An estimate of prostate cancer prevalence for a demographically similar workforce population

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Abstract

To obtain an estimate of prostate cancer prevalence when screening is applied to a workforce, we conducted a search of the English world literature from West Virginia University. Thirty-one papers which met selection criteria for screening were followed by histopathologic diagnosis. Publications using Prostate Specific Antigen (PSA) as a screening test were reviewed. The data from these papers were combined. Population characteristics were then selected to represent the demographics of a working population. Prostate cancer prevalence estimates for the demographics of a working population were calculated using a weighted mean after relevant studies lacked homogeneity and therefore failed meta-analysis. The expected prevalence of prostate cancer in a workplace surveillance population is 2.03% (95% C.I. from 1.69% to 2.37%). This information is useful to entities considering workplace surveillance. Selection bias, geographic location, and uncertainty in prediction of a representative workforce population may strongly influence estimates.

Introduction

Each year thousands of men undergo prostate screening tests as a part of the routine physical examination or when being seen for other health problems. Current recommendations by the American Cancer Society are for annual screening Prostate Specific Antigen (PSA) tests for men greater than 50 years old (1).

Prostate cancer will be diagnosed in more than 200,000 men yearly; 41,800 will die of the disease, making it the second leading cause of death after lung cancer. Prostate cancer accounts for 15% of cancer related deaths in men (2,3).

Screening recommendations are made in hope of detecting prostate cancer in an early stage so that appropriate medical intervention can be made which ultimately will cure the disease. Prostate cancer screening has been promoted as a reasonable and effective workplace health promotional intervention (4).

A long-standing concern about prostate cancer surveillance is absence of population evidence that available interventions result in decreased morbidity, increased life expectancy, or improvement in quality of life (5,6). The ultimate justification of a screening test is the cost effective reduction in mortality and morbidity which an intervention subsequently provokes. In the absence of increased survival or decreased morbidity, the application of a screening test fails to meet standard public health principles of medical surveillance (7). In fact, concern has been expressed that therapeutic interventions provoked by surveillance may increase morbidity without improvement in quality of life or survival.

The National Institute of Health has launched a 15-year prospective multi-center Prostate Cancer Detection Project which addresses the questions of screening and treatment effectiveness (8). A secondary need exists for sound data on the prevalence/incidence of prostate cancer in the general public when undergoing screening. For example, data concerning expected rates are essential if environmental relatedness of the disease is to be assessed. Current screening recommendations are based upon non-randomized studies whose interpretations are complicated by the many unknowns surrounding the natural history of prostate cancer.

There is a real need for sound prevalence data, particularly if we are to recommend screening in settings such as the workplace where population outcomes will be closely scrutinized for efficiency and utility as well as for deviations from expected norms that might be hypothesized to reflect environmental causation.

When routine screenings are performed, they occur over a period of time. During this time frame,

detectable disease occurs adding incidence to prevalence. Some disease present in the survey population may be missed. The expected outcome of screening is prevalence at outset plus any new incident disease during testing, minus any existing disease missed by the survey.

This outcome creates the "harvest" which closely approximates prevalence when survey tests are sensitive and administration time is limited. Screening closely approximates incidence when periodic testing is performed. This is primarily because frequent screening decreases prevalence at onset if known existing cases are excluded.

In our study, the expected harvest of prostate cancer was estimated when screening is performed on the general public. This estimate can be applied to the workforce of an industrial setting. From a public health perspective, the data on the expected number of prostate cancer cases are crucial to the identification of risk factors (or protective behaviors) for developing prostate cancer. Since physicians feel uncomfortable ruling out the diagnosis of prostate cancer in a male greater then 50 years old with a digital rectal exam (DRE) alone, the Prostate Specific Antigen (PSA) test is used alone or in combination with the physical examination. Prostate Specific Antigen is relatively inexpensive ($17-$112), easily administered, and hence amenable to worksite intervention (9,10).

