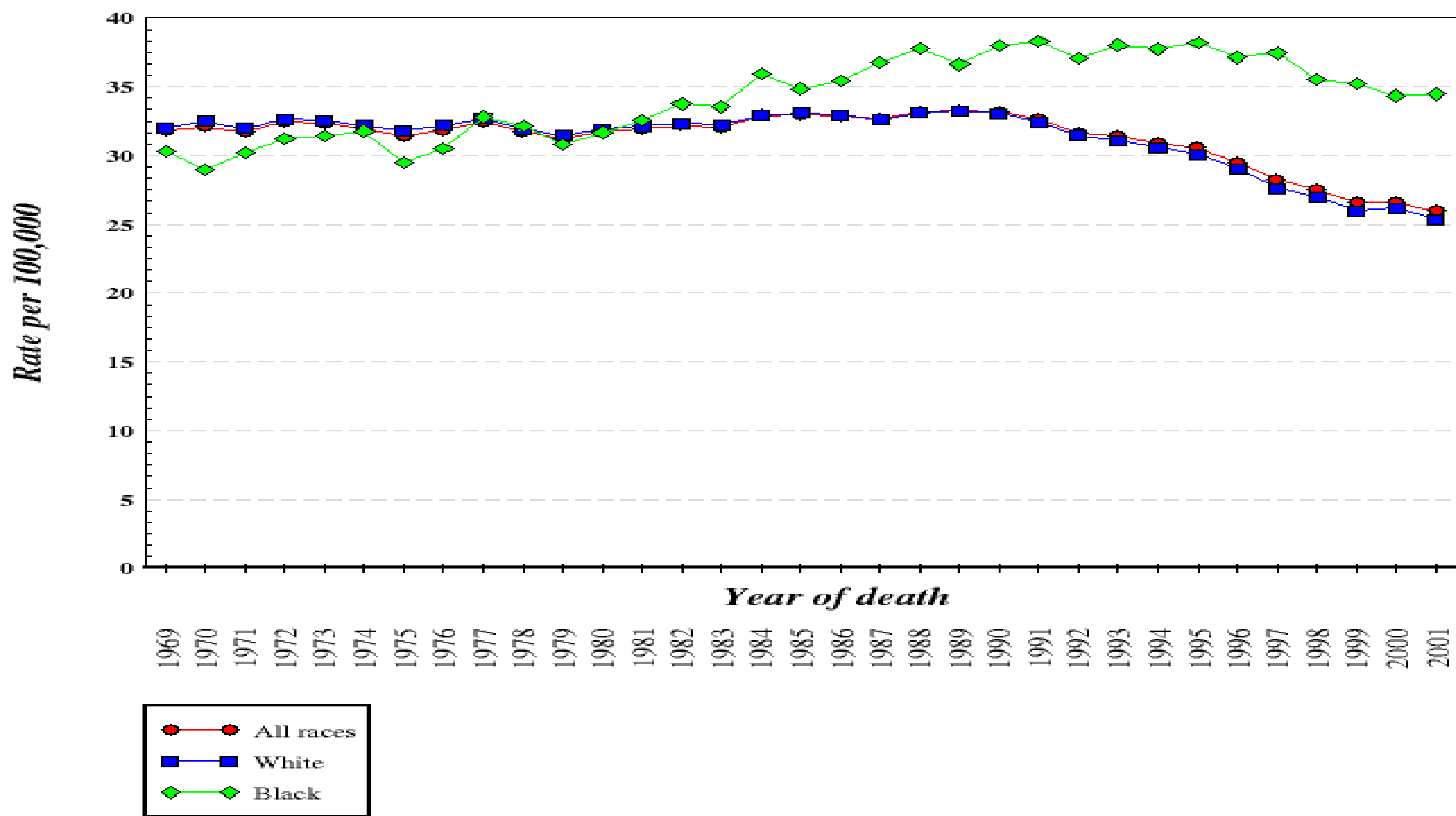
Breast Cancer – World map



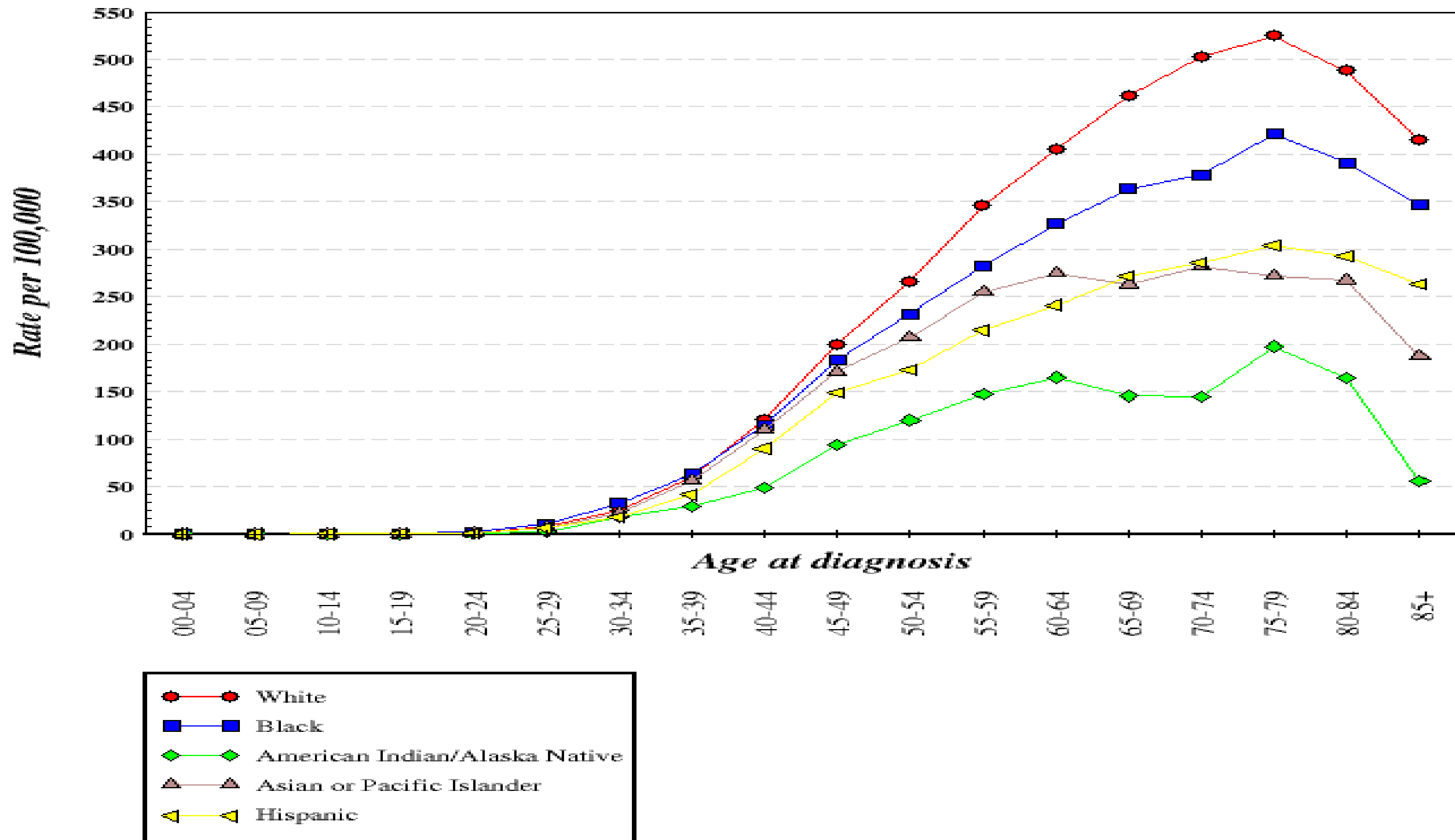
Breast Cancer Incidence in US: to 2001



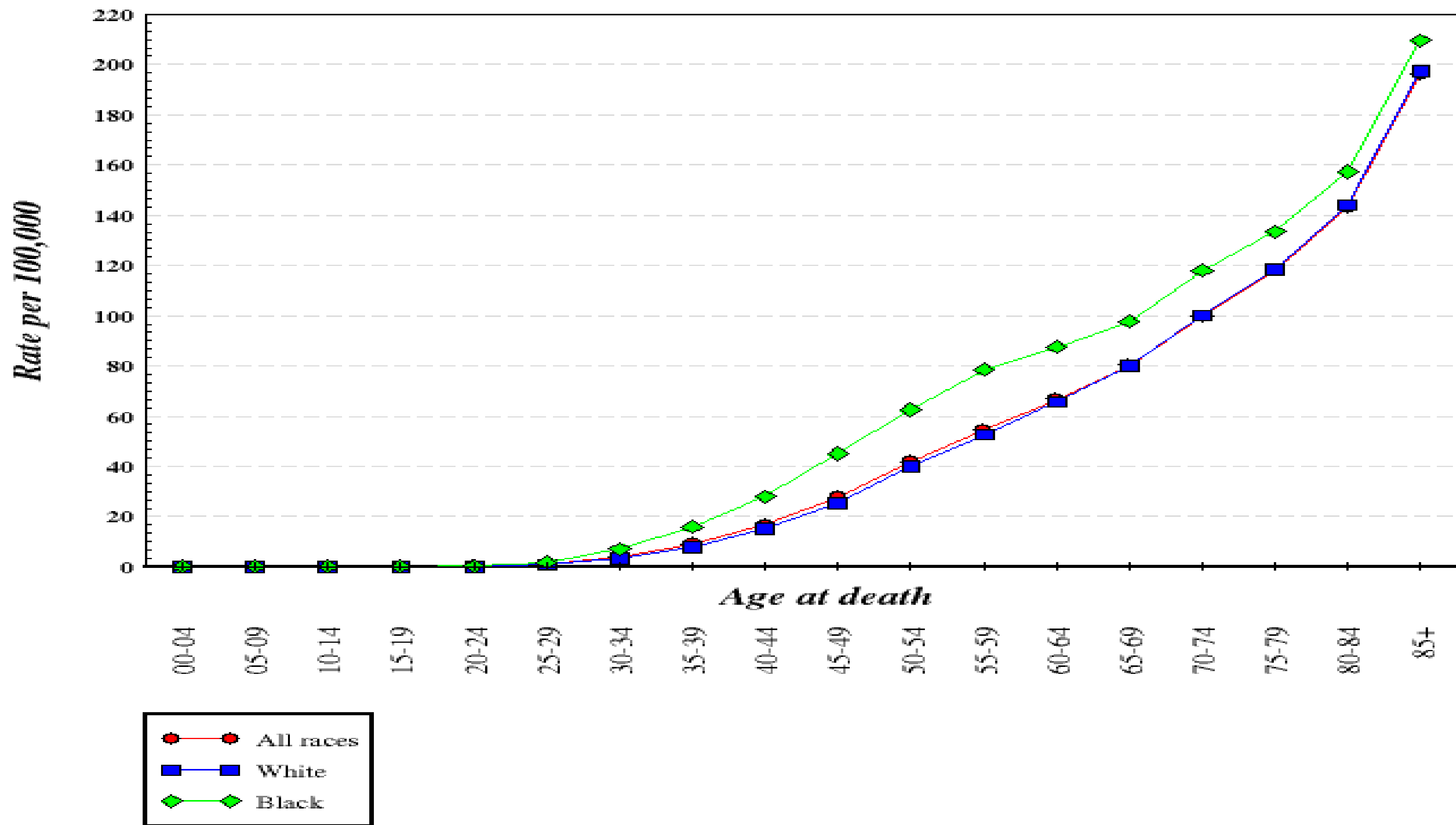
