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Award Number: DAMD17-02-1-0252

TITLE: Prostate Cancer Mortality in Puerto Rican Men: The
Effect of Body Habitus and Physical Activity

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REPORT DATE: February 2003

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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20030702 058

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE February 2003	3. REPORT TYPE AND DATES COVERED Annual (1 Feb 02 - 31 Jan 03)	
4. TITLE AND SUBTITLE Prostate Cancer Mortality in Puerto Rican Men: The Effect of Body Habitus and Physical Activity			5. FUNDING NUMBERS DAMD17-02-1-0252	
6. AUTHOR(S) Carlos J. Crespo, Dr. P.H.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) State University of New York Amherst, New York 14228-2567 E-Mail: ccrespo@buffalo.edu			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) Prostate cancer kills more Puerto Rican men than cancers of the lung, trachea and bronchus. Physical activity has an inconsistent relationship with prostate cancer. It is not clear what the relationship between body habitus and physical activity is among non-Whites population. The underlying hypothesis of this epidemiological research is that excess body adiposity and sedentary lifestyles are independent risk factors for prostate cancer mortality in Puerto Rican men. The specific aims of this proposal are (1) to investigate the association between anthropometric measurements or changes in body weight and prostate cancer mortality, and (2) to study the relationship between physical activity and prostate cancer mortality. This study uses an observational longitudinal design with a random sample of 9,824 Puerto Rican men aged 35-79 years at baseline (1964) who were part of the Puerto Rico Heart Health Program (PRHHP). Using a survival analysis approach and a total follow-up time of approximately 35 years we plan to examine the relationship of the above risk factors with prostate cancer mortality. There continues to be health disparities in prostate cancer incidence and mortality in minorities and our findings will improve our knowledge of the relationship between prostate cancer and other lifestyles.				
14. SUBJECT TERMS Epidemiology			15. NUMBER OF PAGES 47	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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Annual Report
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**Title: Prostate Cancer Mortality in Puerto Rican Men: The effect of
body habitus and physical activity**

INTRODUCTION:

Subject: Prostate cancer kills more Puerto Rican men than the combined cancer mortality rates of the lung, trachea and bronchus. The most extensively studied risk factors for prostate cancer include age, race/ethnicity, family history, diet, androgen metabolism, alcohol consumption, obesity, physical activity and smoking. Of these, age, race and family history are well documented but poorly understood risk factors. The fact that prostate cancer rates change in migrant populations and vary dramatically in ethnically similar populations residing in different geographic locations strongly suggest that environmental factors can greatly influence the risk of this cancer.

Purpose: The purpose of this investigation is therefore, to study the relationship of physical activity and body habitus with prostate cancer mortality among Puerto Rican men. This study uses an observational longitudinal design with a random sample of 9,824 Puerto Rican men aged 35-79 years at baseline (1964) who were part of the Puerto Rico Heart Health Program (PRHHP). The Puerto Rico Heart Health Program provides a unique epidemiological cohort of men who took part in multiple examinations including extensive information on lifestyle, diet, body composition, exercise, and smoking habits. Survival analyses will be used to study the relationship between prostate cancer mortality and physical inactivity and obesity with approximately 35 years of follow up data. **Scope of the research:** The scope of the research this research is to generate new knowledge of how sedentary lifestyles or excess body weight are related to prostate cancer mortality, and to increase our knowledge of prostate cancer in a population where prostate cancer is the number one killer. Additionally, once prostate cancer mortality is identified, other exposures such as diet, smoking and alcohol intake can also be studied.

BODY:

The research accomplishment will be described based on their accomplishments associated with each task outlined in the "Statement of Work." Below is the itemized list of activities planned for year 1 of the research and progress in completing these tasks.

Task	Outcome
Meet with consultants and collaborators to confirm the parameters to assess cancer mortality.	Several meetings were held between Dr. Carlos Crespo and co-investigators (Drs. Dan McGee, Christopher Sempos, Garcia Palmieri, I-Min Lee, Paola Muti, and Rosa Perez) to establish the mechanism to assess prostate cancer mortality.
Establish a format to submit request of cause of death.	Dr. Dan McGee produced a data set with the id names, last names, first name, date of birth, and place of birth to collect information on cause of death.
Establish a format to receive data containing cause of death.	Two separate electronic data sets were sent to the Puerto Rico Cancer Registry. One contained father and mother last names and first name with middle initial with an id number, and a second data set that contained the id number and birth dates and place of birth. This was done to protect the confidentiality of the human subjects. Instructions on how to merge the files were provided accordingly.
Determine a time table for submitting requests to and receiving results from the Puerto Rico Demographic Registry, preferably in electronic format	In April, 2002, a time table was determined to obtain preliminary data on cancer mortality in the entire cohort. In January 2003, a preliminary dataset containing cancer mortality was received. Current activities (February to June 2003) include identifying prostate cancer mortality in the entire cohort.
Prepare yearly report	This document is the yearly report and was prepared during the months of January and February, 2003.

KEY RESEARCH ACCOMPLISHMENTS:

1. Analysis of baseline data on participation in physical activity
 - a. Participants were stratified according to activity levels and by quartiles of physical activity index. Quartile 1 represents participants that engaged in no physical activity. Out of approximately 2500 participants in quartile 1, twenty six subjects were reclassified into quartile 2 because they participated in some type of moderate physical activity. Thus, Quartile 1 is considered persons that are sedentary during leisure-time and also during work.

2. Analysis of baseline data on body habitus using body mass index.
 - a. Participants were classified into WHO body weight classification guidelines: underweight (BMI<18.5), normal weight (BMI=18.5-24.9), overweight/pre-obese (BMI=25-29.9) and obese (BMI>=30)
3. A paper was published studying the relationship between physical activity, body weight and all cause mortality in Annals of Epidemiology, October 2002 ¹.