Materials and methods

An analysis of the published English literature was performed. Included was a Medline search using Grateful Med ®, Cancer Lit ® CD ROM, and current journal articles, from 1988 through 1997. Search terms were prostate cancer, prostate specific antigen and cancer screening.

A total of 127 relevant journal abstracts were reviewed. Selection criteria for further review included the following:

1. The total number of persons enrolled to be used as the denominator;
2. PSA testing performed;
3. Number of prostate cancers detected; and
4. All cancers must be histopathologically documented.

Of the 127 abstracts, 31 papers were chosen for closer analysis and Table 1 shows the data recorded. For each study, calculations of the harvest of prostate cancer were made for the tested population. Using the group of studies combined as a whole, harvest data were calculated for the tested population.

After examining the data, criteria were developed to resemble the age distribution of a working population most likely to undergo prostate cancer screening. Based on present screening recommendations, this is males older than 50. Since prostate cancer increases markedly with age, exclusion of males likely to be retired is necessary. This frequently turns out to be persons in their eighth decade of life or older (11). For workplace comparability, we limited our population to ages 50-71.

In addition, the survey population needed to be from the general public for inclusion. They should not be selected from a referral base, which implies population selection factors such as previous abnormal screening (rectal exam, or PSA). Inclusion of pre-screened groups would give a disproportionately high percentage of prostate cancer. Since the PSA has become the screening test of choice in industry, studies which did not use PSA in screening were excluded. Where identifiable subpopulations within an excluded study (when the study was considered as a whole) met inclusion criteria, the subpopulations were included despite the larger population's exclusion. Finally, publications analyzing identical populations represent duplicate data and were therefore excluded.

Meta-analysis was attempted but failed because of statistically different results between the extracted data populations. Reasons for these statistical differences were explored. Ultimately, a weighted mean was calculated using screened populations as denominators with the figures for biopsy-proven prostate cancer as the numerators.

Table 1. Data Recorded From the 31 Studies on Prostate Cancer.

Study Title
Year Performed
Year Published
Author
Where Published
Location
Selection Criteria
Prevalence vs. Incidence Plus Prevalence
Were Digital Rectal Exams Performed and Result
Prostate Specific Antigen Test and Results
Type of PSA Assay Used
Transrectal Ultrasound (TRUS) Used and Results
Number of Subjects Undergoing Biopsy (Direct of Under Ultrasound)
Diagnosis of Prostate Cancer
Population Tested
Age of Population Tested
Age Distribution of Those with Prostate Cancer

Results

Tables 2a and 2b summarize the 31 studies selected. As mentioned in the footnotes of these tables, some of the studies are further broken down into two or three studies to maximize qualifying data (Table 3).

This extraction of data preserved data which might have been lost if exclusion criteria were applied to the whole study. Table 4 shows studies excluded from our analysis and the reason for exclusion. It should be noted that exclusion of studies does not necessarily imply design flaws. Most studies were excluded through failure to meet criteria for a workplace population at increased risk for development of prostate cancer.

The total number of people in the tested population was 275,611 with an aggregate prostate cancer harvest of 1.7%. The harvest ranges from 0.0% to 22.6%. The results in Tables 2a and 2b include data which are clearly skewed by selection of the population that was tested. Table 5 presents the studies which fulfill selection criteria for a working population. The total number of persons tested was 13,799 with an aggregate prostate cancer harvest of 2.5%. The harvest ranged from 0.3% to 3.6%.

Table 2a. Summary Data From Studies of Prostate Cancer Patients.

Main Author	Year Pub.	# Tested	# Diagnosed	% Per Tested Popular.
Mettlin	Jan. 96	2,999	84	0.028
Kantrowitz	Oct. 95	1,219	12	0.01
Egawa	Aug. 95	1,189	16	0.013
Schroder	July 95	2,028	42	0.021
Potosky'*'A	Feb. 95	100,000	1848	0.018
Potosky'*'B	Feb. 95	100,000	1310	0.013
Gann	Jan. 95	14,916	***18	0.001
Abramson	Aug.94	564	18	0.032
Bretton	July 94	1,027	39	0.038
Kirby	Jan. 94	568	11	0.019
Catalona'*'A	Aug. 93	1,0251	296	0.029
Catalona'*'B	Aug. 93	266	60	0.226
Gerber'*'A	Jan. 93	2,005	'+'19	0.009
Gerber'*'B	Jan. 93	2,131	'++'19	0.009
Imai	Vol. 51,'93	9,067	87	0.010
Gustavsson	Dec. 92	1,782	65	0.036
Brawer'*' A	Mar. 92	822	22	0.027
Brawer'*' B	Mar. 92	427	10	0.023