Breast Cancer Mortality in US: to 2001



BrCA Incidence by Age in US: 1997-2001



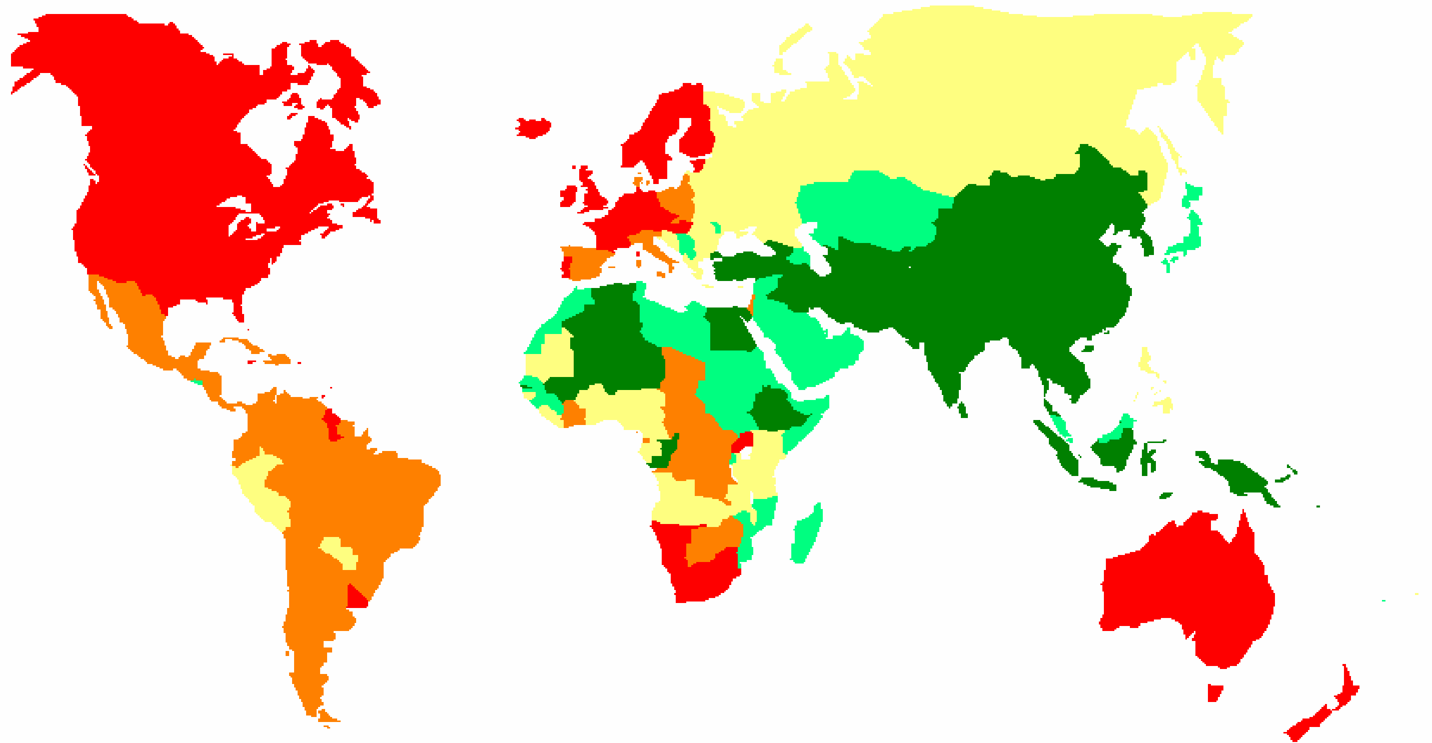
BrCA Mortality by Age in US: 1997-2001



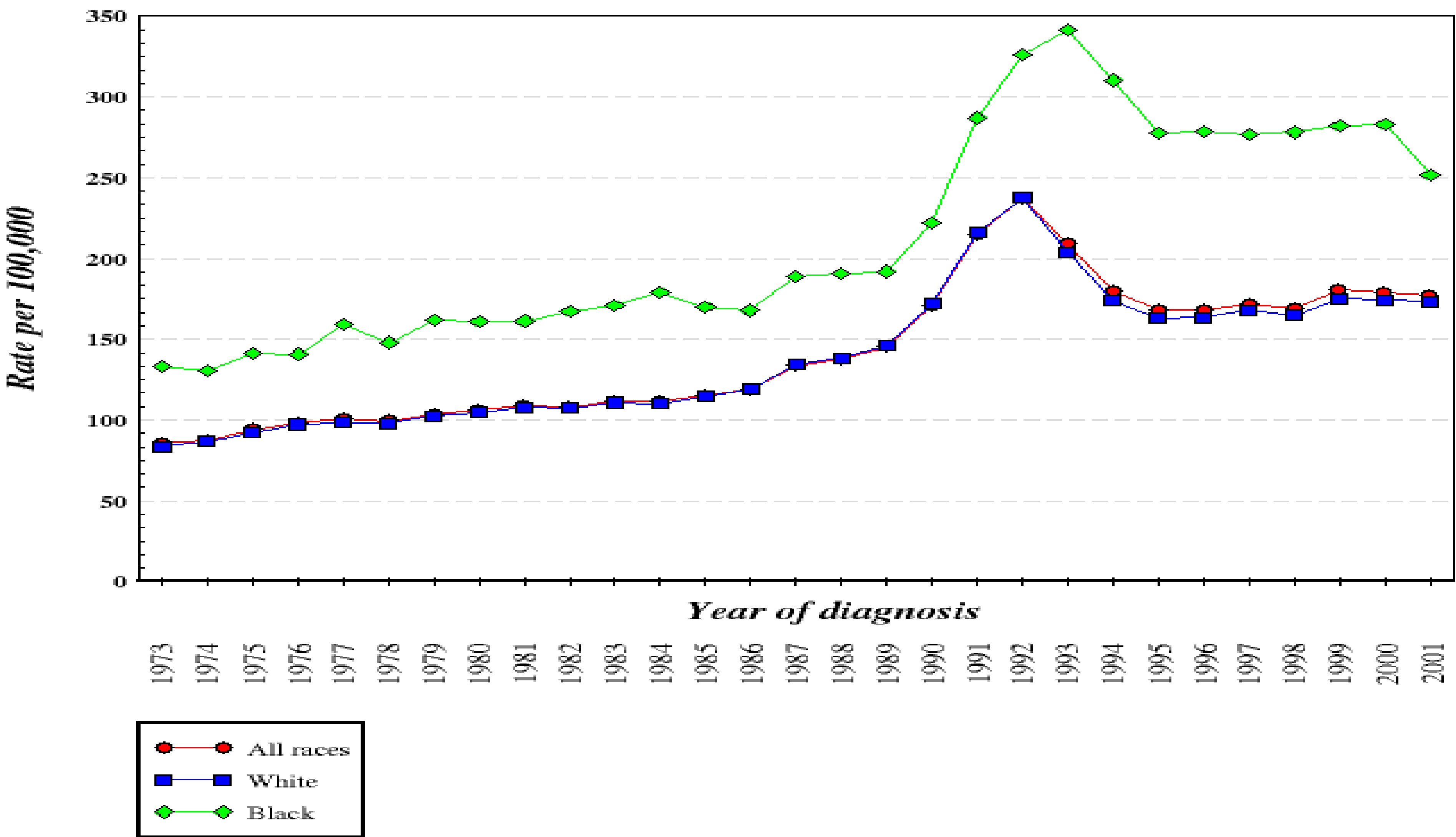
International Variation in Prostate Cancer Incidence Rates

China	***0.5 per 100,000***
Sweden	***55.3 per 100,000***
United States	***102.1 per 100,000***
West Africa	***~ 5-10 per 100,000***

