2006

A Case-Control Study of Farming and Prostate Cancer in African-American and Caucasian Men

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ORIGINAL ARTICLE

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Occup Environ Med 2007;**64**:155–160. doi: 10.1136/oem.2006.027383

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Accepted 7 July 2006
Published Online First 15 August 2006

Objective: To determine the risk of prostate cancer associated with farming by duration, recency and specific activities among African-Americans and Caucasians.
Methods: This population-based case–control study had information on farming-related activities for 405 incident prostate cancer cases and 392 controls matched for age, race and region in South Carolina, USA, from 1999 to 2001. Cases with histologically confirmed, primary invasive prostate cancer who were aged between 65 and 79 years were ascertained through the South Carolina Central Cancer Registry. Appropriately matched controls were identified from the Health Care Financing Administration Medicare Beneficiary File. Data were collected using computer-assisted telephone interviewing, and adjusted odds ratios (aOR) were estimated using unconditional logistic regression.
Results: Farming was associated with increased risk of prostate cancer in Caucasians (aOR 1.8; 95% confidence interval (CI) 1.3 to 2.7) but not in African-Americans (aOR 1.0; 95% CI 0.6 to 1.6). Regarding specific farming activities, farmers who mixed or applied pesticides had a higher risk of prostate cancer (aOR 1.6; 95% CI 1.2 to 2.2). Increased risk of prostate cancer was observed only for those farming <5 years.
Conclusions: Increased risk of prostate cancer for farmers in this study may be attributable to pesticide exposure. Racial differences in the association between farming and prostate cancer may be explained by different farming activities or different gene–environment interactions by race.

Meta-analyses indicate that farming is more frequently associated with an increased risk of prostate cancer in North America than in other countries.[1–3] A total of 8 of 15 studies investigating incidence of prostate cancer in North America found a modestly increased risk among farmers compared with non-farmers, with effect estimates ranging from 1.1 to 4.3,[4–11] whereas 7 studies reported no association.[12–18] Interestingly, Krstev *et al*.[9] found a decreased risk for prostate cancer in farm workers, but an increased risk in those working in agricultural production or with livestock. Studies of mortality from prostate cancer in North America suggest an increase in mortality from prostate cancer among farmers compared with other occupations in 12 of 23 studies, ranging from 1.1 to 1.6.[19–30]

Some investigations have assessed prostate cancer risks associated with duration of farming or types of farming (crop, livestock and hay farming, and licensed pesticide application).[5 6 8–10 12 13 16 26 31–33] However, only one study assessed prostate cancer risk by farming duration and type of farming among African-Americans.[9] Although African-Americans have the highest incidence of prostate cancer in the world,[34] most studies that have evaluated the association between farming and prostate cancer have been carried out on Caucasian men. By contrast, only five studies have reported this association in non-white men[24 28 29 35 36] with an even fewer number of investigations in African-American men.[9 25] Two of these studies had <100 exposed cases in one or both of the racial categories, and one additional study failed to report the number of non-white cases in farmers. Therefore, we carried out a population-based case–control study to investigate the risk of prostate cancer among both African-American and Caucasian farmers using more refined measures of exposure (duration, recency of farming and specific farming-related activities) while controlling for potential confounders.

METHODS

Study population

The methods of data collection have been reported previously.[37] This population-based case–control study included cases with histologically confirmed, primary invasive prostate cancer who were residents of South Carolina, USA, aged between 65 and 79 years and ascertained through the South Carolina Central Cancer Registry (SCCCR) between 1999 and 2001. Of the 964 cases of prostate cancer reported to the SCCCR during the study period, attempts were made to include all 168 men with advanced disease (stages III and IV) and a random sample of cases with localised disease (stages I and II). African-American men were over sampled from those with localised disease (42% of Caucasian and 82% of African-American cases). Selected cases were contacted after obtaining permission from the diagnosing doctor. From 692 selected cases, 425 (61.4%) completed the interview; 90 (13.0%) doctors refused, 71 (10.3%) patients refused, 24 (3.5%) patients died before the interview, 59 (8.5%) were not located and 23 (3.3%) were too sick to participate. In all, 7 cases with prevalent prostate cancer were excluded from the case group, and 13 cases who did not provide complete interview data including farming-related exposures were excluded leaving 405 cases for analyses.