*' Studies broken down further for isolation of variables

***'Eighteen men were diagnosed with prostate cancer after the first year of study (i.e. initial harvest plus some incidence)

*' '++'68% of the total amount of prostate cancer was diagnosed in the first year (56 dx of prostate cancer divided by 2 study groups multiplied by 68% which equals 19) (i.e. initial harvest plus a minimal amount of incidence)

Calculations

Using the data in Table 5, a meta-analysis was attempted. There was no homogeneity for all 10 studies; and therefore, no common proportion could be estimated.

Three statistically different homogeneous strata were identified. If there were a reason to stratify the studies then a common proportion could be assumed; however, none was noted despite investigating geography, exclusively working populations, and the specialty department performing the study. Table 5 demonstrates the lack of medical reasons for stratification.

Having failed meta-analysis, a weighted mean effect of 2.03% (95% C.I. from 1.69% to 2.37%) was calculated.

Discussion

The harvest of prostate cancer in a tested population is 2.03%. When industry successfully screens a working population ages 51 to 71 years old, the figure for the expected prostate cancer prevalence is 2.03%. This decreased figure is slightly higher than prostate cancer harvest across the 275,611 whose screening harvest is known.

Having not met the criteria of a meta-analysis, it is important to consider this result in the context of its range 0.3% to 3.6%. This range reflects the harvest in those who accepted invitations and went through surveillance to biopsy when appropriate and is probably most closely aligned with the information needs of corporate planners.

There are a number of levels of uncertainty in these numbers. From an epidemiological standpoint, many of the studies fell short of acceptable standards. Most notable is that many of the studies fail to provide the total number of population invited. Due to the fact that it is difficult to determine exactly how many people a public announcement reaches, most studies failed to report the number of people invited. All studies provided the number of people tested, but the response rate of those accepting the invitation to be screened, is unclear among these studies. The characteristics (health status, age, race, etc.) of those declining to be screened is not known, making it difficult to ascertain sources of bias.

Table 2b. Summary Data From Studies of Prostate Cancer Patients.

Main Author	Year Pub.	# Tested	# Diagnosed	% Per Tested Populat.
Babaian	Mar. 92	**' 2425	88	0.036
Labrie	Mar. 92	1002	57	0.057
Thomson	Apr. 92	2736	5	0.002
Chadwick	Sept. 91	472	7	0.015
Moon'*'A	Sept. 91	190	0	0.000
Moon'*'B	Sept. 91	224	5	0.022
Mettlin	June 91	2425	52	0.021
Catalona	Apr. 91	1653	37	0.022
Vallancien	Mar. 91	100	14	0.140
Babaian	1991	287	10	0.035
Littrup'*'A	Feb. 91	368	'^^'10	0.027
Littrup'*'B	Feb. 91	400	'^^^'12	0.030
Paiken	Jan. 91	323	23	0.071
Muschenheim*A	v. 21#6 '91	342	16	0.047
Muschenheim*B	v. 21#6 '91	223	4	0.018
Perrin'*'A	1991	863	3	0.003
Perrin'*'B	1991	370	6	0.016
Perrin'*'C	1991	370	67	0.181
Cooner	June 90	1807	263	0.146
Teillac	Vol. 18, '90	685	22	0.032
Normura	June 88	6860	103	0.015
Cooner	Apr. 88	225	28	0.124
Totals		**275,611**	**4,808**	**0.017**

*' Studies broken down further for isolation of variables

^^'Plus 2 cases of dysplasia ^^^'Plus 3 cases of dysplasia

**'The number of the total population was over a 3 year period with annual exams occuring each year, resulting in initial harvest plus 3 years of incidence collected with an annual exam

Furthermore, who responded? Although age groups were chosen to reflect a working population at risk, actual work status is unknown in all but one study (4). Are responders with extra time (retirees) over represented? Or those with symptoms? Or those who have not yet been tested and therefore less likely to have symptoms?

