
Temporal trends and racial disparities in global prostate cancer prevalence

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Introduction: To inform historical trends and racial disparities in prostate cancer across time and geography.

Materials and methods: Data from 58 autopsy studies of latent prostate cancer from 1898-2013 were identified and analyzed accounting for histopathological methods, which may have varied over time.

Results: Prostate cancer is most prevalent in African descent men, less prevalent in European descent men, and least prevalent in Asian descent men. Fifty percent of Asian men have latent prostate tumors by 90. This 50% prevalence is reached by age 80 in Caucasians, and by age 60 in African descent men. While men are rarely diagnosed with prostate cancer before age 40, 4% of Asian men, 9% of Caucasian men, and 37% of African descent men have latent prostate cancer before age 40. However, prostate cancer is under-ascertained in Africa. An increase in prostate cancer prevalence was observed by observing historical trends in prostate cancer prevalence.

This increase is only significant in men of European descent, who experienced a 0.3% increase in prostate cancer prevalence per calendar year since the 1930's ($p = 0.043$). Evaluation of incidence-prevalence-duration data suggest that men are living longer with prostate cancer in recent years, perhaps due to early detection and improved treatment.

This information has relevance for the design of clinical trials of prostate cancer detection, chemoprevention and treatment, and has been incorporated into recent guidelines for the early detection of prostate cancer and biopsy recommendations.

Conclusions: Prostate cancer is common at all ages and varies by race, and prevalence is increasing over time. Autopsy-based prevalence data provide a means of examining historical trends and comparison of diverse demographic groups and help guide clinical practice and trial design for the diagnosis and treatment of prostate cancer.

Key Words: Pautopsy, prostate cancer prevalence, temporal trends, disparities

Introduction

Prostate cancer was first reported in 1817 by Langstaff and rigorously defined by Thompson in 1857.¹ Albarran and Hallé² first suggested that prostate

cancer was likely to be a common disease in 1898 after identifying 12 (16%) cases among 86 autopsied prostates. Since that time, it has become clear that prostate cancer is the most common non-cutaneous male cancer in most populations.³ African Americans suffer from among the highest incidence rates of prostate cancer in the world, with an average annual incidence rate of 165 per 100,000 in the period 2004-2008 and 229 per 100,000 in the period 2006-2010.^{4,5} The *International Agency for Research on Cancer* estimates that prostate cancer is also the leading cancer in terms of incidence and mortality in men from Africa and the Caribbean.⁶ Incidence and mortality rates are generally lower in men of European descent and even lower in men of Asian descent.^{4,5}

Estimates of prostate cancer incidence are highly variable around the world, and are influenced by

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health care access including screening and detection practices.⁷ Detection of indolent prostate tumors has been common in the United States, where prostate-specific antigen (PSA) screening has been widely used.⁸ On the other hand, it is likely that prostate cancer rates in Sub-Saharan Africa (SSA) are substantially higher than those reported in existing registries.⁹ In SSA, the infrastructure for population-based (or even hospital-based) capture of cancer cases is limited, and clinic-based studies are subject to referral and other forms of bias that may not accurately represent prostate cancer rates in a population. Autopsy studies provide an alternative and valid metric of prostate cancer in populations.

The prevalence of prostate cancer can be accurately determined if a representative cross section of a population is evaluated in post-mortem examination. If comparable techniques are used to analyze autopsied prostate specimens, comparisons of prostate cancer rates can be made across time, geography and other demographic characteristics. Here, a summary of prostate cancer prevalence is provided that informs differences across populations and changes over time that is difficult to obtain using other approaches.

Accurate knowledge of the true prevalence of prostate cancer among different populations and age groups provide important information for the design and conduct of clinical trials and therapeutic decision making. Autopsy studies may indicate not only the presence or absence of prostate cancer in given population, but can characterize these cancers to a degree that is often not possible in clinical studies. For example, data from autopsied prostates can characterize grade, stage, multifocality and geographical locations of tumors within the prostate gland, and thus direct detection efforts.

Materials and methods

Search strategy

A systematic literature search of the PubMed and Web of Science databases was conducted searching on relevant terms "prostate cancer", "latent", "autopsy", and "prevalent". Relevant articles included those that examined autopsy (cadaver) prostates and did not include data ascertained via surveys using cystoprostatectomy or other clinical approaches including treatment or screening series. In addition, reference and citation lists of all relevant publications found by this search (including review articles) were manually reviewed to identify additional articles. Summaries, comments and reviews were reviewed for reference but not used for the analysis in this study

if they did not present primary data. All potentially eligible articles were reviewed in detail to confirm that the abovementioned inclusion/exclusion criteria were met. After exclusions were applied, 58 papers were identified that met all inclusion criteria, Table 1-4.