REPORTABLE OUTCOMES:

1. Manuscripts: We finalized publication of a manuscript (see **Crespo CJ**, Garcia-Palmieri M, Sorlie P, Perez-Perdomo Rosa, McGee DL, Smit E, Sempos C, Lee IM. The relationship between physical inactivity, body weight, and all cause mortality in Puerto Rican men: Results from the Puerto Rico Heart Health Program. Annals of Epidemiology. 2002;12:543-552.)
2. Presentations:
 - a. As a result of the funding provided in this grant we presented a paper during the First Puerto Rican Public Health Conference and talked about cancer mortality among Hispanic minorities. San Juan, Puerto Rico, April 4-5, 2002.
 - b. We submitted a poster that has been accepted to the American College of Sports Medicine on physical activity and breast cancer mortality in US older women. The abstract will be published in the journal Medicine and Science in Sports and Exercise in the April, 2003 issue.
3. Funding applied for based on work supported by this award: We have submitted 2 grants.
 - a. Aging and prostate cancer in Puerto Rican men. This was an R01 grant responding to a NIH/NIA request for applications RFA # AG-02-003 titled "Aging, Race/ethnicity and Prostate Cancer." Our proposal aim was to study prostate cancer risk factors' relationship (i.e., race, familial aggregation, and diet) with prostate cancer incidence and mortality in Puerto Rican men of different age groups. As a result of writing this grant we identified a large number of the participants in the PRHHP to have one or more siblings who were also part of the cohort. This finding has the potential to identify familial aggregation of risk factors. Table 1 lists preliminary work done examining the prevalence of members of the cohort who were biological brothers. This grant was reviewed but not funded. The reviewer's comments from this grant have been incorporated into a new smaller grant to study the relationship of diet and cancer in PR men (see item (b) below). Table 1 illustrates the potential to conduct familial aggregation studies using the 2249 participants who had at least one biological brother in the cohort.

Table 1. Number of siblings in cohort of PRHHP		
Biological family members	siblings	Total
1 person only	7,575	7,575
2 brothers	795	1,590
3 brothers	149	447
4 brothers	33	132
5 brothers	12	60
6 brothers	1	6
7 brothers	2	14
Number of Brothers		2,249
Total Participants		9,824

- b. Diet and Cancer in Puerto Rican Men. We have submitted a small cancer epidemiology research grant (R03) to NIH/NCI Grant number 1R03 CA-103475-01 that will be reviewed during the month of March, 2003. More specifically, this grant intends to examine the relationship of consumption of legumes and prostate cancer in PR men.
 4. Research opportunities applied for based on training supported by this award.
 - a. We have applied for a "Long-Term Minority Investigator Research Supplement" to the National Institutes of Health, National Cancer Institute. This supplement provides long-term research support for minority staff or faculty members to conduct research in the biomedical or behavioral sciences. Support is provided for up to four years at a minimum of 30 percent effort during each 12-month period. During this research supplement we plan to work with Dr. Jo Freudenheim (Interim Chair of the Department of Social and Preventive Medicine) to examine the relationship of exercise and oxidative stress with breast cancer in a case control study in Western New York. This training will pay a percent of my salary, and more importantly will provide funds for training in genetic and molecular epidemiology. This grant was reviewed and is recommended for funding when NIH budget for 2003 is approved.

CONCLUSIONS:

The implications of completed research are that we have been able to find it feasible to obtain cause of death using multiple sources of data from the Puerto Rico Demographic Registry and the Puerto Rico Cancer Registry. We accomplished what we set out to do during the first year and that was to work with these agencies to ascertain prostate cancer mortality in men from the Puerto Rico Heart Health Program.

The data we have obtained so far is better than expected. As of now, we have data on all members of the cohort to move to the next stage of ascertaining prostate cancer mortality. We now need to go over names where we have more than one corresponding person, and to match according to father and mother last names, date of birth, and place of birth. Another important accomplishment is to be able to work with the Puerto Rico Cancer Registry. We have established a good working relationship with the Director of the Puerto Rico Cancer Registry. This Registry is currently updating all of its data to be able to provide incidence data.

Our current accomplishment also includes being able to analyze the exposure data on physical activity and body habitus. As a result we completed the submission of a paper to examine the relationship of physical activity, body mass index and all cause mortality. The findings from this paper show that even among overweight individuals who are physically active there is significant reductions in the odds ratio of all cause mortality when compared with overweight individuals who are not physically active.

REFERENCES:

1. C. J. Crespo, M. R. Palmieri, R. P. Perdomo, D. L. McGee, E. Smit, C. T. Sempos, I-Min, and P. D. Sorlie, "The relationship of physical activity and body weight with all-cause mortality. Results from the Puerto Rico Heart Health Program," *Ann Epidemiol*, 2002, 543-552.

APPENDICES:

1. Reprint of article entitled "The Relationship of Physical Activity and Body Weight with All-Cause Mortality: Results from the Puerto Rico Heart Health Program."
2. Abstract entitled "Physical Activity and Breast Cancer Mortality in Older US Women: Findings from NHIS 1990-91" accepted by the American College of Sports Medicine.
3. CV-Biosketch
4. Copy of abstract and body of grant entitled "Diet and Cancer in Puerto Rican Men" submitted to NIH review in December 2002.

Appendix

Project title: Prostate Cancer Mortality in Puerto Rican
Men: The Effect of Body Habitus and Physical Activity

Award Number: DAMD 17-02-1-0252

Principal Investigator: Carlos J. Crespo, DrPH,MS, FACSM

The Relationship of Physical Activity and Body Weight with All-Cause Mortality: Results from The Puerto Rico Heart Health Program

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PURPOSE: To study the relationship of physical activity and obesity with all-cause mortality in Puerto Rican Men.