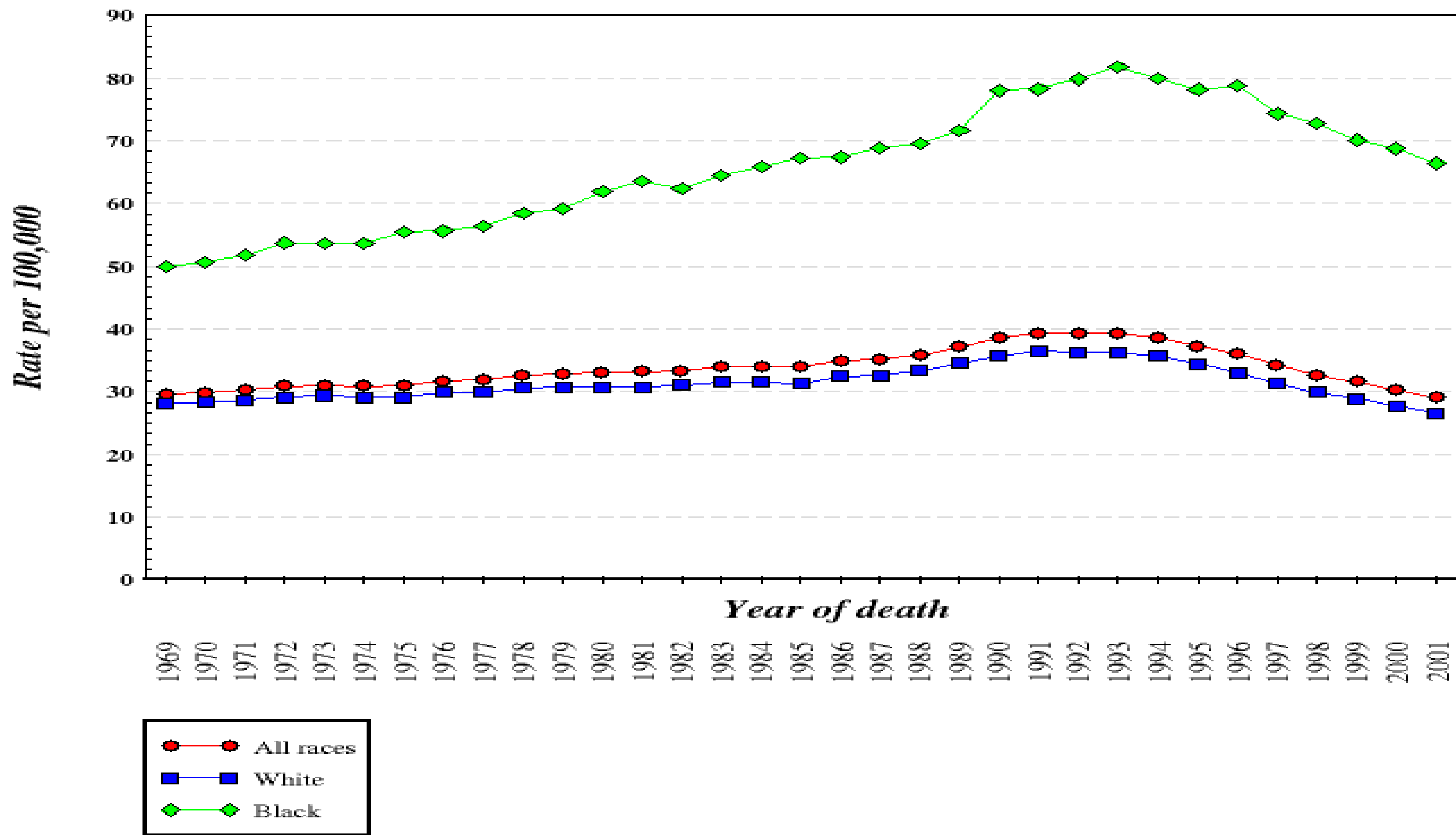
Prostate Cancer – World Map



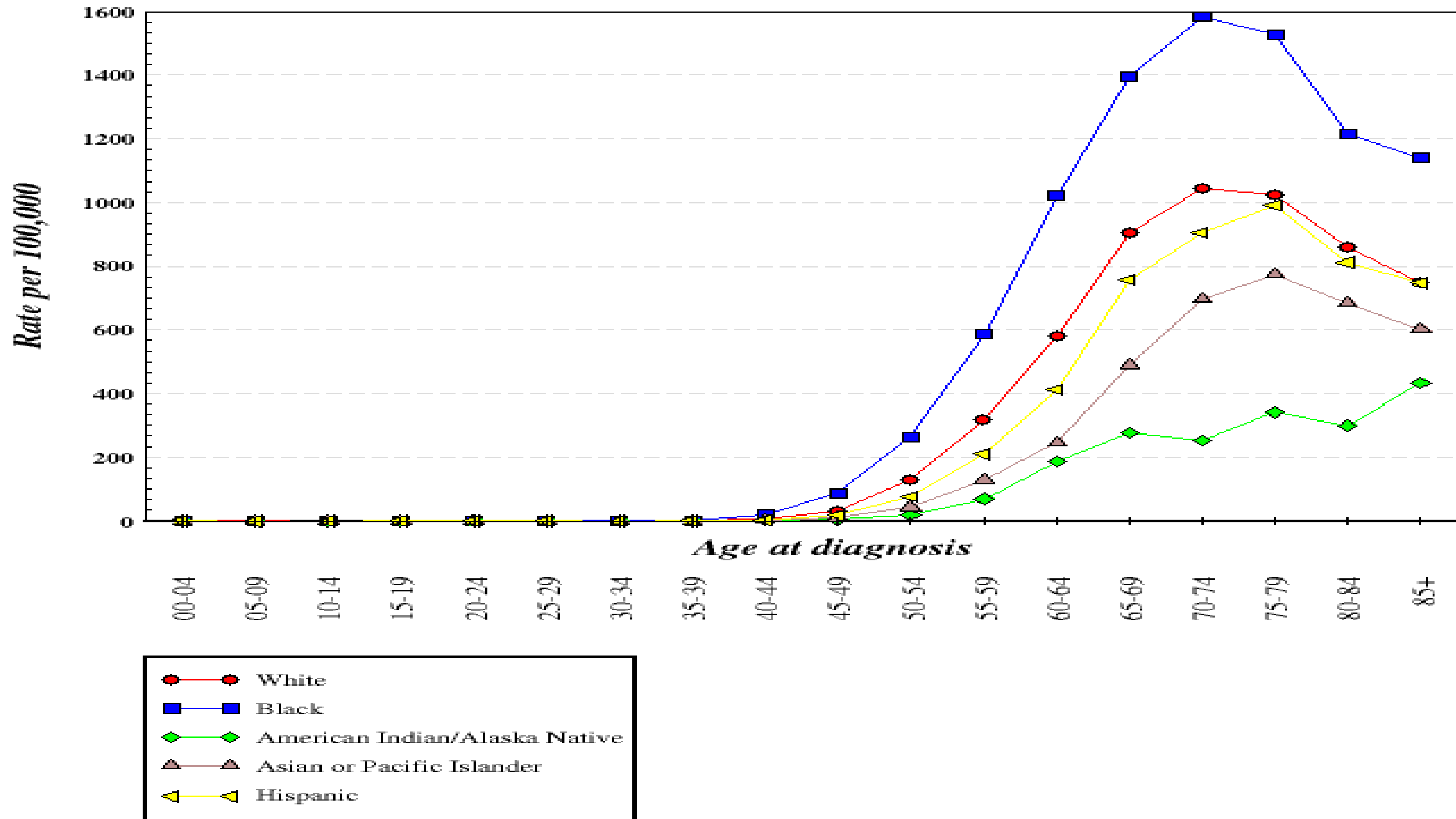
Prostate Cancer Incidence in US: to 2001