It has been well-documented that differences in methods for the detection of tumors in autopsy prostates can lead to very different estimates of prostate cancer prevalence.¹⁰⁻¹² Therefore, autopsy evaluation technique information was determined that included step-sectioning methods¹² ("S"), random/single sections ("R") of the prostate.

Analysis of prevalence, incidence, and duration

Incidence is defined here as the number of new cases of a disease in a population, and the incidence (density) rate is the number of new cases of disease in given time period divided by the total number in population at risk at that time period (i.e., person-time).¹³ Prevalence is defined here as the number of individuals in a population who have the condition in a particular time period, i.e., the number of cases existing at the start of the period and the number of new cases that arise during that period.¹³ The prevalence rate is the proportion of a population affected by the condition in a specified time period. We use here the term "prevalence" to be the period prevalence rate, defined as the total number of individuals accrued over a time period. This period differed from study to study.

Assuming a population is stable and the incidence and prevalence rates are unchanging, the relationship of incidence and prevalence rates are well known as $I_t = P_p / D(1 - P_p)$, where I_t is the person-time incidence rate, P_p the period prevalence rate, and D the average duration of the disease from diagnosis until recovery or death.¹³ This relationship was used to evaluate prevalence data with a subset of studies for which incidence data were available.

Statistical analyses were performed to evaluate the relationship of prevalence rates by age, year of report, and race using descriptive methods, non-parametric Kruskal-Wallis analysis of variance, and linear regression. Analytic weights were used to consider the sample size involved in the reported averages. We used weights that were proportional to the variance of an observation (e.g., mean prevalence in a group) such that the variance of the j th observation is assumed to be σ^2 / w_j , where σ^2 is the total variance and w_j are the weights defined by the number of observations used to determine the sample means and variances. Spearman rank correlation coefficients were also estimated. All computations were undertaken using STATA 12.0 (College Station, TX, USA).

Results

Table 1-4 summarizes the literature of latent prostate cancer identified by autopsy studies. Data in African descent men (particularly at older ages) are limited, with more data in Asian men, and the most data in European descent men. Earlier studies tended to use random or single section prostate evaluations, while more recent data rely on serial section evaluations.

The reasons for differences in cancer rates across time or by geography can be explained by a number of factors, including differences in methods for the detection of prostate tumors in an autopsy sample.¹⁰⁻¹² A comparison of step section versus random/single section data, Table 1-4 indicate the mean prevalence of prostate cancer is higher (25.2%) among step sectioned tissues than random/single section tissues (16.1%; $\chi^2_2 = 0.02, p = 0.002$). This difference remained even after adjustment for study year. Therefore, most analyses considered the method of sectioning used to report prevalences. However, year of publication

was significantly correlated with section technique (Spearman's rho = 0.3755, $p = 0.0014$), so the potential for multicollinearity among these variables limited out ability to include both in the same linear model.

Unlike incidence, it is not expected that the use of PSA screening should change prostate cancer prevalence. A comparison of prevalences before and after the widespread use of PSA screening suggested no substantial differences before or after 1990 ($\chi^2_1 = 0.021, p = 0.885$). Therefore, all subsequent analyses considered only step-section data, and did not consider whether the study occurred before or after the PSA era.

Effect of age, race, geography, and time on prevalence

Using only prevalences estimated from serial section data, Table 1-4 the overall weighted prevalence of prostate cancer was 19.9% in men of Asian descent, 26.7% in men of European descent, and 26.2% in men of African descent. These prevalences were not significantly different from one another overall ($\chi^2_2 = 4.05, p = 0.132$), but prevalences

TABLE 1. Prevalence of latent prostate cancer as estimated by autopsy studies: pre 1940