Controls were identified from the Health Care Financing Administration (HCFA) Medicare Beneficiary File and were eligible for participation if they were residents of South Carolina, USA, and aged between 65 and 79 years. 96% of South Carolina residents aged 65–79 years are included in the HCFA Beneficiary Files (according to the South Carolina Lieutenant Governor's Office on Aging). A total of 482 controls,

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; BPH, benign prostatic hyperplasia; CI, confidence interval; DRE, digital rectal examination; HCFA, Health Care Financing Administration; OR, odds ratio; PSA, prostate-specific antigen; REF, reference; SCCR, South Carolina Central Cancer Registry.

Table 1 Comparison of cases and controls for demographic and lifestyle factors

	Cases (n = 405), n (%)	Controls (n = 392), n (%)
Age (years)		
65–69	188 (46.4)	170 (43.4)
70–74	130 (32.1)	114 (29.1)
75–79	87 (21.5)	108 (27.6)
Data missing	0	0
Race		
African-American	166 (41.0)	167 (42.6)
Caucasian	239 (59.0)	225 (57.4)
Data missing	0	0
Region		
Low country	228 (56.3)	220 (56.1)
Midlands	104 (25.7)	86 (21.9)
Upstate	73 (18.0)	86 (21.9)
Data missing	0	0
Education		
< 8th grade	102 (25.4)	84 (21.4)
Grades 9–11	53 (13.2)	64 (16.3)
High-school graduate	98 (24.4)	90 (23.0)
Some college/technical school	53 (13.2)	70 (17.9)
College graduate	95 (23.7)	84 (21.4)
p Value for trend	0.39	
Data missing	4	0
BMI(kg/m^2)		
<24.4	90 (22.8)	90 (23.6)
24.4–27.2	114 (28.9)	100 (26.2)
27.3–29.8	96 (24.3)	96 (25.1)
⩾29.9	95 (24.1)	96 (25.1)
p Value for trend	0.67	
Data missing	10	10
Family history		
No	277 (69.8)	328 (84.5)
Yes	120 (30.2)	60 (15.5)
Data missing	8	4
History of BPH		
No	239 (59.9)	287 (73.8)
Yes	160 (40.1)	102 (26.2)
Data missing	6	3
Number of PSA tests in the past 5 years		
0	59 (14.6)	85 (21.7)
1–2	127 (31.4)	142 (36.3)
3–4	64 (15.8)	64 (16.4)
⩾5	155 (38.3)	100 (25.6)
p Value for trend	<0.001	
Data missing	0	1
Number of DRE tests in the past 5 years		
0	46 (11.4)	48 (12.3)
1–2	81 (20.0)	107 (27.4)
3–4	75 (18.5)	81 (20.7)
⩾5	203 (50.1)	155 (39.6)
p Value for trend	0.02	
Data missing	0	1

BMI, body mass index; BPH, benign prostatic hyperplasia; DRE, digital rectal examination; PSA, prostate specific antigen.

frequency matched to cases for age, race and geographical region, were randomly selected from the beneficiary file. The participation rate among the controls was 63.8%. Of the remaining eligible controls, 108 (14.3%) refused), 22 (2.9%) died before the interview, 112 (14.8%) were not located and 32 (4.2%) were too sick to participate. A total of 52 cases with prevalent prostate cancer were identified through medical chart review and excluded from the control group. After eliminating the 52 controls with prevalent prostate cancer and 38 controls whose interviews were incomplete, 392 controls remained for analyses.

Farming exposures

Participants were interviewed by telephone using computer-assisted technology. Information collected included demographics, alcohol and tobacco use, medical history and farm-related exposures. Participants were dichotomously classified as farmers using the question, ''Since you were 14 years old, have you ever worked on a farm?''. Specific farming activities, exposure to pesticides, duration and recency of farming were evaluated for the farmers. Duration of farming was assessed using the question, ''After age 14, how many years have you farmed or worked on a farm?''. Non-farmers were the referent group and were compared with those farming for 0–4 years, 5–9 years, 10–20 years or 21–65 years. Recency of farming was classified using last year of farming and obtained with the question, ''In what year did you last work on a farm?''. Those who last farmed before 1950, from 1950 to 1959, from 1960 to 1979 and from 1980 to 2001 were compared with non-farmers. Farming activities were assessed using the question, ''During the time you worked on a farm, did you do any of the following activities?''. Responses to the questions regarding 17 farming activities were evaluated to identify activities that all farmers carried out (eg, planting crops, tilling soil, harvesting crops), as well as activities that consistently co-occurred. Similar activities were combined to yield six activity groups: handled hay/grain/silage, harvested tobacco, planted/picked crops or tilled soil, picked cotton, repaired pesticide equipment, or fed animals/worked with poultry or swine. Indicator variables were created to compare (a) farmers who reported the activity (exposed farmers) and (b) farmers not reporting the activity (unexposed farmers) with (c) non-farmers. In addition, pesticide use among farmers was assessed with the question, ''Have you personally mixed or applied any of the following: herbicides, insecticides, fumigants, or fungicides?''. In a similar manner, three groups were created to compare (a) farmers exposed to pesticides and (b) farmers not exposed to pesticides with (c) non-farmers.