Prostate Cancer Mortality in US: to 2001



PrCA Incidence by Age in US: 1997-2001



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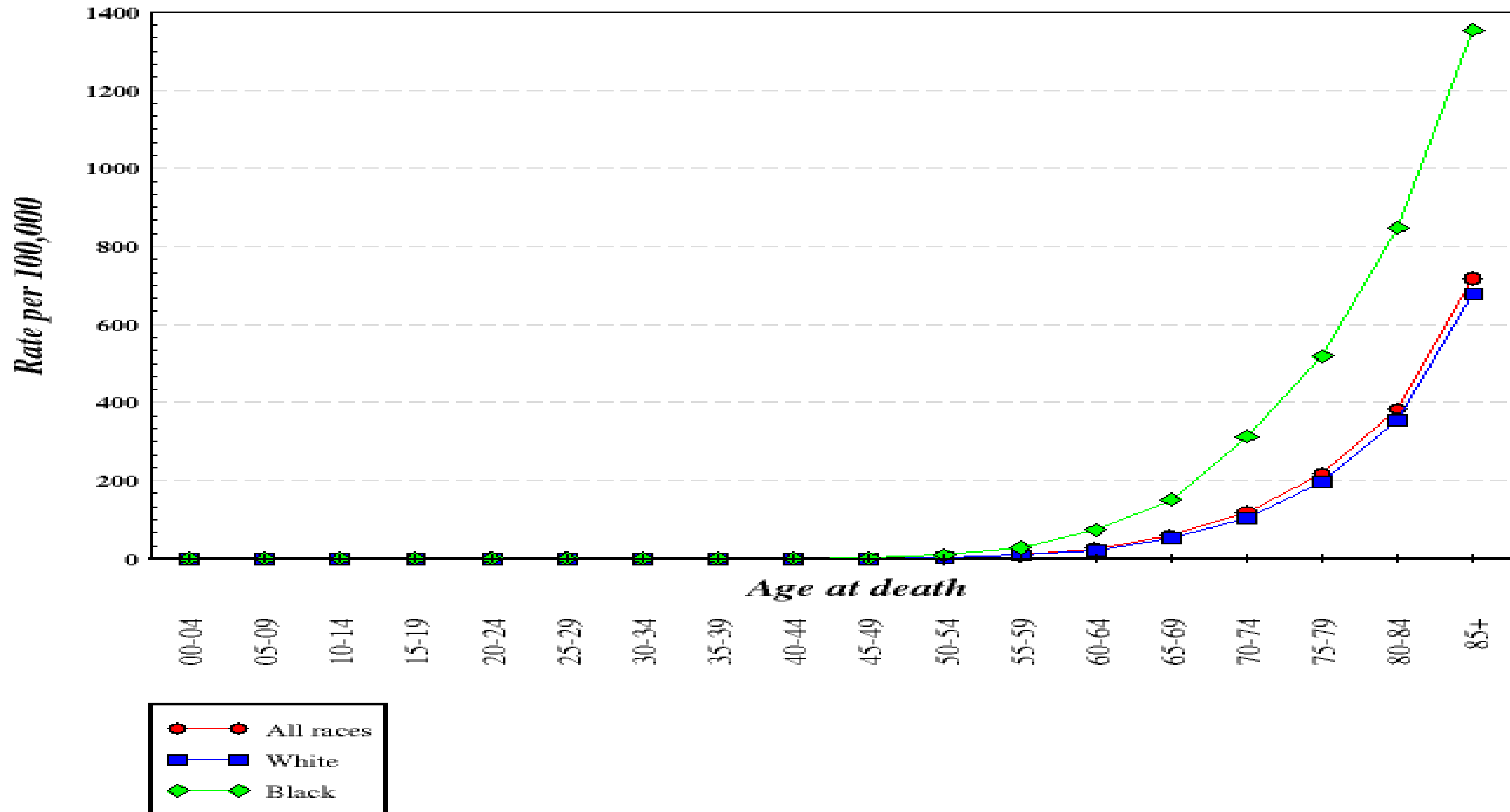


Overview of Epidemiology of Breast Cancer in South Carolina

- Incidence is lower, by 13%, in African-American women (this is slightly larger than the differential observed nationally); state rate is in the lowest quartile
- BrCA mortality, however, is much higher in African-American women, i.e., by 45% vs the national differential of 32%

Relevant Prostate Cancer Facts

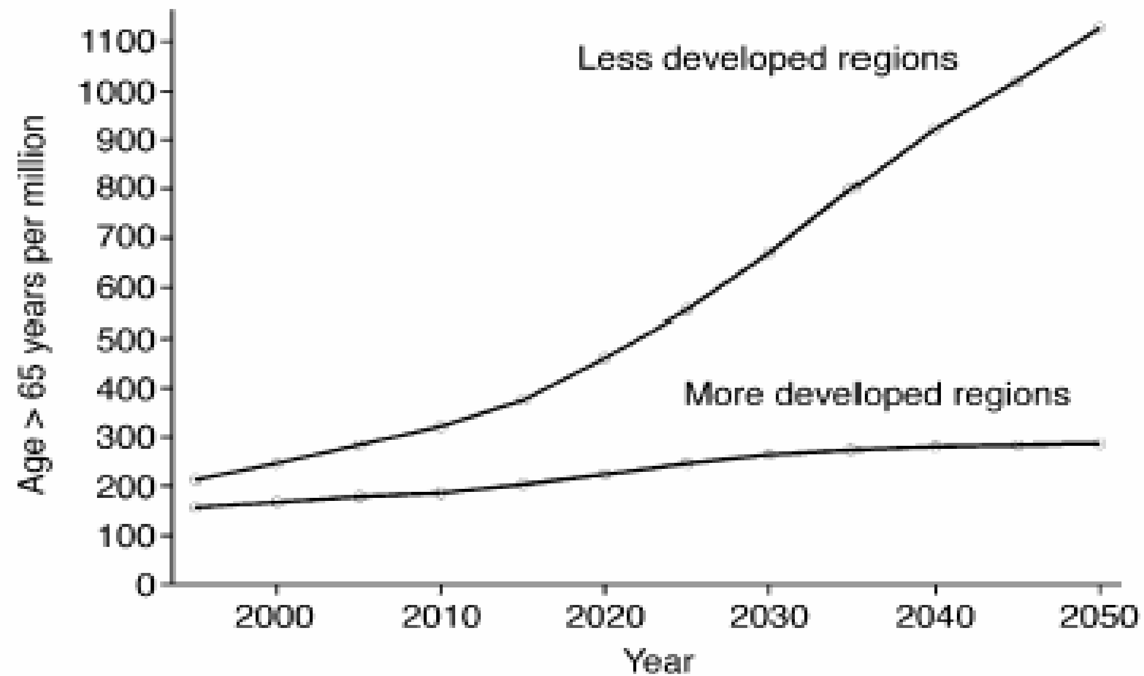
PrCA Incidence in South Carolina among the highest in the United States.