First author/ year	N	Ethnicity/ location	Ages	Dates ^a	Age-specific prevalence (%)									Overall	Section method
					20- 29	30- 39	40- 49	50- 59	60- 69	70- 79	80- 89	90+			
Albarran ² 1898	86	France	NR	NR										16.3	NR
Neller ³¹ 1926	40	Caucasian	30-70	NR										17.5	NR
Caulk ³² 1932	NR	Caucasian	NR	NR										20.0	S
Mintz ³³ 1934	100	Caucasian	NR	NR										13.0	NR
Muir ¹ 1934	54	English	> 50	NR										13.0	NR
Rich ³⁴ 1935	292	American ^b	> 50	NR				5.4	8.1	20.3	0 ^c	0 ^c		14.0	R: 3-4 mm
Moore ³⁵ 1935	375	Austrian	20-90	1931-32	0	0	17	14	23	21	29			20.5	R: 4 mm
Graves ³⁶ 1935	NR	Caucasian	NR	NR										17.5	S
D'Abreu ³⁷ 1936	NR	Caucasian	NR	NR										16.0	S
Barringer ³⁸ 1937	NR	Caucasian American	NR	NR										17.4	S
Myers ³⁹ 1937	NR	Caucasian American	NR	NR										29.4	S
Waltherd ⁴⁰ 1937	100	Swiss	> 40	NR										30.0	S: 3-4 mm
Gaynor ⁴¹ 1938	1040	Austrian	20-90	1935-37	0	4.0	4.9	10.4	17.8	28.3	38.7	40.0		18.4	R: 3-4 mm
Yotsuyanagi ⁴² 1938	100	Japanese	NR	NR										3.0	NR
Kahler ⁴³ 1939	195	Caucasian American	> 50	NR										17.3	R: 3-4 mm

^aperiod prevalence interval; ^brace/ethnicity not specified; ^cages 80+; NR = not reported; S = step sectioned; R = single, routine or random sections. Value in mm indicates the section interval, if available.

TABLE 2. Prevalence of latent prostate cancer as estimated by autopsy studies: 1941-1970

First author/ year	N	Ethnicity/ location	Ages	Dates ^a	Age-specific prevalence (%)								Overall	Section method
					20- 29	30- 39	40- 49	50- 59	60- 69	70- 79	80- 89	90+		
Baron ⁴⁴ 1941	364	Caucasian	> 50	1935-39				6.4	8.1	16	21		9.9	R
	50	American						42.1	38.1	66.7	100		46.0	S
Lowsley ⁴⁵ 1941	120	Caucasian	> 40	NR									12.5	NR
Abe ³⁷ 1943	550	Japanese	NR	NR									1.8	R
Quinland ⁴⁶ 1943	188	African American	> 50	NR									18.0	NR
Vernet ⁴⁷ 1944	210	Caucasian	NR	NR									25.0	S
Buchert ⁴⁸ 1947	135	Caucasian	NR	NR									13.0	R
Mathé ⁴⁹ 1947	130	Caucasian	NR	NR									8.4	R
Meyenburg ⁵⁰ 1948	100	Caucasian	> 40	NR									23.0	NR
Andrews ⁵¹ 1949	142	English	15-79	1949	0	4	5.3	17.9	31.8	48	83		12.0	S: 3-4 mm
Horstman ⁵² 1952	118	Caucasian	40-86	NR									10.2	NR
Labess ⁵³ 1952	98	Caucasian	44-95	NR									9.2	R
Edwards ⁵⁴ 1953	81	Canadian	> 40	1942-45									14.8	R: 4 mm
	173						3.9	5.2	9.1	8.1	2.9		16.7	S: 4 mm
Hirst ¹¹ 1953	39	Caucasian American	> 80	1950-51							42.7	80.0	35.6	S: 4 mm
Franks ⁵⁵ 1954	178	English	> 50	1954	0	0	0	28.9	30.2	40.0	66.7	100	37.6	S: 3-4 mm
Oota ⁵⁶ 1958	203	Japanese	NR	NR									13.3	NR
Viitanen ⁵⁷ 1958	NR	Finnish	> 50	NR				14	21	30	0		22.0	S
Butler ⁴⁶ 1959	220	American ^b	> 50	NR									32.2	R: 6-8 mm
Sugihara ⁵⁸ 1959	157	Japanese	> 40	NR			2.5	4.9	19.4	30.0	0.0		10.9	NR
Imai ⁵⁹ 1960	129	Japanese	> 40	NR			0	8.8	9.7	16.7	25.0		7.7	NR
Oota ^{59c} 1961	259	Japanese- Japan	> 45	1959			5.0	6.6	13.6	35.8	45.5	50.0	18.1	S: 3-4 mm
Karube ⁶⁰ 1961	229	Japanese- Japan	> 40	1954-58			2.2	5.1	18.2	22.9	0		10.9	S: 3-4 mm
Strahan ⁶¹ 1963	85	Caucasian	60-80	NR									17.6	S: 5 mm
Schmalhorst ⁶² 1964	98	American ^b	80-90	NR									17.5	R
													57.0	S
Halpert ⁶³ 1966	407	American ^b	70-79	NR									17.4	R
	100												41.0	S
Scott ¹⁰ 1969	5000	American ^b	30-80+	1949-63	1	1	3	5	9	10 ^d	10 ^d			R
	158		70+						36	45 ^d	45 ^d		39	S: 4 mm
Halpert ⁶⁴ 1963	4696	Caucasian American	33-91	NR									8.8	S:3-4 mm
Liavåg ⁶⁵ 1968	324	Norwegian	> 40	NR			8.0	20.4	23.7	28.9	48.8	66.7	26.9	R: 4 mm
Lundberg ⁶⁶ 1970	3034	Swedish	> 40	1962-66			0.8	7.4	14.8	21.9	35.5		20.9	R: 5 mm ^a