In general, we suspect most biases would increase the estimated harvest in the present circumstance because of greater prevalence in the older age group. This assumption would change if screening becomes more generally accessible.

How well do the studies selected after the exclusion criteria have been applied resemble a working population? Many workers retire at age 65, and the age range selected here would bias toward higher harvest percentages. It could also be argued that retirement age is advancing upwards (at least in the United States) and that a group that includes those in the seventh decade of life is becoming more representative of a working population (12).

One would also have to consider the racial make-up of the working population. The prevalence of prostate cancer is apparently lower in Japanese men and higher in African-American men. This difference is hypothesized to be

Table 3. Rationale for Dividing Up Studies (Variable Isolated by Splitting Up Study).

Potosky	Race: A = White; B = African American
Catalona	Two Pre-screened Populations: A = No hx of Prostate Ca or Prostatitis B = No normalities (all abnl DRE, PSA or TRUS)
Gerber	Two Different Geographic Populations: A = Texas; B = Illinois
Brawer	Age: A = 50-70 years old; B = greater than 70 y.o.
Moon	Age: A= 40-49 y.o.; B = greater than 50
Littrip	PSA assay: A = Tandem R (Hybritech) S.D. CA; B = Pros Chek Yang Labs; Bellevue WA
Muschenheim	Two Different Geographic Populations: A = Based out of Oneida City Hospital B = Based out of Hamilton, NY
Perrin	Subject selection pool: A = Quinquennial Health Check; B = Consult a General Practitioner; C = New Urological Patient

Table 4. Studies Excluded.

Age of Patients < 50 or > 71	PSA Not Performed	Referred Patient Population	Duplicated Patient Population
Egawa	Perrin B	Perrin C	Babian**
Schroder	Littrup A*		
Potosky A	Littrup B*		
Potosky B			
Gann			
Abramson			
Bretton			
Catalona A			
Catalona B			
Gerber A			
Gerber B			
Imai			
Brawer B			
Labrie			
Thomson			
Moon A			
Catalona			
Vallancien			
Babaian			
Palken			
Muschenheim A			
Muschenheim B			
Teillac			
Normura			
Gooner			

*Littrup did not use P.S.A. in decision to bx.

**Babian '92 and Mettlin '91 both used identical study populations (American Cancer Society NPCDP data). Babian was excluded instead of Mettlin because Babian included some incidence data with initial harvest data.

due to differences in hormonal androgen secretion and metabolism in differing ethnic groups (13). The utility of ethnic/racial risk factors, independent of socioeconomic status has been questioned in some quarters (14), but best present evidence suggest future harvest predictions for prostate cancer screening would improve with ethnic and racial data. Self-selection bias presents an additional measure of uncertainty, which will change if more men are surveyed routinely.

An interesting finding is that the estimated harvest increased after applying our exclusion criteria. This is contrary to expectation and we offer no explanation. It does not appear that the final data (Table 5) are from a period of time when testing was more intense (1991-93) relative to the summary tables (Tables 2a, 2b). If anything, Table 5 appears to reflect a slightly younger age group, where the prevalence of prostate cancer would be expected to be less. One possibility is that stronger study designs identify a higher prevalence of disease. If this is the case, the explanation relates to some unknown detection bias.

As long as the public is screened for prostate cancer, there will be a need to know the prevalence of (or more precisely, the harvest of) prostate cancer in a cross-section of the general public if comparisons of potential ecological significance are to be made. As we become more successful at preventing surgical complications and treating other comorbid conditions, prostate cancer interventions may then prove to decrease morbidity and mortality. Similarly physicians may be able to identify a subclass of prostate cancer that, if detected early is curable. The workplace is a convenient place to undertake detection strategies, and, as the U.S. population ages, prostate cancer prevalence data will become increasingly important.