Information about education, body mass index, family history of prostate cancer, benign prostatic hyperplasia (BPH), prostate cancer screening behaviour (prostate-specific antigen (PSA) and digital rectal examination (DRE)), drinking, smoking, leisure-time physical activity and dietary factors was ascertained by a questionnaire[37] and each factor was evaluated as a potential confounder. Body mass index, smoking duration (in years), drinking duration (in years) and dietary factors (consumption of animal fat, fruits and vegetables, and dairy products) were treated categorically on the basis of quartiles of the distribution in the controls. Family history and BPH were treated as dichotomous variables. The PSA and DRE variables were categorised by the number of tests in the past 5 years (0, 1–2, 3–4, ⩾5).

Statistical analysis

Unconditional logistic regression was used to calculate adjusted odds ratios (aORs) and 95% confidence intervals (CI) for farming exposures for all men, and separately by race. None of the potential risk factors that were tested met the 10% change between crude and adjusted point estimates criteria for confounding, hence ORs were adjusted only for the three matching variables (age, race and South Carolina region). Effect modification was evaluated using the likelihood ratio test with a p value of 0.05.

Ethics approval

This study received institutional review board approval from the University of South Carolina, South Carolina, USA, Centers for Disease Control and Prevention and National Cancer Institute.

RESULTS

The 405 cases and 392 controls included in this analysis were similar with respect to age, race and region (table 1), indicating

Table 2 Farming exposures and risk of prostate cancer

Exposure measure	Cases, n = 405 (%)	Controls, n = 392 (%)	OR*	95% CI
Farming				
Non-farmers	181 (44.7)	205 (52.3)	1	Ref
Ever farmed	224 (55.3)	187 (47.7)	1.4	1.1 to 1.9
Data missing	0	0		
Years of farming				
Non-farmers	181 (45.8)	205 (53.7)	1	Ref
Farmers				
⩽4	100 (25.3)	75 (19.6)	1.5	1.1 to 2.2
5–9	47 (11.9)	40 (10.5)	1.4	0.9 to 2.3
10–20	33 (8.4)	26 (6.8)	1.5	0.9 to 2.7
21–65	34 (8.6)	36 (9.4)	1.1	0.7 to 1.9
p Value for trend	0.51			
Data missing	10	10		
Recency of last farming				
Non-farmers	181 (48.8)	205 (58.2)	1	Ref
Farmers				
Before 1950	64 (17.3)	34 (9.7)	2.1	1.3 to 3.4
1950–9	90 (24.3)	73 (20.7)	1.5	1.0 to 2.2
1960–79	21 (5.7)	18 (5.1)	1.3	0.7 to 2.6
1980+	15 (4.0)	22 (6.3)	0.8	0.4 to 1.6
p Value for trend	0.02			
Data missing	34	40		
Mixed/applied pesticides				
Non-farmers	181 (44.8)	205 (52.4)	1	Ref
Farmers				
Never mixed	46 (11.4)	56 (14.3)	1	0.6 to 1.5
Ever mixed	177 (43.8)	130 (33.3)	1.6	1.2 to 2.2
Data missing	1	1		
Handle hay, grain, silage				
Non-farmers	181 (44.8)	205 (52.3)	1	Ref
Farmers				
Never handled	22 (5.5)	18 (4.6)	1.4	0.7 to 2.7
Ever handled	201 (49.8)	169 (43.1)	1.4	1.1 to 1.9
Data missing	1	0		
Harvest tobacco				
Non-farmers	181 (44.8)	205 (52.3)	1	Ref
Farmers				
Never harvested	136 (33.7)	114 (29.1)	1.4	1.0 to 2
Ever harvested	87 (21.5)	73 (18.6)	1.4	0.9 to 2
Data missing	1	0		
Plant/pick crops, till soil				
Non-farmers	181 (44.7)	205 (52.3)	1	Ref
Farmers				
Never planted	10 (2.5)	8 (2.0)	1.4	0.5 to 3.6
Ever planted	214 (52.8)	179 (45.7)	1.4	1.1 to 1.9
Data missing	0	0		
Pick cotton				
Non-farmers	181 (44.7)	205 (52.3)	1	Ref
Farmers				
Never picked	86 (21.2)	45 (11.5)	2.1	1.4 to 3.3
Ever picked	138 (34.1)	142 (36.2)	1.1	0.8 to 1.6
Data missing	0	0		
Repair pesticide equipment				
Non-farmers	181 (44.8)	205 (52.3)	1	Ref
Farmers				
Never repaired	172 (42.6)	141 (36.0)	1.5	1.1 to 2
Ever repaired	51 (12.6)	46 (11.7)	1.3	0.8 to 2
Data missing	1	0		
Feed animals, work with poultry/swine				
Non-farmers	181 (44.8)	205 (52.3)	1	Ref
Farmers				
Never fed	23 (5.7)	17 (4.3)	1.6	0.8 to 3.1
Ever fed	200 (49.5)	170 (43.4)	1.4	1.0 to 1.9
Data missing	1	0		