^aperiod prevalence interval; ^brace/ethnicity not specified; ^conly the larger or more recent of studies from a group are included here; earlier studies with possible sample overlap are not presented; ^dages 80+; NR = not reported; S = step sectioned; R = single, routine or random sections. Value in mm indicates the section interval, if available.

TABLE 3. Prevalence of latent prostate cancer as estimated by autopsy studies: 1973-1992

First author/ year	N	Ethnicity/ location	Ages	Dates ^a	Age-specific prevalence (%)							Overall	Section method	
					20- 29	30- 39	40- 49	50- 59	60- 69	70- 79	80- 89			90+
Akazaki ⁶⁷ 1973	158	Japanese- Hawaii	> 50	1969-72				10.7	20.8	22.9	57.1 ^b	57.1 ^b	29.1	S: 3 mm
	239	Japanese- Japan						12.3	18.0	18.3	35.9 ^b	35.9 ^b	28.4	
Breslow ¹⁸ 1977	145	German	> 45	NR									28.4	S: 5 mm
	306	Swedish											31.6	
	173	Hong Kong											15.8	
	242	Singapore											13.2	
	168	Jamaican											29.8	
	150	Ugandan											19.5	
Guileyardo ¹⁹ 1980	207	African American	> 50	NR	0.0	50 ^c	20 ^d	34.4	44.2 ^e	44.2 ^e	44.2 ^e	44.2 ^e	31.4	S: 3 mm
	293	Caucasian American	> 50	NR	0.0	0.0 ^c	23 ^d	31.6	40.7 ^e	40.7 ^e	40.7 ^e	40.7 ^e	29.0	
Yatani ^{68f} 1982	253	Caucasian American	> 50	1969-78									34.6	S: 3 mm
	178	African American		1969-78									36.9	
	182	Colombian		1967-70									31.5	
	417	Japanese- Hawaii		1969-78									25.6	
	576	Japanese- Japan		1965-79									20.5	
Yatani ^{69f} 1988	576	Japanese -Japan	> 50	1965-79									22.5	S: 3 mm
	576	Japanese- Japan		1982-86									34.6	
Gatling ⁷⁰ 1990	1641	American	NR	1974-87									10.5	R
Stemmermann ⁷¹ 1992	293	Japanese- Hawaii	NR	1970-99				19.0	22.0	33.0	63.0 ^b	63.0 ^b	27.0	NR
Takahashi ⁷² 1992	29	Japanese	> 90	NR									58.6	S

^aperiod prevalence interval; ^bages 80 +; ^cages 30-44; ^dages 44-60; ^eages 60 +; ^fonly the larger or more recent of studies from a group are included here; earlier studies with possible sample overlap are not presented; NR = not reported; S = step sectioned; R = single, routine or random sections. Value in mm indicates the section interval, if available.

were higher in African and European descent men combined (26.6%) than in Asian descent men (19.9%, $\chi^2_1 = 4.05, p = 0.044$)

The age-specific prevalence distribution reflects these overall race-specific prevalences, Figure 1. The age-specific distribution of mean prostate cancer prevalence was generally highest at all ages in African, lower in European, and lowest in Asian descent populations. Asian descent men reached a mean peak

value of 50% prevalence in men over age 90, while the prevalence at the oldest age group reached a mean of 91.1% in European descent men. Prevalences in older African descent men (i.e., over age 70) have not been reported in the literature. Prostate cancer prevalence in African descent men in their 60's (56.7%) was similar to European descent men in their 80's (49%) and Asian descent men in their 90's (50%; Figure 1). While essentially no men are clinically diagnosed with

TABLE 4. Prevalence of latent prostate cancer as estimated by autopsy studies: 1994-2013