- Prostate incidence in African-Americans is ≈80% higher than in European-Americans here in SC (vs a national differential of about 55%)
- Mortality is about 150% (2.5 times that of Whites), causing us to have the world's highest death rate from PrCA
- Rates are among the highest in the world & nation

Studying Populations in Transition Allow:

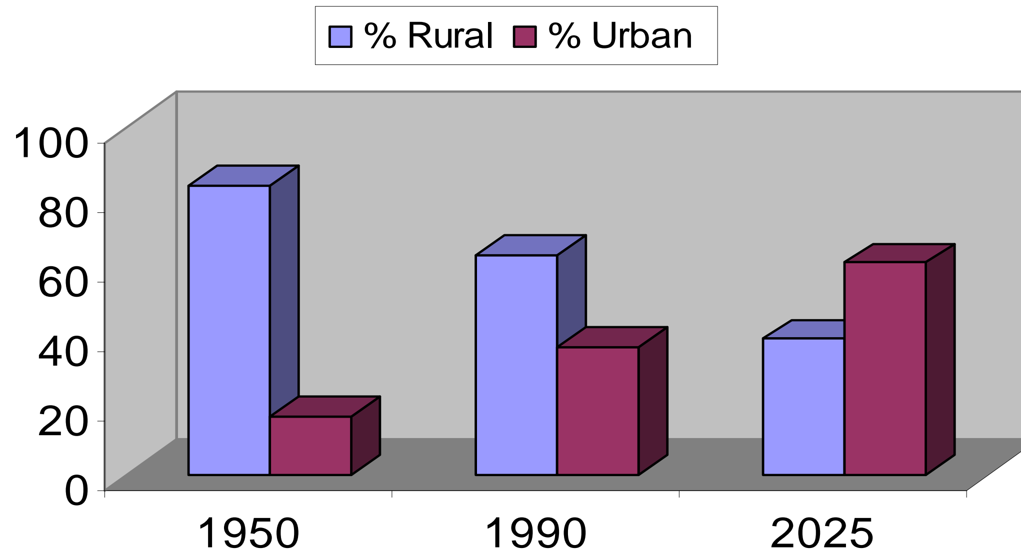
- examining exposure-outcome relationships in situations of high contrast
- us to see relationships longitudinally and not just cross-sectionally (e.g., the serum lipid example – $\rho=0$ in cross-section)

Transition: Aging



Source: Parkin et al. Cancer burden in the year 2000. The global picture. Eur J Cancer 2001; 37: S4-S66

Transition: Urbanization



Source: Parkin et al. Cancer burden in the year 2000. The global picture. Eu J Cancer 2001; 37: S4-S66

Indian BrCA & PrCA Comparison Study - Methodology

See: Hebert JR, Ghumare SS, Gupta PC. Stage at diagnosis and relative differences in breast and prostate cancer incidence in India: And comparison to the United States. Asian Pacific J Cancer Prev 2006;7(4):547-55.

Data sources:

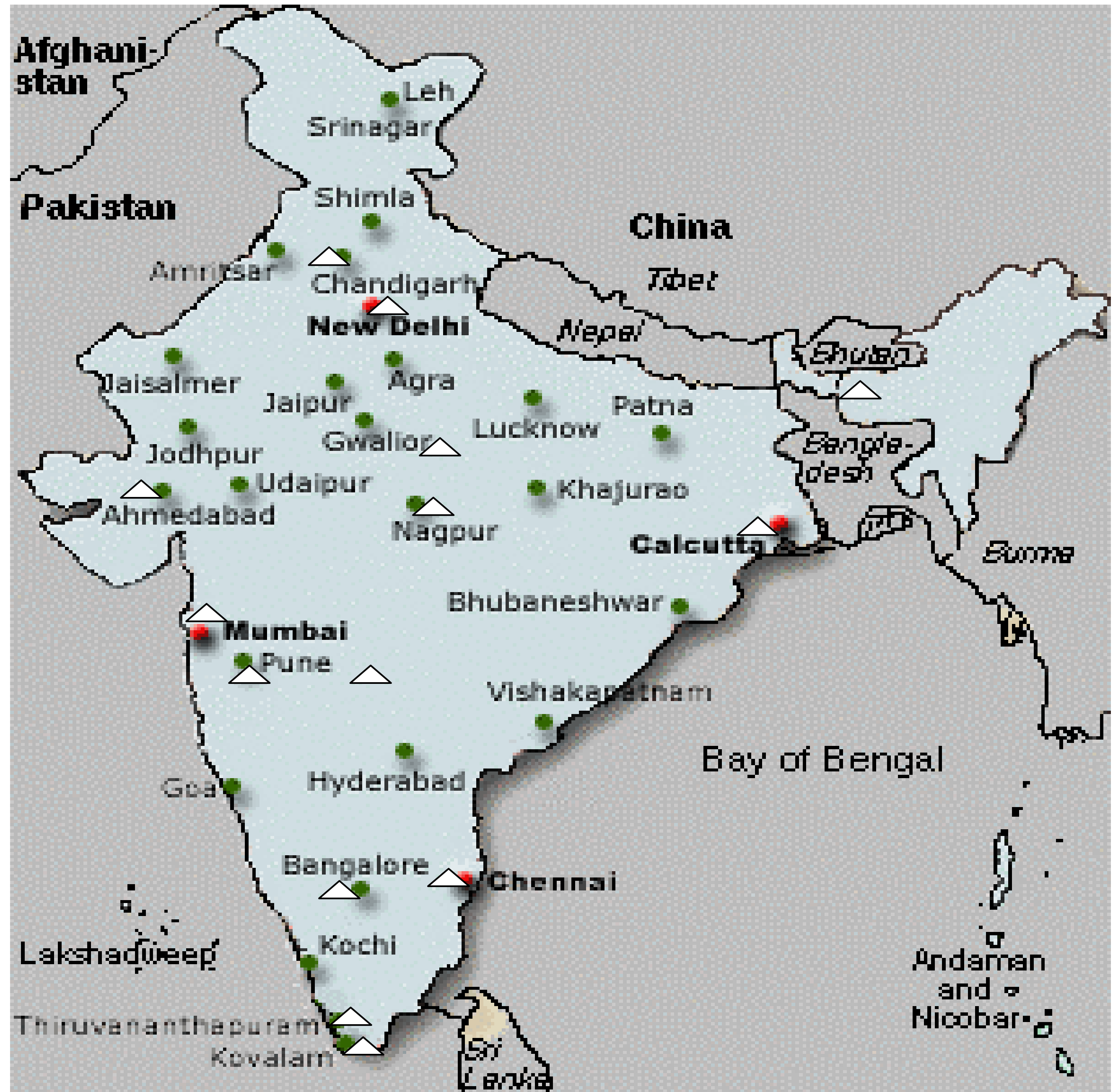
- National Cancer Registry Program- Consolidated report of the **population-based** cancer registries
- Non-NCRP population-based registries
- Cancer incidence in five continents Vol VIII (IARC)
- SEER (USA)