On a final note, it is critical to be cognizant of the way the various professional groups develop their screening recommendations. The U.S. Preventive Services Task Force

(USPSTF) has epidemiologists and clinicians making screening recommendations. These are preventive medicine experts practicing preventive medicine. The USPSTF states "Routine screening for prostate cancer with digital rectal examinations, serum markers (e.g. PSA), or transrectal ultrasound is not recommended" (1).

Other organizations advocate a more aggressive screening approach (Table 6) (1). These organizations have a lower threshold at which they will invoke the use of public resources for unproven benefit. Their recommendations are worthy of consideration but do not reflect prudent use of an ever-shrinking healthcare dollar or prudent recommendations for patient care. Alternatively, the more aggressive recommendations, by virtue of their potential to improve prostate cancer research and development, may be wisely investing today's healthcare resources for decreased future prostate cancer morbidity and mortality. This sequence occurred with the development and modification of surgery and medical interventions for breast cancer - a disease whose natural history resembles prostate cancer in some ways, a glandular cancer with a

Table 5. Demonstration of the lack of medical reasons for stratification.

Stratification Group	Study	Location
Low values	Kantrowitz ('95)*	Cambridge MA
	Perrin A ('90)	Lyons France
Middle values	Mettlin ('96)	Multicenter: U.S. & Canada
	Kirby ('94)	London England
	Brawer A ('92)	Seattle WA
	Chadwick ('91)	North Bristol U.K.
	Mettlin ('91)	Multicenter: U.S.
	Moon ('91)	New Orleans LA
High Value	Gustavsson ('92)	Stockholm Sweden

Multicenter: U.S. & Canada = MI, OH, IL, MA, GA, TX, CA, OR, WA, Toronto

Multicenter: U.S. = NY, MI, OH, GA

* The only study from an Occupational Medicine Department and of a work force population. All other studies were from Urology, Oncology or Epidemiology Departments and were of general public populations and therefore not necessarily employed (i.e. no healthy worker effect).

Table 6. Prostate Cancer Screening Recommendations (1)

Organization	Recomendation
United States Preventive Task Force	Routine Screening not reccomended
Canadian Task Force on Periodic Health Examination	Routine Screening not reccomended
American Cancer Society	Digital rectal exam (DRE) @ age 40 and up, DRE plus PSA @ age 50 and up. For African-American men and those with a family history of prostate Cancer, DRE plus PSA @ age 40 and up.
American Urological Association	DRE @ age 40 and up, DRE plus PSA @ age 50 and up. For African-American men and those with a family history of prostate Cancer, DRE plus PSA @ age 40 and up. TRUS is not recommended as routine screening tool.
American College of Radiology	DRE @ age 40 and up, DRE plus PSA @ age 50 and up. For African American men and those with a family history of prostate cancer, DRE plus PSA@ age 40 and up.

more aggressive course in younger individuals. Improvements are likely to occur in invasive prostate cancer detection and treatment, and affect future recommendations.

The work survey population who will test positive are interesting from several perspectives. First, they face important choices in the face of tremendous scientific uncertainty, a trait they share with the general population screened in private clinics. Second, the predicted size of the worksite screening harvest populations is a moving target, probably affected by survey techniques, threshold for diagnosis and existence of competing access to testing in other settings. Third, it is unclear what work survey populations learn concerning the present state of knowledge about prostate cancer, its detection, treatment, treatment benefit and morbidity.

Conclusion

The workplace provides a highly advantageous setting for detecting prostate cancer. A relatively high but fluctuating percentage of the survey population will have the condition. The percentage is presently estimated at 2.03%.

Surveys that adequately inform workers of the uncertain present benefits of participation in prostate cancer screenings hold a potentially important role in public health.

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(An appendix of the 31 studies mentioned in this article, is available from the first author.)