First author/ year	N	Ethnicity/ location	Ages	Dates ^a	Age-specific prevalence (%)								Overall	Section method
					20- 29	30- 39	40- 49	50- 59	60- 69	70- 79	80- 89	90+		
Sakr ^{20b} 1994	249	Caucasian	20-69	NR	0.0	33.0	36.0	62.0	60.0				36.0	S: 2-3 mm
	249	African American			3.0	26.0	29.0	44.0	67.0				23.0	
Shiraishi ⁷³ 1994	18	Caucasian American	< 50	1965-79	0.0	0.0							0.0	S: 3 mm
	18	African American			0.0	20.0							16.7	
	16	Japanese-Hawaii			0.0	9.0							6.3	
	47	Japanese-Japan			0.0	4.0							4.3	
	128	Japanese-Japan			6.0	17.0							14.1	
Sanchez- Chapado ¹⁴ 2003	162	Spanish	20-80	NR	3.6	8.8	14.3	23.8	31.7	33.3			18.5	S: 3-4 mm
Stamatiou ¹⁵ 2006	212	Greek	30-98	2002-04	0.0	0.0	2.6	5.2	13.8	30.9	40.0 ^c	40.0 ^c	18.8	S: 4 mm
Konety ⁷⁴ 2005	3307	American ^d	> 40	1955-60		0	1.0	4.5	7.4	8.9	22.9	4.8	R: 4 mm	
	2938			1991-01		0	0.8	2.0	2.5	3.2	0.0	1.2		
Soos ¹⁶ 2005	139	Hungarian	18-95	NR	0.0	15.0	26.6	32.1	50.0	64.7	86.6 ^c	86.6 ^c	38.8	S: 3-5 mm
Haas ⁷⁵ 2007	164	Mixed	54-73	NR									29.0	S: 4 mm
Zare-Mirzaie ¹⁷ 2012	149	Iranian	50-91	2008-09									9.4	S: 3-5 mm
Zlotta ⁷⁶ 2013	220	Russian	22-80	2008-11									37.3	S: 4 mm
	78	Japanese- Japan	24-89										34.6	

^aperiod prevalence interval; ^bonly the larger or more recent of studies from a group are included here; earlier studies with possible sample overlap are not presented; ^cages 80 +; ^drace/ethnicity not specified; NR = not reported; S = step sectioned; R = single, routine or random sections. Value in mm indicates the section interval, if available.

prostate cancer before age 40, 4% of Asian descent men, 8% of European descent men, and 35% of African descent men were estimated to have latent prostate cancer in their 30's.

As suggested by the near complete overlap of prevalence estimates by geography in Figure 2, there was no difference in prevalence between Asians living in Asia or North America (including Hawaii; $\chi^2_1 = 0.451$, $p = 0.502$), or African Americans versus Africans ($\chi^2_1 = 0.150$, $p = 0.699$). However, the sample sizes available for these comparisons remain small. While not depicted in Figure 2, there was also no difference in prevalence between European descent men living in Europe versus North America ($\chi^2_1 = 0.001$, $p = 0.970$).

Figure 2 suggests that there have been increases in prostate cancer prevalence over time. However, these effects are enhanced when including older, non-step-section data. Using step section data, only

European descent men showed significant weighted regression effects with time ($\beta = 0.32$, $p = 0.043$), with non-significant regression coefficients for men of Asian descent ($\beta = 0.31$, $p = 0.137$) or African descent ($\beta = -0.30$, $p = 0.420$). These data suggest that for every year of observed data, there has been an increase in prostate cancer prevalence of 0.32% in European descent men.

Incidence, prevalence, and duration

Incidence and prevalence data representative of major ethnic/geographical groups representing Europeans,¹⁴⁻¹⁶ Iranians,¹⁷ Ugandans,¹⁸ Japanese, Caucasian Americans,¹⁹ African Americans.^{19,20} Only prevalence studies that used a consistent step-sectioning method for prostate evaluation were included. Incidence rates were obtained for US men by using SEER⁴ data and for non-US men using GLOBOCAN data.³ Ugandan incidence