Years covered:

- 1990-1998

Cancer Registries in India

△ Cancer Registry

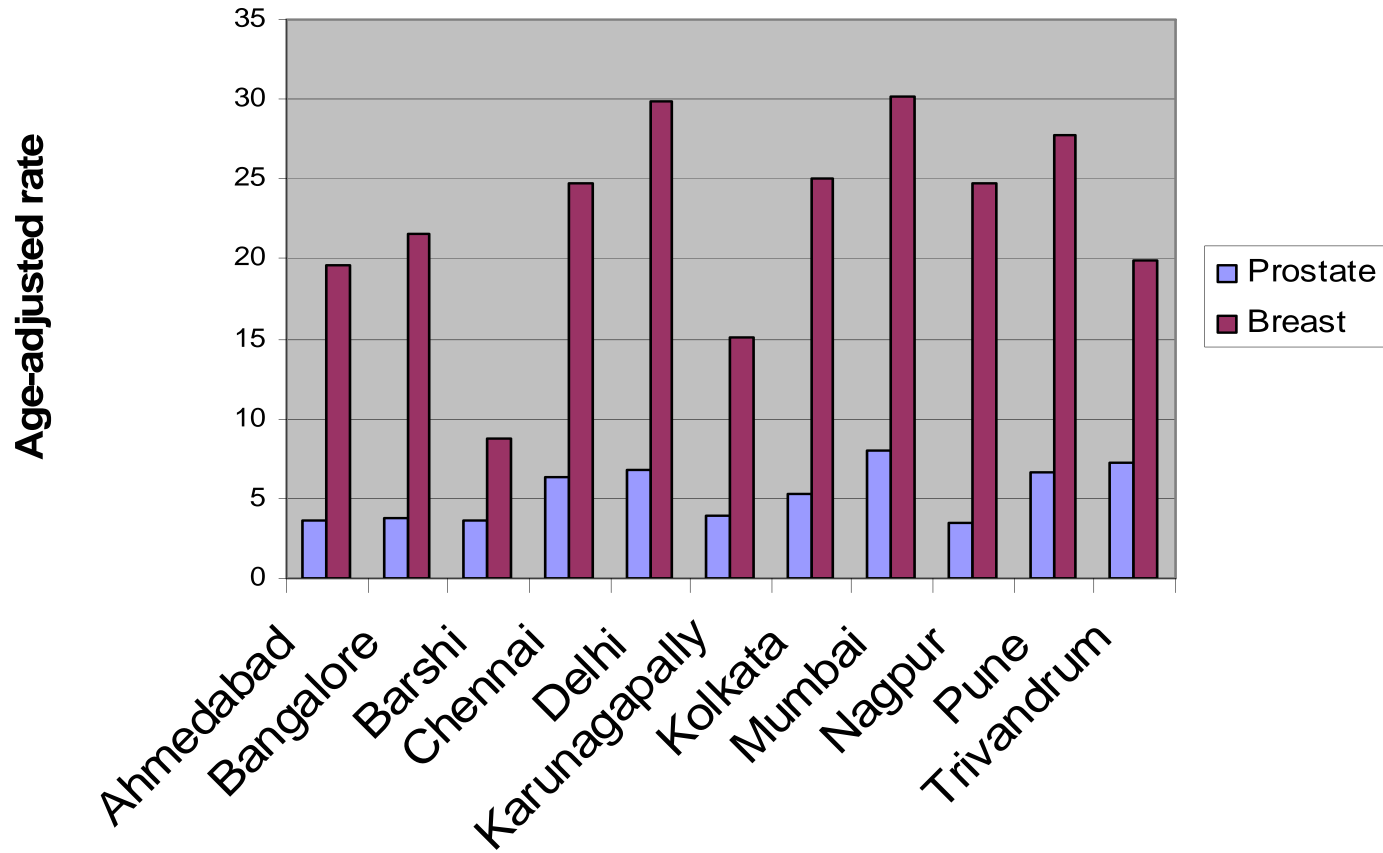


Results: Age-adjusted rates in India (All sites)

Setting	Registry	Males	Females
Rural	Barshi	42.8	52.5
Urban	Bhopal	117.0	107.8
Metropolitan	Bangalore	92.1	115.5
	Chennai	112.3	124.4
	Mumbai	116.8	126.7
	Delhi	126.1	142.0

Source: National Cancer Registry Program-First All India Report 2001-2002

Results – Comparing Breast and Prostate Cancer Rates in India

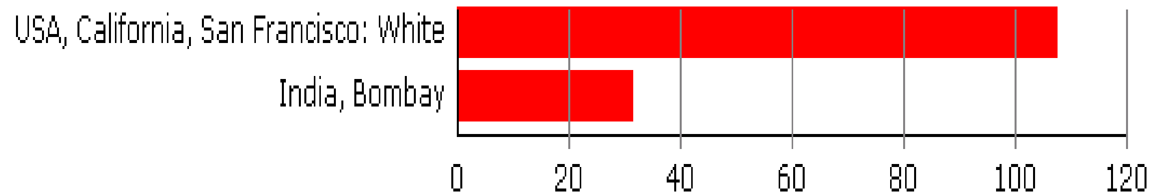


Results-comparison with SEER rates (1997)

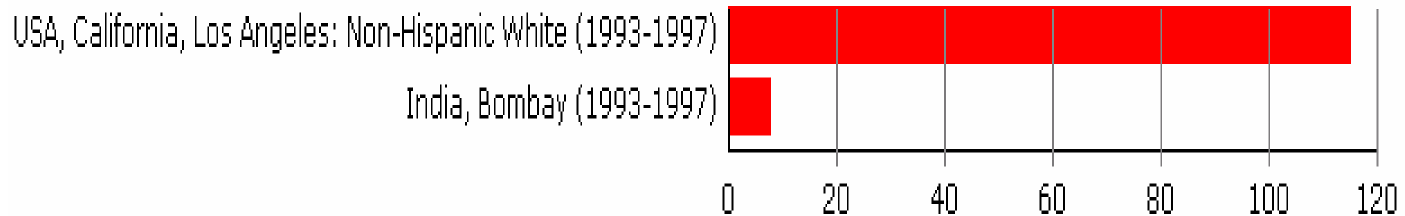
Site	India		US, Whites		US, Blacks	
	Male	Female	Male	Female	Male	Female
All sites	97.8-121.9	92.2-135.3	369.5	290.1	478.0	277.9
Prostate	4.6	-	110.4	-	180.9	-
Breast	-	19.1	-	96.4	-	86.6