ref, reference.
*Adjusted for age, race and region.

effective frequency matching in the design phase. Cases were more likely than controls to report a family history of prostate cancer, a history of BPH and greater frequency of PSA and DRE in the past 5 years.

Table 2 presents aOR and 95% CI for various measures of farming exposures and prostate cancer. Men who reported ever working as farmers had an increased risk of prostate cancer compared with those who had never farmed (aOR 1.4; 95% CI 1.1 to 1.9). When considering the duration of farming, only those farming for a short period (0–4 years) had an increased risk of prostate cancer compared with non-farmers. Furthermore among farmers there was no dose–response relationship between increasing years of farming and risk of prostate cancer (p value for trend 0.51). Regarding the recency of farming, only men who last farmed before 1960 had an increased risk of prostate cancer compared with non-farmers. Regarding specific farming activities, mixing or applying pesticides (aOR 1.6; 95% CI 1.2 to 2.2) and not picking cotton (aOR 2.1; 95% CI 1.4 to 3.3) were associated with an increased risk of prostate cancer compared with non-farmers.

Table 3 presents the risk of prostate cancer associated with farming by race. Race modified the association between farming and prostate cancer (Breslow–Day χ^2 p value for interaction = 0.04). Farming was associated with prostate cancer among Caucasians (aOR 1.8; 95% CI 1.3 to 2.7) but not among African-Americans (aOR 1.0; 95% CI 0.6 to 1.6). As was observed among all men, farming for shorter duration (<10 years) and year last farmed occurring before 1960 were associated with prostate cancer risk, but only for Caucasian men. Mixing or applying pesticides was associated with an increased prostate cancer risk only for Caucasian men (p value for interaction = 0.11 by race for pesticide use and prostate cancer risk). For both Caucasian and African-American men, never picking cotton was associated with an increased prostate cancer risk that was more pronounced among African-American than among Caucasian men (p value for interaction = 0.08).

DISCUSSION

Our finding that farming was associated with a modest increase in prostate cancer risk is consistent with other studies conducted in the USA and Canada. We did not find any dose–response relationship between increasing years of farming and prostate cancer risk, which is also consistent with the existing literature.[12 13] Furthermore, our finding of an increased risk of prostate cancer among individuals who farmed for the shortest duration (⩽4 years) was consistent with prior studies with incidence[9] or mortality[26] from prostate cancer as the outcome. As suggested in the literature, short-term workers in general may be exposed to higher levels of contaminants or may differ from long-term workers in lifestyle and health-related factors.[38] Among farmers, short-term workers are more likely to be manual labourers, whereas those who participate in farming for longer periods are more likely to be farm owners and managers. Farm labourers may have higher or more direct exposure to pesticides than farm owners.[3 39] To restrict the window of exposure to include only those years of farming likely to be aetiologically relevant to prostate cancer, we repeated our analyses on duration of farming and excluded years farmed within (a) 5 and (b) 10 years of case diagnosis for cases and in (1) 5 and (2) 10 years of the year 2000 for controls. Adjusted odds ratios remained insignificant in all cases.