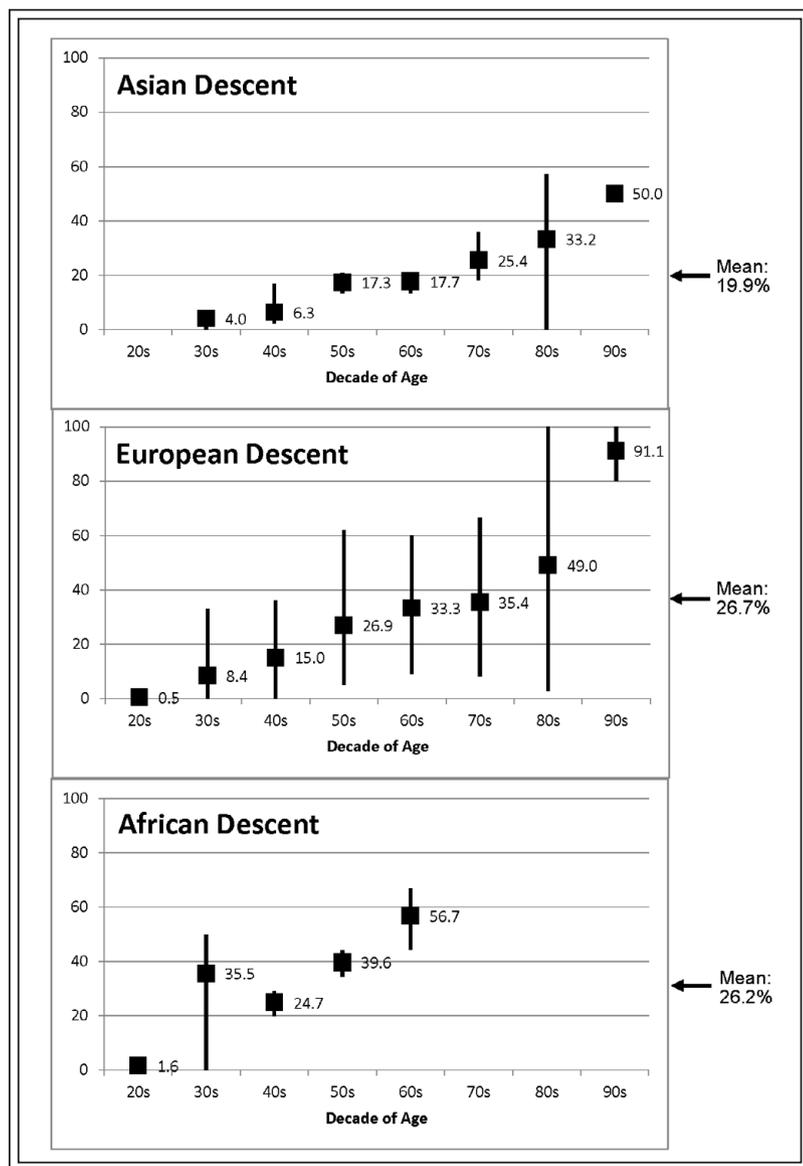


Figure 1. Prostate cancer prevalence estimates by decade of age and race: weighted mean percentage of prostates found to have prostate cancer; vertical bars denote observed ranges.

rates were obtained from the report of Wabinga et al.²¹ Incidence rates estimated closest to the period in which the prevalences were estimated. Figure 3 shows that over time, the duration of disease, measured by the metric D, has increased, with a correlation between year and D of 0.826 (p value = 0.0061). However, this strong relationship was only apparent when one data point (Uganda²¹) was excluded. As shown in Figure 3, the estimate of D (2.87) for Uganda is substantially greater than in any other country or time period. This suggests either that prostate cancer duration was substantially longer among Ugandans in the 1970s than in any other

group, or the estimate of prevalence is inflated, or the reported estimate of prostate cancer incidence is lower than it should be. It is unlikely that prostate cancer duration in that period was significantly longer in Ugandan men than in any other population, including more recent data. It is possible that the prevalence estimate was inflated if the ascertainment of autopsy subjects was preferential toward men at high risk of prostate cancer. However, there is no evidence from the original publication that this was the case.¹⁸ While the data reported by Wabinga et al²¹ appear to be accurate given the information that was available (i.e., prostate cancers that came to clinical attention), the most likely explanation is that the incidence of prostate cancer was underestimated in Uganda. This inference is supported by other data that support the hypothesis that prostate cancer is under-ascertained in Sub-Saharan Africa.⁷ These data also support the hypothesis that the duration of prostate cancer is increasing with time (i.e., men are living longer with prostate cancer than in the past). This may in part be explained by the observation that screening and improved treatment have had beneficial effects on prostate cancer survival.

Discussion

Most of the data used to characterize prostate cancers in clinical populations come from either biopsy or radical prostatectomy specimens. This information, however, is only available for those tumors which became clinically

evident and detected; the characteristics of early prostate cancers which have not been diagnosed are much more difficult. Only cystoprostatectomy and autopsy studies can accurately describe the characteristics of these clinically undetected tumors. Recent studies²² evaluated size, grade, multifocality, location and even optimal biopsy strategies to locate such lesions. This knowledge has been incorporated into strategies of risk stratification,²³ prostate biopsy strategies²⁴ and guidelines for the early detection of prostate cancer.²⁵

This report demonstrates that autopsy studies of latent prostate cancer can provide information about