METHODS: The Puerto Rico Heart Health Program collected physical activity and anthropometric measurements in 9,824 men between 1962 and 1965. After excluding those with known coronary heart disease at baseline, and those who died within the first three years of the study we analyzed the data for the relationship between physical activity and overweight status to all-cause mortality in 9,136 men. We stratified our participants by quartiles of physical activity. Participants were classified into four categories of body weight: underweight (BMI < 18.5), healthy weight (BMI = 18.5–24.9), overweight (BMI = 25–29.9), and obese (BMI = 30+).

RESULTS: After adjusting for age, education, smoking status, hypertension status, hypercholesterolemic status, urban/rural residence, and overweight status, physical activity was independently related to all-cause mortality. All-cause mortality was lower in those in quartile 2 (OR = 0.68, CI = 0.58–0.79) than quartile 1 (reference, sedentary group). Mortality among those in quartile 3 and 4 (0.63, CI = 0.54–0.75; and 0.55, CI = 0.46–0.65, respectively) were also significantly lower than those observed in quartile 1, but not significantly lower than those observed in quartile 2. Furthermore, within every category of body weight, those who were most active had significantly lower odds ratio of all-cause mortality.

CONCLUSION: Our findings support the current recommendation that some physical activity is better than none, in protecting against all-cause mortality. The benefits of an active lifestyle are independent of body weight and that overweight and obese Puerto Rican men who are physically active experienced significant reductions in all-cause mortality compared with their sedentary counterparts.

Ann Epidemiol 2002;12:543–552. © 2002 Elsevier Science Inc. All rights reserved.

KEY WORDS: Mortality, Obesity, Exercise, Puerto Ricans, Epidemiology, Puerto Rico Heart Health Program.

INTRODUCTION

Lack of exercise and obesity are two independent major public health problems (1–9). Physical inactivity and excess body weight have also been found to be major risk factors for several chronic diseases such as coronary heart disease

(CHD), type 2 diabetes, hypertension, and cancer (8, 9). These chronic conditions are responsible for a large percent of the overall mortality observed in the U.S. (5). It is unclear how much of the higher mortality seen in overweight and obese individuals results from excess body weight and how much results from physical inactivity (10–16).

One hypothesis that has been raised is that moderate to high levels of cardiorespiratory fitness are protective against the excess mortality observed in overweight and obese individuals (10–12, 15–17). Most of the evidence that has examined the relationship between obesity or physical inactivity and all-cause mortality has been conducted in cohorts of non-Hispanic populations (18–41). The purpose of this study is to examine the effects of physical inactivity and excess body weight in a cohort of Puerto Rican men who were part of the Puerto Rico Heart Health Program using mortality follow-up data collected from 1965 to 1980. In addition, this study explores if higher physical activity

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Received June 7, 2001; revised September 10, 2001; accepted September 26, 2001.

Selected Abbreviations and Acronyms

BMI	= body mass index
BRFSS	= Behavioral Risk Factor Surveillance System
CHD	= coronary heart disease
CVD	= cardiovascular disease
MET	= metabolic equivalent
OR	= odds ratio
SD	= standard deviation

levels can attenuate the increased risk of mortality in overweight and obese Puerto Rican men.

MATERIAL AND METHODS**Study Subjects**

The Puerto Rico Heart Health Program is a prospective cohort study designed to examine morbidity and mortality from CHD in urban and rural Puerto Rican men (42-45). The original sampling was designed to recruit men aged 45 to 64 years who were free from CHD at time of first examination in 1965. These men were sampled from 3 urban areas and 4 rural areas in the northeast part of Puerto Rico by the personnel who participated in the United States decennial census (44). All of these men were encouraged to attend the baseline examination, and an 80% response rate was achieved. The original sample of the cohort consisted of men ages 45 to 64 years of age. Other participants ages 35-44 years and 65 to 79 years of age, who had been inappropriately included in the enumeration, were also included in this study. Thus, the total number of examined participants used in this analysis includes 9,824 men between the ages of 35 to 79 years.

All men completed an extensive self-report of demographic characteristics, personal and family health history, and health habits, including education, occupation, income, a history of smoking, and place of residence among other characteristics. Our analytic sample include Puerto Rican men without CHD at baseline and who were alive after three years of the beginning of the study.

Physical Activity Classification

During the first examination each participant provided sociodemographic information and a complete medical history with a physical examination that included laboratory determination, and a resting 12-lead electrocardiogram was conducted. At this first examination complete physical activity status was assessed using the Framingham Physical Activity Index (43, 47). This questionnaire assesses occupational, leisure-time and other physical activities, measured as usual activity over the course of a 24-hour day, and was interviewer-administered. Usual physical activity was

determined by a review of the number of hours spent at various activities. For analysis, the number of hours at each activity was converted to an index of usual daily energy expenditure. This was accomplished by grading activities into different categories using estimated oxygen consumption per hour for each activity or metabolic equivalents (METs). One MET is equivalent to energy expenditure at rest, approximately 3.5 ml of O₂ per kilogram of body weight per minute. The usual activities were classified as sedentary (MET = 1.0), slight (MET = 1.1-2.3), slightly moderate to moderate (MET = 2.4-4.9) and strenuous (MET = 5.0+). The product of this grade and duration in hours gave a score of a physical activity index. A score of 24 meant the individual slept or reclined for 24 hours in a day. Higher scores indicated either strenuous activity for short periods or moderate activity for a longer time. Estimates of consistency of administration between the first test and 2- to 3-year post-test in this group of Puerto Rico men provided Pearson correlation coefficients of 0.30 to 0.59 using the Framingham Physical Activity Index (43, 46).