We found an inverse trend between the recency of last year farmed and risk of prostate cancer with a significantly increased OR for those farming before 1960. One explanation for this finding may be that exposures to pesticides and other contaminants may have varied in time on the basis of pesticides used, pesticide application methods, pesticide regulations, crop planting and harvesting methods, and personal protective equipment availability and use.[1] Another possible explanation is that a greater percentage (58%) of those who farmed before 1960 farmed for ⩽4 years, whereas 56% of those farming after 1960 farmed for >21 years.

Table 3 Farming and risk of prostate cancer by race

	Caucausians			African-Americans		
Exposure measure	**Cases, n = 239**	**Controls, n = 225**	**OR* (95% CI)**	**Cases, n = 166**	**Controls, n = 167**	**OR* (95% CI)**
Farming						
Never farmed	122 (51.1)	147 (65.3)	1 Ref	59 (35.5)	58 (34.7)	1 Ref
Ever farmed	117 (49.0)	78 (34.7)	1.8 (1.3 to 2.7)	107 (64.5)	109 (65.3)	1 (0.6–1.6)
Data missing	0	0		0	0	
Years of farming						
Non-farmers	122 (51.5)	147 (65.9)	1 Ref	59 (37.3)	58 (36.5)	1 Ref
Farmers						
⩽4	63 (26.6)	40 (17.9)	1.9 (1.2 to 3)	37 (23.4)	35 (22.0)	1.1 (0.6–1.9)
5–9	24 (10.1)	14 (6.3)	2.1 (1 to 4.3)	23 (14.6)	26 (16.4)	0.9 (0.5–1.8)
10–20	13 (5.5)	9 (4.0)	1.8 (0.7 to 4.3)	20 (12.7)	17 (10.7)	1.2 (0.6–2.6)
21–65	15 (6.3)	13 (5.8)	1.4 (0.6–3.1)	19 (12.0)	23 (14.5)	0.8 (0.4–1.7)
p Value for trend	0.53			0.84		
Data missing	2	2		8	8	
Recency of last farming						
Non-farmers	122 (55.0)	147 (69.7)	1 Ref	59 (39.6)	58 (41.1)	1 Ref
Farmers						
Before 1950	32 (14.4)	13 (6.2)	2.9 (1.4 to 5.8)	32 (21.5)	21 (14.9)	1.5 (0.8–2.9)
1950–9	54 (24.3)	37 (17.5)	1.8 (1.1 to 3)	36 (24.2)	36 (25.5)	1.1 (0.6–2.1)
1960–79	8 (3.6)	5 (2.4)	1.9 (0.6 to 6.1)	13 (8.7)	13 (9.2)	0.9 (0.4–2.1)
1980+	6 (2.7)	9 (4.3)	0.8 (0.3 to 2.3)	9 (6.0)	13 (9.2)	0.7 (0.3–1.8)
p Value for trend	0.05			0.14		
Data missing	17	14		17	26	
Mixed/applied pesticides						
Non-farmers	122 (51.3)	147 (65.3)	1 Ref	59 (35.5)	58 (34.9)	1 Ref
Farmers						
Never mixed	20 (8.4)	14 (6.2)	1.7 (0.8 to 3.5)	26 (15.7)	42 (25.3)	0.6 (0.3–1.2)
Ever mixed	96 (40.3)	64 (28.4)	1.8 (1.2 to 2.7)	81 (48.8)	66 (39.8)	1.2 (0.8–2.0)
Data missing	1	0		0	1	
Handle hay, grain, silage						
Non-farmers	122 (51.3)	147 (65.3)	1 Ref	59 (35.5)	58 (34.7)	1.0 Ref
Farmers						
Never handled	14 (5.9)	6 (2.7)	2.7 (1.0 to 7.2)	8 (4.8)	12 (7.2)	0.7 (0.3–1.8)
Ever handled	102 (42.9)	72 (32.0)	1.7 (1.2 to 2.6)	99 (59.6)	97 (58.1)	1.0 (0.7–1.7)
Data missing	1	0		0	0	
Harvest tobacco						
Non-farmers	122 (51.3)	147 (65.3)	1 Ref	59 (35.5)	58 (34.7)	1 Ref
Farmers						
Never harvested	79 (33.2)	53 (23.6)	1.8 (1.2 to 2.8)	57 (34.3)	61 (36.5)	1 (0.6–1.7)
Ever harvested	37 (15.6)	25 (11.1)	1.8 (1.0 to 3.1)	50 (30.1)	48 (28.7)	1 (0.6–1.8)
Data missing	1	0		0	0	
Plant/pick crops, till soil						
Non-farmers	122 (51.1)	147 (65.3)	1 Ref	59 (35.5)	58 (34.7)	1 Ref
Farmers						
Never planted	7 (2.9)	6 (2.7)	1.4 (0.4 to 4.2)	3 (1.8)	2 (1.2)	1.6 (0.2–9.9)
Ever planted	110 (46.0)	72 (32.0)	1.9 (1.3 to 2.8)	104 (62.7)	107 (64.1)	1 (0.6–1.6)
Data missing	0	0		0	0	
Pick cotton						
Non-farmers	122 (51.1)	147 (65.3)	1 Ref	59 (35.5)	58 (34.7)	1 Ref
Farmers						
Never picked	65 (27.2)	38 (16.9)	2.1 (1.3 to 3.3)	21 (12.7)	7 (4.2)	2.9 (1.1–7.3)
Ever picked	52 (21.8)	40 (17.8)	1.6 (1.0 to 2.6)	86 (51.8)	102 (61.1)	0.8 (0.5–1.4)
Data missing	0	0		0	0	
Repair pesticide equipment						
Non-farmers	122 (51.3)	147 (65.3)	1 Ref	59 (35.5)	58 (34.7)	1 Ref
Farmers						
Never repaired	88 (37.0)	58 (25.8)	1.9 (1.2 to 2.8)	84 (50.6)	83 (49.7)	1 (0.6–1.7)
Ever repaired	28 (11.8)	20 (8.9)	1.7 (0.9 to 3.1)	23 (13.9)	26 (15.6)	0.9 (0.4–1.7)
Data missing	1	0		0	0	
Feed animals, work with poultry/swine						
Non-farmers	122 (51.3)	147 (65.3)	1 Ref	59 (35.5)	58 (34.7)	1 Ref
Farmers						
Never fed	13 (5.5)	7 (3.1)	2.4 (0.9 to 6.1)	10 (6.0)	10 (6.0)	1 (0.4–2.6)
Ever fed	103 (43.3)	71 (31.6)	1.8 (1.2 to 2.6)	97 (58.4)	99 (59.3)	1 (0.6–1.6)
Data missing	1	0		0	0	