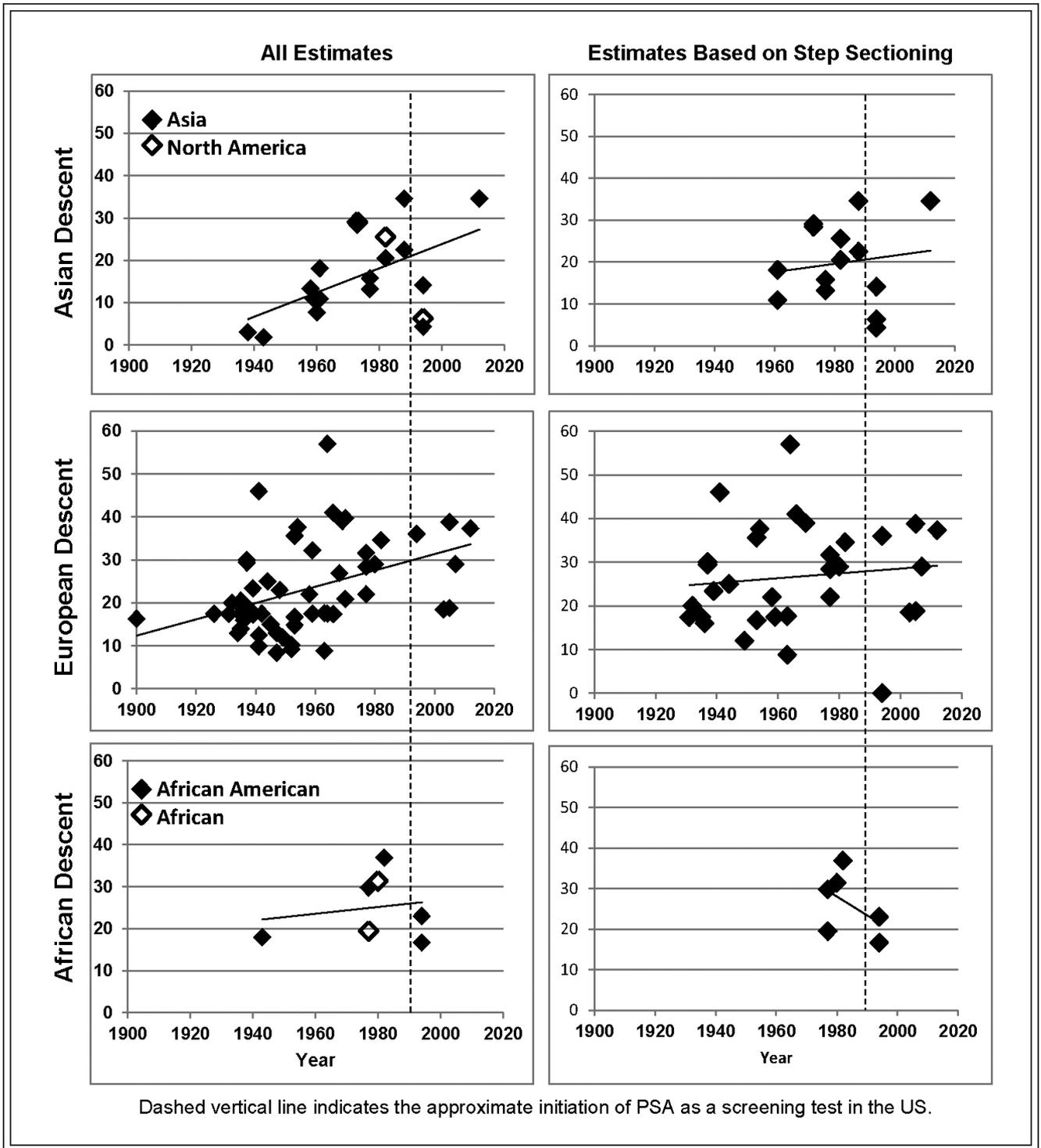


Figure 2. Prostate cancer prevalence estimates by year and race.

differences by race as well as changes in prostate cancer occurrence over time using data from historical data. The data presented here confirm that prostate cancer prevalence is highest in men of African descent, lower in men of European descent, and lowest in men of

Asian descent. These data also demonstrate that these relative differences are present at most ages, and that prostate cancer increases with age in all races. Why may these trends have been observed? Changes in methodology and clinical practice could change the