We stratified our analytic sample by quartiles of physical activity. The physical activity index ranged from 24 to 71. We further examined patterns of physical activity within quartile by hours spent doing no activity such as sleeping or resting; sedentary or very light activities such as sitting; light activities such as walking at level; moderate physical activity such as brisk walking, climbing stairs or walking uphill; and vigorous physical activity such as cutting sugar cane or other strenuous activities. The cutoff point for quartile 1 was a physical activity index of 27 or less and represents the group that is most inactive. To assure quartile 1 reflects those who are sedentary, we reclassified 18 participants (out of 2401) in quartile 1 who reported participating in moderate physical activities into quartile 2 (N = 2277). Thus, quartile 1 of physical activity includes participants who engaged in no physical activities, sedentary activities or light physical activities. The range of physical activity index for quartile 2 was greater than 27 but less than 30, for quartile 3 the range was greater than or equal to 30 but less than 37 (N = 2171), and for quartile 4 scores were greater than or equal to 37 (N = 2287).

Obesity Classification

We used the most recent guidelines released by the National Heart, Lung, and Blood Institute; National Obesity Education Initiative to classify our participants based on body mass index (BMI) (8). Briefly, underweight individuals are those whose BMI is less than 18.5; normal or healthy weight represent persons with BMI between 18.5 and 24.9; overweight are persons with BMI between 25 and 29.9; and obesity of stages 1, 2, and 3 represent BMI of 30-34.9, 35-39.9, and 40 or more, respectively. We collapsed stages 1, 2 and 3 into one category because few of our participants had BMI greater than 35 (stage 2, N = 96, stage 3, N = 20).

Other Covariates

A physician conducted a detailed physical examination and measured blood pressure twice on the left arm with the participant in the sitting position. The first reading was taken at the beginning of the physical examination and the second reading at the end, allowing an interval of 15 to 20 minutes between readings. Hypertensive status was defined as systolic blood pressures greater than or equal to 140 mm Hg or diastolic blood pressure greater than or equal to 90 mm Hg, or currently taking anti-hypertensive medication (47, 48). During the first examination, and subsequently, blood was drawn for blood chemistry analysis, including lipid profiles (42). High blood cholesterol represents participants whose serum cholesterol levels were greater than or equal to 240 mg/dl, borderline high blood cholesterol reflect those with levels between 200-239 mg/dl, and normal blood cholesterol are those with values below 200 mg/dl (49).

Education level was determined from history by ascertaining the highest grade completed in school. For our analysis, participants were grouped into five categories: No formal schooling, and those who attended or completed grades 1-4, grades 5-8, high school, or college. The detailed smoking history provided the basis to classify participants into non-smokers, previous smokers, and smokers for the multivariate analysis. Rural-urban residence was determined based on place of residence at baseline. The characterization of the rural area was composed primarily of small farms located on very hilly terrain while the urban area consisted of a more dense cluster of houses, many of whose residents worked in the business and industry around San Juan.

Exclusion Criteria

Diagnosis of CHD was made according to predetermined criteria such as chest pain and pathologic Q waves, or evidence of muscle necrosis by enzyme studies, or both. The classification of coronary disease other than angina pectoris included evidence of heart attacks, coronary heart disease, myocardial infarction, and coronary insufficiency, but not angina pectoris. In our attempt to exclude participants with any pre-existing conditions, we excluded those with CHD at first examination or who died within the first three years of follow up (from 1965 to 1967). Any deaths within the first three years of follow up may be indicative of cancer or other chronic conditions not screened for during the first examination (16, 40).

Statistical Analysis

The study uses all-cause mortality as the outcome variable. The multivariate logistic function model was used to analyze relationships between known risk factors and all-cause mortality. The model adjusted for the covariables age (years), education (no formal schooling, grades 1-4, grades

5-8, attended or completed high school, attended or completed college), body weight classification (underweight, healthy weight, overweight, obesity), baseline smoking status (non-smokers, former smokers, current smokers), urban-rural residence (urban, rural), hypertension status (hypertensive or normotensive), and hypercholesterolemic status (ideal, borderline, high blood cholesterol) as described earlier. Additionally, we examine the effects of physical activity on all-cause mortality stratifying the cohort according to body weight classification (underweight, healthy weight, overweight, and obese) (50-52).

RESULTS

Our original study population consisted of 9824 men, of which only 9 men were lost to follow up after a mean follow up of 12 years. Our analytic sample consisted of the 9136 Puerto Rican men free of coronary disease at exam 1, who had complete physical activity information, and who were alive after three years of follow up. Table 1 shows the distribution of the analytic sample according to age, education, body weight, smoking status, place of residence, hypertension and hypercholesterolemic status during baseline. There were 1445 total deaths. The crude death rate was greatest among those 65-79 years, those with no formal education, those who were underweight, and hypertensive men.

We found physical inactivity to be an independent risk factor for all-cause mortality. Table 2 shows the effect of physical activity and body weight categories on all-cause mortality. We found higher all-cause mortality rates among the inactive men (quartile 1) than among those in quartile 3-4, even after controlling for age. Each exposure (physical activity and body weight categories) were adjusted for the other characteristics and covariates in both model 1 (age-adjusted), and model 2 (age, high blood pressure, high blood cholesterol, education, smoking and urban/rural living) (see Table 2). Consistently, physical inactivity was a better predictor of all-cause mortality than being overweight or obese. After controlling for physical activity and other correlates, underweight men experienced higher risk of all-cause mortality than men of healthy weight. An interaction effect between overweight status and physical activity was not significant and did not alter the results.