Ref, Reference.
*Adjusted for age and region.

Mixing or applying pesticides was strongly associated with the risk of prostate cancer in our data. This is similar to findings reported by Fleming *et al*[8 26] of twice the expected incidence and 2.5 times the expected mortality from prostate cancer in agricultural pesticide applicators compared with the general Florida population. Alavanja *et al,*[4] also reported an excess in the incidence of prostate cancer among agricultural pesticide applicators compared with the general North Carolina and Iowa populations. A recent meta-analysis of prostate cancer among pesticide applicators by Van Maele-Fabry *et al*[2] reported a small but marked increase in the risk of prostate caner among pesticide applicators. Taken together, these studies suggest that exposure to pesticides may play an important role in increasing prostate cancer risk, and that protective gear should be worn when mixing or applying pesticides.

As a class of agents, pesticide exposure provides a biologically plausible link between farming and increased risk of prostate cancer. Keller-Byrne *et al*[40] in their meta-analysis of prostate cancer and farming provide support for this association on the basis of their review of toxicological studies of pesticide binding to steroid hormone receptors, which then induces proliferation of prostate cancer cells. A later review of environmental endocrine modulators (including pesticides) and human health effects[41] proposed a number of mechanisms of action that disrupt the endocrine system, including interactions of chemicals with endogenous hormones or their carrier proteins to prevent receptor binding. The mechanism through which pesticide exposure may lead to prostate cancer is complex, probably differs by pesticide, and deserves attention in future research.

Our finding of an increased risk of prostate cancer among farmers who never picked cotton is difficult to explain, although those who never picked cotton were more likely to have farmed for shorter durations, and this group of farmers had the highest prostate cancer risk. Thus, the observed increased risk associated with never picking cotton may be related to a shorter duration of farming and only spuriously associated with not picking cotton. Further, among Caucasian men only, both picking and not picking cotton were associated with prostate cancer risk, indicating that this activity is not probably aetiologically linked with prostate cancer. Many of the remaining farming activities were common in all farmers (eg 86% of farmers handled hay, grain or silage, 96% planted or pick crops, or tilled soil; and 90% fed animals, worked with poultry or swine), and thus the power to consider these activities and prostate cancer risk was limited.