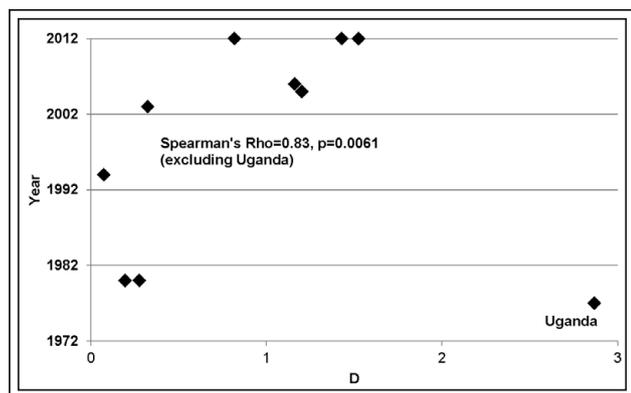


Figure 3. Relationship of incidence, prevalence and duration.

probability of detecting a prostate tumor. This is likely given the effects on prevalence we identified that compared serial section versus random or single section methods. However, the effect of technique cannot completely explain the differences observed here. PSA screening would be likely to change the clinical detection of cancers, but it is not expected to influence the prevalence of cancer in a population. The present data suggest no differences in prostate cancer prevalence before or after the onset of widespread PSA screening. Demographics or changes in lifestyle or exposure may also explain increases in prostate cancer over time or with age. Increasing lifespan is one reasonable explanation for increasing prostate cancer prevalence. Since the data presented here stretch back as far as 1900, these differences could well reflect lifespan changes. According to the US Census, European descent men in the US had a life expectancy at birth of 48.2 years in 1900, 66.3 years in 1950 and 74.8 years in 2000. Given that age is the single most salient risk factor for prostate cancer, this is a likely explanation for the temporal trends in prevalence.

Changing lifestyle is also a potential explanation for differences in the occurrence of prostate cancer over time. However, few if any risk factors have been identified that may explain changes in prostate cancer occurrence (risk).²⁶ Thus, if changes in exposure or lifestyle explain these changes over time, it is not possible at this time to know which factors may have played a role. Finally, the short period of time over which these data were collected suggests that genetics is not a major explanation for the increase in prostate cancer prevalence, although genetic susceptibility to changing environments could explain these observed patterns.

While these data present a unique perspective about prostate cancer, there are limitations that temper the

inferences that can be made using the information presented here. While an advantage of autopsy studies is that a relatively consistent approach can be used across time and populations to estimate cancer prevalence, there is still likely to be a great deal of variability in methods and data quality that cannot be adequately evaluated. This is particularly true for older studies (e.g., before 1960) where methods may not have been presented in detail. Thus, increases in prostate cancer prevalence over time could reflect actual changes to the prevalence of prostate cancer, or improvements in pathology methods that allowed improved detection of tumors over time. The data presented here clearly suggest that systematic step sectioning methods may have improved the capture of prostate tumors compared with random or single sections that have been used in some reports, Table 1-3. In addition, the epidemiological methods for many studies do not clearly define the sampling design or any inclusion/exclusion criteria used. In addition, data from populations in the developing world (e.g., Africa, South America, South and Southeast Asia) are particularly limited.

Information derived from autopsy studies also has relevance to the design of recent clinical trials which can lead to public health policy, detection and treatment guidelines, and everyday clinical practice. The recently conducted Prostate Cancer Prevention Trial²⁷ utilized data from autopsy studies to predict baseline prostate cancer prevalence in the target population. Their finding of nearly 25% prostate cancers in the control arm of the study (in men aged 55-70 with PSA < 4 ng/mL, who received placebo only), presumably represent typical men biopsied only due to study requirement, is consistent with data from the autopsy study of Sakr et al.^{28,29}

Recent efforts to develop nomograms and Risk Calculators to help guide physician recommendation and patient decision to undergo prostate biopsy and to select appropriate management also rely on autopsy studies to inform of the prevalence and characteristics of prostate cancers in particular populations.²³

The American Urological Association (AUA) recommendations on the technique of prostate biopsies to detect cancer were based, at least partially on information on the location of cancers and optimum targeting of specific regions of the prostate as derived from autopsy data.^{22,30} The autopsy prevalence of prostate cancer in young US and European men was also a key consideration in the recently published AUA Guidelines for the Early Detection of Prostate Cancer. The guidelines advised against prostate cancer screening in men under the age of 40 and referred

to the low prevalence of cancers found in US and European men under the age of 40 in autopsy studies.²⁸ These examples demonstrate the importance of the identification and characterization of prostate cancers in autopsy studies for the design of rational studies and clinical recommendations. Prostate cancer is common in men at all ages, even in young men, and varies by race. Temporal trends in prostate cancer prevalence in all populations suggest that increased use of screening is the only explanation for increased prostate cancer occurrence. Autopsy studies of latent CaP can provide valuable information to inform epidemiological, etiological, and clinical research at a variety of levels. Limitations in the data, including more limited data in men of African descent, are required to fill gaps in this body of knowledge. □

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