Figure 1 shows that Puerto Rican men who engage in small amounts of physical activity (quartile 2) had lower number of deaths than those who were inactive (quartile 1). Adjustment by age at first examination did not change this relationship. Further increases in physical activity (quartiles 3 and 4) did not lead to further decreases in the number of deaths, especially non-cardiovascular disease mortality. Additional analysis using quartile 2 as the reference demonstrated that odds ratios (OR) observed in quartile 3 (0.95, 0.80-1.13) and 4 (0.84, 0.70-1.01) of physical

TABLE 1. Description and mortality follow up among participants who were free from CHD at baseline and alive after 3 years of follow up in the Puerto Rico Heart Health Program (N = 9136) (12-yr follow up)

	N	%	Number of deaths	Crude death rates, %
Age groups	9136		1445	
35-44 y	337	3.7	20	5.9
45-54 y	4680	51.2	477	10.2
55-64 y	3527	38.6	741	21.0
65-79 y	592	6.5	207	35.0
Education	9115		1441	
No formal schooling	914	10.0	216	23.6
Grades 1 to 4	3205	35.2	543	16.9
Grades 5 to 8	2625	28.8	399	15.2
Attended or completed HS	1629	17.9	205	12.6
Attend/completed College	742	8.1	78	10.5
Body weight classification	9136		1445	
Underweight (BMI < 18.5)	292	3.2	86	29.5
Healthy weight (BMI = 18.5-24.9)	4306	47.1	672	15.6
Overweight (BMI = 25-29.9)	3434	37.6	495	14.4
Obese (BMI = 30+)	1104	12.1	192	17.4
Baseline smoking status	9128		1444	
Nonsmokers	3126	34.2	478	15.3
Previous smokers	2017	22.1	303	15.0
Smokes 1-10 cigarettes	576	6.3	86	14.9
Smokes 11-20 cigarettes	691	7.6	125	18.1
Smokes 20+ cigarettes	1410	15.4	263	18.7
Cigar Smoker	1073	11.8	155	14.5
Pipe Smoker	235	2.6	34	14.5
Urban/Rural Living	9136		1444	
Rural	2785	30.5	425	15.3
Urban	6351	69.5	1019	16.0
Hypertension status	9136		1444	
Hypertensive	3231	35.4	734	22.7
Normotensive	5905	64.5	711	12.0
Blood cholesterol	9136		1444	
Desirable cholesterol (less than 200 mg/dl)	4652	50.9	735	15.8
Borderline high blood cholesterol (200-239 mg/dl)	3032	33.2	471	15.5
High blood cholesterol (240 mg/dl or greater)	1452	15.9	238	16.3

activity were not different from the OR observed in quartile 2 (data not shown). Approximately half of all the deaths observed were from cardiovascular disease (CVD). There was a linear trend toward lower cardiovascular mortality among those who were more physically active. The largest dropped in cardiovascular mortality was noted among quartile 1 (the most inactive group) and quartile 2.

Table 3 shows that even small amounts of physical activity were associated with lower all-cause mortality in healthy weight and overweight Puerto Rican men. Among obese Puerto Rican men, participation in high amounts of physical activity seems to exert the most protective benefit against all-cause mortality. Puerto Rican men who were underweight and participated in relatively high amounts of physical activity (quartile 3 and 4) lowered their odds of dying more so than underweight men who were in the lower two quartiles of physical activity. Figure 2 shows that those who were underweight had the greatest probability of death in the next 12 years when compared to other body weight

categories. Figure 3 shows the cumulative survival curve plots of Puerto Rican men who participated in physical activity in different levels. Those in quartile 1 (the sedentary group) experienced greater mortality than those in quartiles 2-4. The number of deaths in quartile 3 and 4, who represent those who exercised the most had the lowest number of deaths at the end of the follow-up period when compared to those in quartile 1.

DISCUSSION

Our results show that physical activity is associated with lower all-cause mortality in this group of Puerto Rican men. Small increments of physical activity beyond sedentary behaviors, such as those observed in quartile 2 when compared to quartile 1, exerted a significant protective effect against all-cause mortality. Participation in more physical activity such as those observed in quartiles 3 and 4, exerted little extra benefits when compared to those in quartile 2.

TABLE 2. Multivariate odds ratio (O.R.) for all cause mortality in Puerto Rican men aged 35-74 years according to levels of participation in physical activity. Results from the Puerto Rico Heart Health Program. Excludes men with pre-existing CHD or who died within 3 years of study. (12-yr follow up).

	Beta Coefficient (SE)	P-value	O.R.	(95% C.I.)
Model 1* (N = 9136)				
Body weight categories				
Underweight	0.64 (0.14)	<0.0001	1.89	(1.43-2.50)
Healthy weight	Reference		1.00	
Overweight	-0.05 (0.07)	0.4697	0.95	(0.84-1.09)
Obese	0.17 (0.09)	0.0617	1.19	(0.99-1.43)
Physical activity categories				
Q1 Physical Activity (Low)	Reference		1.00	
Q2 Physical Activity	-0.40 (0.08)	<0.0001	0.67	(0.57-0.78)
Q3 Physical Activity	-0.46 (0.08)	<0.0001	0.63	(0.54-0.74)
Q4 Physical Activity (High)	-0.61 (0.08)	<0.0001	0.54	(0.46-0.64)
Model 2** (N = 9118)				
Body weight categories				
Underweight	0.64 (0.15)	<0.0001	1.90	(1.43-2.54)
Healthy weight	Reference		1.00	
Overweight	-0.08 (0.07)	0.2497	0.92	(0.80-1.06)
Obese	0.07 (0.10)	0.4640	1.07	(0.89-1.30)
Physical Activity categories				
Q1 Physical Activity (Low)	Reference		1.00	
Q2 Physical Activity	-0.39 (0.08)	<0.0001	0.68	(0.58-0.79)
Q3 Physical Activity	-0.45 (0.08)	<0.0001	0.63	(0.54-0.75)
Q4 Physical Activity (High)	-0.60 (0.09)	<0.0001	0.55	(0.46-0.65)

*Adjusted for age (in years as a continuous variable).

**Adjusted for age (in years as a continuous variable); smoking (never smokers, previous smokers, current smokers); education (no formal education, grades 1-4, 5-8, up to HS, and College or more); urban residence (rural or urban); hypertension (Yes = 140/90 mm Hg or on antihypertensive medication, or No hypertension); and high blood cholesterol (<200 mg/dl, 200-239 mg/dl and 240+ mg/dl).