Results

Breast Cancer rates comparison
Age Standardized Rate (World), per 100,000

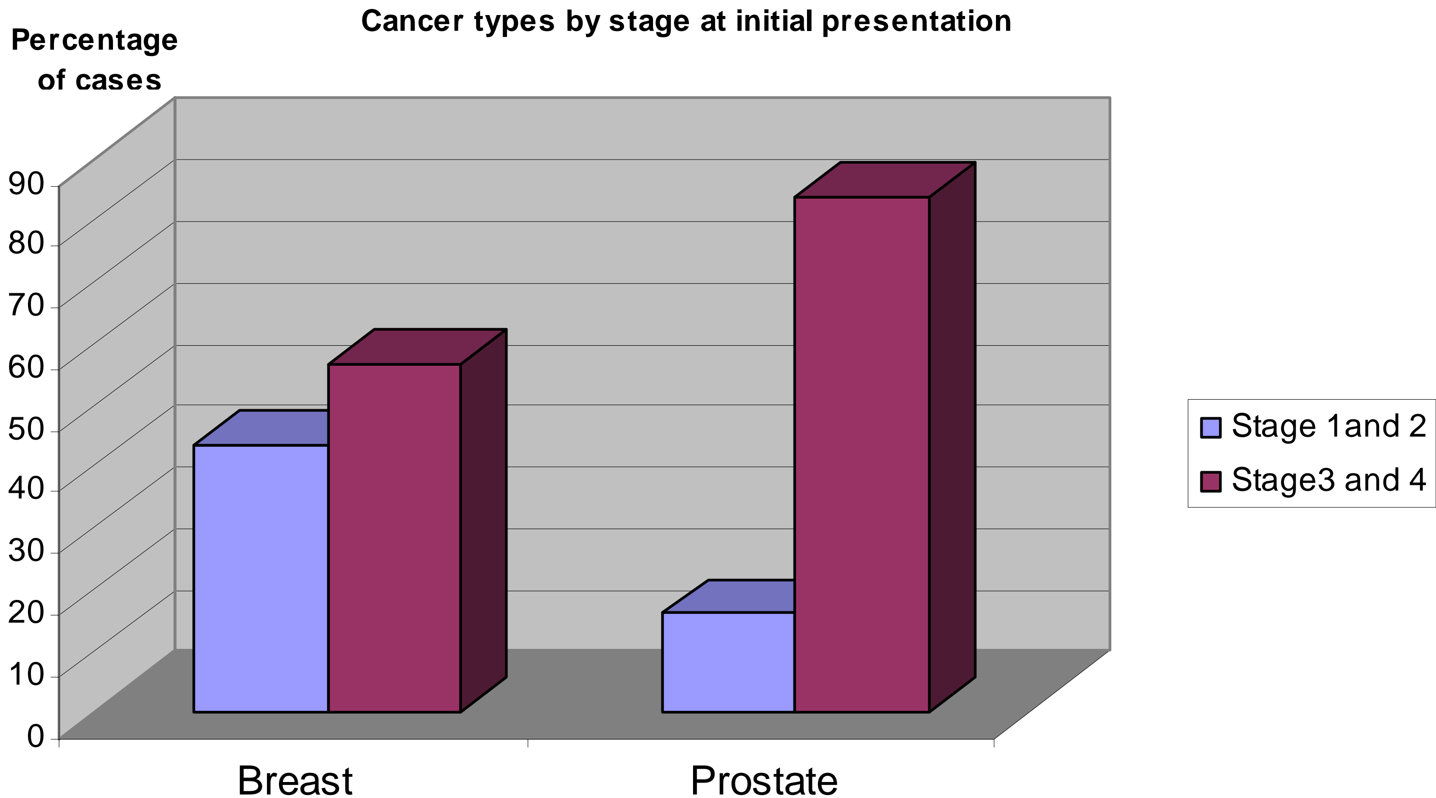


Prostate Cancer rates comparison
Age Standardized Rate (World), per 100,000



Adapted from: Cancer Incidence in Five Continents Vol. VIII, IARC

Stage at initial presentation (Excluding “stage unknown”)



Source:

1. National Cancer Registry Program-First all India report 2001-2002
2. Srinivas et al. Carcinoma of the prostate-state at initial presentation. Int Urol Nephrol. 1995; 27 (4): 419-22.

Clues from immigrant studies: breast cancer example

Population	Location	Years Covered	Incidence rate
Indian residents [a]	Karunagapally	1993-1997	15.0
	Delhi	1997-1999	33.4
Immigrant Asians and descendents			
South Asian [b]	UK	1990-1992	46.6
South Asian [c]	California (USA)	1993-1997	66.6
South Asian [d]	USA	1992-1999	61.0
Western			
All [e]	England (UK)	1993-1997	74.4
White [d]	US	1992-1999	98.3
White [d]	San Francisco, California (USA)	1992-1999	112.0

Mumbai Cohort Study (MCS)

provides an unparalleled opportunity to examine the role of dietary, and other environmental, factors in cancer etiology in a population in the midst of a demographic, nutrition, and epidemiologic transition. In the MCS we will be able to: 1) measure a wide range of dietary factors that control inflammation and 2) identify genetic factors that determine who will get cancer. This will allow us to develop new cancer prevention strategies, including adoption or retention of dietary patterns that are protective, but would be virtually impossible to study in conventional, Western populations.

Hebert JR. Epidemiologic studies of diet and cancer: The case for international collaboration. Austro-Asian J Cancer 2005;4(3):125-34.

In the meantime:

We have seen that reductions in cancer rates in the US in recent years result from the conceptually simple (if sometimes behaviorally difficult) decisions that people make in the living of their lives (e.g.,

- Quitting using tobacco
- Being screened by colonoscopy
- Deciding not to use HRT

Must work to deepen our understanding of the causes of these cancers, with a special focus on letting people know what they can do to modify risk

Thanks to the Many People and Institutions that have influenced my thinking, especially

University of Washington

- Cole P. Dodge (UNICEF)
- Ross Prentice (FHCRC)

Harvard University

- Glorian Sorensen (DFCC)
- Karen Peterson (Nutrition)
- Mohamed el Lozy (DFCC)
- Walter Willett (Nutr, Epid, CL)
- Larry Kushi (Kaiser P.)

Bombay University – Healis

- Prakash C. Gupta (USC)

Boston University – Bedford VA

- Donald Miller

American Health Foundation

- Ernst Wynder (deceased)
- Geoffrey Kabat

University of Massachusetts

- Ira Ockene (Prev Cardiology)
- Judy Ockene (Prev & Behav Med)
- Jon Kabat-Zinn (emeritus)

University of South Carolina

- Tom Hurley (EPID-BIOS)
- Bill Hrushesky (Dorn VA)
- Frank Berger (Biol – CAS)
- Jane Teas (SCCC)
- Harris Pastides (EPID-BIOS)