Our finding of an interaction between race and farming on risk of prostate cancer is consistent with the only other study[9] to deal with prostate cancer risk in African-American and Caucasian men. Krstev *et al*[9] also found that farming was associated with an increased risk of prostate cancer among Caucasians but not among African-American men. Heterogeneity of effects by race could be explained by different distributions of genetic factors by race and interactions between these genetic factors and environmental exposures.

This study is not without limitations. As 96% of South Carolina residents aged 65–79 years are included in the HCFA Beneficiary Files and as we have a nearly complete sampling frame for the population that would have given rise to the cases, this can be considered a population-based sample, which limits the potential for selection bias. However, the response rate was only fair among cases and controls (61.4% and 63.8%, respectively), and we were unable to locate a larger proportion of African-Americans (19.3%) compared with Caucasians (6.0%). Selection bias may be introduced with lower response rates. Among participants with correct contact information, we were able to interview 76.4% (78.3% of cases and 74.8% of controls) of potential participants. We identified and excluded prevalent cases in both the controls and the cases using medical chart reviews to reduce outcome misclassification. To reduce exposure misclassification, we used computer-assisted telephone interviewing rather than self-administered questionnaires or information about occupation collected only from cancer registries or death certificates. Nonetheless, there was potential for recall bias in reporting attributes of farming exposure. Cases and controls may differentially remember or report their farming-related exposures. Typically, cases have an incentive to more carefully recall exposures than controls. If this pattern holds in this case–control study, recall bias would be expected to bias the resulting OR away from the null. However, if recall bias were truly observed in these data, we would expect a bias away from the null for both Caucasian and African-American men, whereas we observed an increased risk only among Caucasian men. Although we had sufficient numbers to investigate farming activities for the entire study population, we had limited study power to investigate some specific farming activities by race. As we did not collect information on whether farmers were farm workers or owners, we could not examine differences in years of farming by type of farming. Information on farming type may have provided support for the theory that short-term farmers are more likely to be farm labourers rather than farm owners.

Although a number of associations between specific activities (which represent crude surrogates of pesticide exposure) and increased prostate cancer risk were evaluated, issues of multiple comparisons may have arisen. Nonetheless, an interesting finding relates to the pattern of differences in the strength of the association between Caucasians and African-Americans for many of the farm activity–prostate cancer risk associations that were evaluated. As the associations between farming and prostate cancer were typically stronger among Caucasians compared with African-Americans, this general finding may inform future studies to consider race as an effect modifier of the farming–prostate cancer association.

Our study adds to the existing literature by investigating the risk of prostate cancer associated with years of farming, recency of farming, and specific farming activities, stratified by race, which have not been reported previously in the literature. Although most specific farming-related exposures were not associated with prostate cancer, farmers who mixed or applied pesticides were at increased risk of prostate cancer compared with non-farmers and farmers who never mixed or applied pesticides. It is biologically plausible that pesticide exposures may be aetiologically linked with an increased risk of prostate

Main messages

- Farming-related exposures were associated with an increased risk of prostate cancer among Caucasians but not among African-Americans.
- Prostate cancer risk was highest for those farming for shorter periods and for those who mixed or applied pesticides.
- Exposure to pesticides may play a role in increasing the risk of prostate cancer among farmers.

Policy implications

- Prostate cancer is the most common cancer in men, yet the aetiology remains unclear.
- Consistent use of protective gear when applying pesticides is strongly recommended to minimise the effect of pesticide exposure that may be associated with the risk of prostate cancer.
- Future studies should develop and apply exposure assessments that incorporate information about the intensity, frequency and duration of exposure to specific pesticides in studies evaluating the risk of prostate cancer among agricultural workers.
- Race should be considered as an effect modifier in future studies on prostate cancer and farming.

cancer and other hormone-dependent cancers.[40] Further studies considering polymorphisms in genes that regulate the metabolism of pesticides or other chemicals common in farming-related work and prostate cancer risk would advance our understanding of the mechanism by which exposures experienced while engaged in farming-related activities may increase prostate cancer risk.

ACKNOWLEDGEMENTS
This research was supported by funding to M S from the Association of Schools of Public Health/Centers for Disease Control and Prevention and the National Cancer Institute. MS was partially supported by a career development award DAMD-17-00-1-0340 from the US Army Medical Research and Material Command.

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Competing interests: None.

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