Similar findings were observed for cardiovascular disease mortality. Comparing the percent of cardiovascular deaths between those in quartile 1 and 2 we found that those who reported being sedentary had 38% more cardiovascular deaths than those in quartile 2. These findings are in agreement with those stated by the Surgeon General's Report on Physical Activity and Health, the American College of Sports Medicine and the Centers for Disease Control and Prevention, the National Institutes of Health and others (6, 9, 16, 25, 26, 29, 53-56).

Few prospective epidemiological studies have been able to assess body habitus and physical activity simultaneously, and examine their independent effect on all-cause and cause-specific mortality. The Aerobics Center Longitudinal Study found low cardiorespiratory fitness to be independently associated with CVD mortality and all-cause mortality, independent of body habitus (10, 13, 15, 27, 56). These findings have been reproduced by others (16, 31, 53). The available literature on the independent effect of physical activity, physical fitness, and obesity have been conducted on White men not of Hispanic origin, and underscores the need to replicate these studies in traditionally understudied population, such as racial/ethnic minority groups. Our findings support the statement that small increments in physical activity can confer significant benefits for health in this group of Puerto Rican men. The higher number of survivors

in quartile 4 shown in Figure 3, is supportive of the theory that those who engage in more exercise—those with a higher physical activity score, either by exercising more hours or exercising more strenuously—tend to live longer. Further analysis revealed that the age distribution in these quartiles were very similar. The mean age in years, standard deviation (SD) and age range by quartiles were: Q1 = 55.4 years, SD = 6.8, range 37-79; Q2 = 53.9 years, SD = 6.4, range 35-75; Q3 = 53.7 years, SD = 6.3, range 35-76; and Q4 = 53.7 years, SD 6.4, range 36-77. It is not clear, however, if those who exercise the most are also genetically predisposed to live the longest.

We found that overweight status was not highly correlated to all-cause mortality in this group of Puerto Rican men after controlling for physical activity, education, smoking, urban/rural dwelling, high blood cholesterol and high blood pressure. This finding is in agreement with other studies that found that overweight status (BMI 25-29.9) is not related to all-cause mortality (18, 19, 57-61). Other prospective longitudinal studies have found excess body weight, assessed via body mass index, to be positively correlated with cardiovascular and all-cause mortality (1, 8, 20). In our study the likelihood of premature death among men who were obese did not reach statistical significance, especially after adjusting for other risk factors. It is possible that more years of follow up are needed in order to provide a

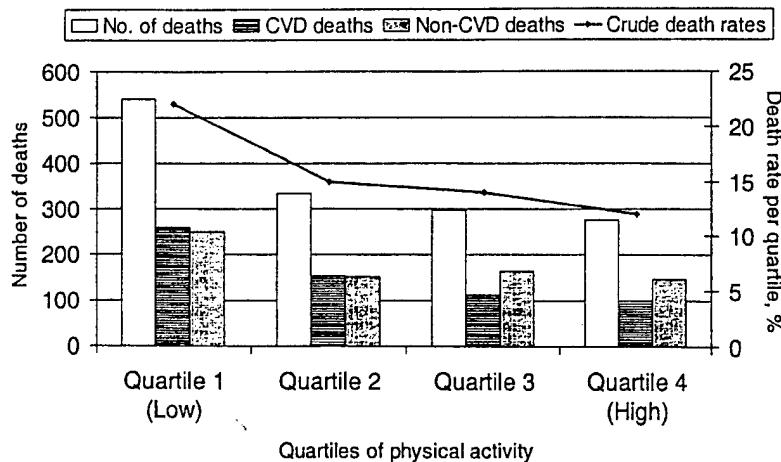


FIGURE 1. Title: Number of deaths due to all causes, cardiovascular disease and non-cardiovascular diseases, and death rate (per 100) of persons dying within quartile of physical activity. (12 yr follow up) Footnote: Mortality rates excludes those with pre-existing heart disease at baseline and those who died within the first 3 years of the study. Number of deaths presented in bars are explained using the right y-axis and crude death rates (per 100) shown by line is explained using the left y-axis.

clearer picture of the relationships between physical activity, obesity (BMI < 30) and all-cause mortality. Another explanation is that obese persons that are physically fit may have an added protection and therefore are less likely to die prematurely when compared to obese persons that are not physically active. For cardiovascular mortality, however, when we compare the percent of deaths from CVD among obese men and men in a healthy weight we observed a

33.6% increase in CVD mortality among the obese. Comparisons between those who were overweight and those who were of healthy weight we observed only a 7% increase in CVD mortality (data not shown).

Hahn et al., (63) observed that lack of physical activity was a more predominant risk factor than excess body weight in explaining cardiovascular mortality using data from the Behavioral Risk Factor Surveillance System (BRFSS). In

TABLE 3. Effect of physical inactivity on all cause mortality among underweight, healthy weight, overweight and obese Puerto Rican men Results from the Puerto Rico Heart Health Program. Excludes men with pre-existing CHD or who died within 3 years of study. Results are adjusted for age, education, smoking, urban residence, and hypertensive status. (12-yr follow-up)

Quartiles of Physical Activity by Body Weight	Sample Size	O.R. 95% C.I.	P-value
Underweight (BMI <18.5)	N = 292		
Quartile 1 (Low)	95	Reference	
Quartile 2	75	0.58 (0.29-1.16)	0.124
Quartile 3	53	0.37 (0.16-0.83)	0.017
Quartile 4 (High)	69	0.44 (0.20-0.94)	0.034
		P-value for trend = 0.059	
Healthy weight (BMI = 18.5-24.9)	N = 4306	O.R. 95% C.I.	P-value
Quartile 1 (Low)	908	Reference	
Quartile 2	882	0.74 (0.58-0.95)	0.0194
Quartile 3	996	0.69 (0.54-0.87)	0.0022
Quartile 4 (High)	1440	0.62 (0.49-0.79)	<0.0001
		P-value for trend <0.001	
Overweight (BMI = 25-29.9)	N = 3434	O.R. 95% C.I.	P-value
Quartile 1 (Low)	973	Reference	
Quartile 2	1001	0.57 (0.44-0.73)	<.0001
Quartile 3	839	0.59 (0.45-0.77)	<.0001
Quartile 4 (High)	621	0.49 (0.36-0.68)	<.0001
		P-value for trend <0.001	
Obese (BMI = 30+)	N = 1104	O.R. 95% C.I.	P-value
Quartile 1 (Low)	345	Reference	
Quartile 2	319	0.83 (0.55-1.24)	0.3656
Quartile 3	283	0.72 (0.47-1.11)	0.1335
Quartile 4 (High)	157	0.44 (0.24-0.79)	0.0063
		P-value for trend = 0.046	

*Adjusted for age (in years as a continuous variable); smoking (never smokers, previous smokers, current smokers); education (no formal education, grades 1-4, 5-8, up to HS, and College or more); urban residence (rural or urban); hypertension (Yes = 140/90 mm Hg or on antihypertensive medication, or No hypertension); and high blood cholesterol (<200 mg/dl, 200-239 mg/dl and 240+ mg/dl).

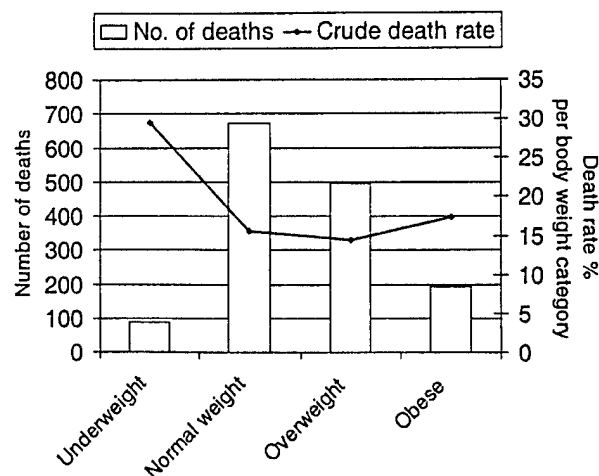


FIGURE 2. Title: Number of deaths and crude death rates (per 100), of persons dying within category of body weight. (12 yr follow up) Footnote: Mortality rates excludes those with pre-existing heart disease at baseline and those who died within the first 3 years of the study. Number of deaths represented by bar is explained by the right y-axis and crude death rate (per 100) shown by a line are explained by the left y-axis.

this ecological study the results suggested that state prevalences of physical inactivity and hypertension were strongly associated with state mortality rates of CVD. Assessment of physical activity in the BRFSS is somewhat different in that participants are allowed to report leisure-time physical activity for a limited number of activities, mainly walking or jogging, and two other activities. Vigorous physical activities are more likely to be remembered in this type of setting where the participant has few questions to report physical activity than light to moderate intensity physical activities. This type of over reporting of vigorous physical activity

may be partially responsible for the strong relationship observed between physical inactivity and CVD mortality. In our study, the participant had the opportunity to account for the usual physical activity in a 24-hour period, and therefore there is a less likelihood of reporting bias. Moreover, this type of assessment allows for the incorporation of occupational physical activity as part of the physical activity index.

Our results showed a significant increase in all-cause mortality among underweight Puerto Rican men, even after excluding men with pre-existing coronary disease at time of the first examination and men who died within the first three years of follow-up. This finding supports the hypothesis that underweight persons are at greater risk for mortality than healthy weight persons (17, 57, 59, 61, 62). Thus, leaner is not always better. Another possibility is that underweight participants may have higher mortality rates due to wasting diseases such as cancer. This unintentional weight loss has been previously associated with higher mortality (64). In our attempt to reduce this bias, we excluded participants who had died within the first three years of the study. We do not know what is the percent of body fat of underweight individuals or the location of the fat tissue. Although smoking may effect body weight, previous analysis of these data, and 14 other diverse observational studies, do not support the need to exclude smokers, but to adjust for smoking status, when examining the relationship between BMI and all-cause mortality (17, 57). More importantly, is that even among underweight men, who experienced increased odds of all-cause mortality, participation in physical activity at the level observed in quartile 3 and 4 were shown to be protective against all-cause mortality.

The biological plausibility of our findings confirm that independent of other known risk factors (e.g., hypertension, high blood cholesterol, and smoking), physical activi-

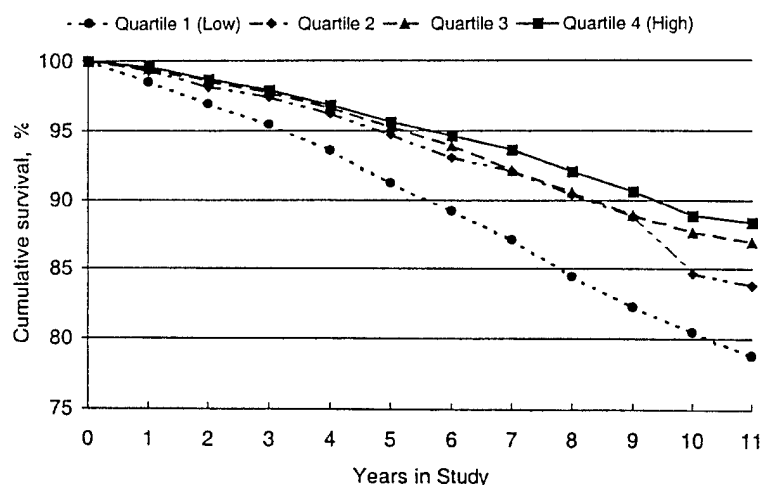


FIGURE 3. Title: Cumulative survival (per 100) among Puerto Rican men aged 35-79 years at baseline by quartiles of physical activity. (12 yr follow up). Footnote: Survival is based on men who did not have any pre-existing heart disease at baseline and who were alive 3 years after the study started.

ity exerts positive health benefits that are also independent of body weight. Several hypothesis have emerged regarding the effect of exercise on the immune system and on other metabolic pathways. Regular moderate-intensity physical activity has been found to increase activity of natural killer cells, greater insulin sensitivity, and increase bone density among others. Much of the effect of physical activity appears to be due to the metabolic adaptations of skeletal muscle (9). What we missed in explaining a biological mechanism of action, is gained in the fact that physical activity is beneficial to the psychosocial wellbeing of the individual. Lifetime physical activity can increase the independence of older persons and substantially contribute to a better quality of life resulting in less chronic diseases, and a longer and healthier life (5, 9, 11, 14, 18, 46).

The results we have presented here are based on all-cause mortality. We need additional research to study the independent effects of body weight and physical activity on other less studied cause-specific mortality such as cancer, stroke, and diabetes. There is increasing evidence to suggest that overweight and obesity are independent risk factors for several chronic diseases and their respective attributable mortality. Less is known, however, regarding how physical activity patterns affect body habitus, and how physical activity is independently related to non-cardiovascular disease mortality and cancer-site specific mortality in minority populations.

One limitation of our study is the utilization of BMI as an indicator of body fat. For example, we are not certain if highly active (quartile 4) Puerto Rican men who are obese (BMI = 30) represent individuals with high amounts of body fat or if this is more representative of individuals with high amounts of lean tissue such as those observed in well conditioned athletes. This phenomenon, however, seems unlikely since our cohort consist of older men who are probably not the well conditioned athlete younger than 35 years of age. The National Obesity Education Initiative suggests that BMI is a good surrogate of excess body fat in epidemiological studies, nevertheless its use in non-White and Hispanic populations should be studied further.

In conclusion, we found that physical inactivity was independently related to all-cause mortality, even after adjusting for body habitus, age, and other co-morbidities. Small amounts of physical activity were shown to be associated with lower all-cause mortality for Puerto Rican men who were of healthy weight and overweight. Overweight men did not experience significantly higher all-cause mortality than healthy weight. Our results suggest that physical inactivity is a stronger predictor of all-cause mortality than body habitus in this group of Puerto Rican men. More research is needed to replicate this results on other minority groups, women, and using specific causes of deaths such as cancer, stroke and diabetes.

This study was supported by a grant 1RO3AG17296-01 from the National Institute on Aging.

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PHYSICAL ACTIVITY AND BREAST CANCER MORTALITY IN OLDER US
WOMEN: FINDINGS FROM NHIS 1990-91

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Purpose: We used data from the 1990 and 1991 National Health Interview Survey (NHIS) to examine the association between self-reported leisure-time physical activity (LTPA) and breast cancer mortality. **Methods:** This cohort study included 16,009 women 55 years of age and older; during an average 8 years of follow-up, 149 deaths occurred attributed to breast cancer. Mortality was determined through the linking of the NHIS and the National Death Index (NDI). Conditional logistic regression analysis was used to estimate odds ratio (ORs) and 95 percent confidence intervals (95% CI). **Results:** After adjustment for potential confounding factors (age, race, marital status, education, health status, body mass index (BMI), alcohol consumption, and smoking), LTPA was associated with a reduced mortality of breast cancer in a dose-response manner. OR for breast cancer for women who participated in LTPA 1-2 times per week was 0.90 (95% CI = 0.51, 1.58), for women who participated in LTPA 3-4 times per week was 0.69 (95% CI = 0.44, 1.07) and for women who participated 5 or more times per week or vigorous 3 times or more was 0.51 (95% CI = 0.28, 0.91), as compared to women that were inactive. Breast cancer mortality was also associated with levels of education and health status. Women with less than a high school education had reduced mortality of breast cancer (ORs 0.50; 95% CI = 0.32, 0.79) when compared to those women who had more than a high school education. Women who self-reported a poor or fair health status had an increased mortality of breast cancer, ORs 4.26, 95% CI = 1.91, 9.49 and ORs 2.04, 95% CI = 1.02, 4.06 respectively. No association was found in age, race, BMI, alcohol consumption, and smoking. **Conclusion:** The findings support a protective effect of LTPA on breast cancer mortality in postmenopausal women. Supported by grant DAMD 17-02-1-0252

February 7, 2003

Free Communication/Slide Presentation Notification

We are pleased to inform you that your abstract entitled "Physical Activity and Breast Cancer Mortality in Older U.S. Women: Findings from NHIS 1990-1991" has been accepted for presentation in a slide session at the 50th Annual Meeting of the American College of Sports Medicine being held at the Moscone Center in San Francisco, California. Your abstract will be published in *Medicine and Science in Sports and Exercise*, Volume 35:5 Supplement. Your presentation date and time are as follows:

Name: Carlos Crespo
Date: Saturday, May 31, 2003
Session: H-13D - Exercise and Chronic Disease
Session Time: 1:00 PM - 2:30 PM
Presentation Time: 1:45 PM - 2:00 PM

Each slide speaker has been allocated exactly 10 minutes for an oral presentation, plus an additional 5 minutes for questions and answers. Session chairs will use timers to keep the program on schedule. The Program Committee has worked diligently to minimize content overlap among the concurrent sessions at the Annual Meeting. As I am sure you will appreciate, it is quite an undertaking to create a meeting program without overlapping sessions in any given topical area. Because changes to the time or day of any sessions would have a ripple effect throughout the program, we cannot consider any change requests related to the date and time of sessions. We appreciate your understanding.

The information you provide to the attendees during your presentation is very important. Therefore, we request that you consider ending your presentation with a CONCLUSION SLIDE - giving the attendees a take-home message. This simple request, if adhered to by most speakers, should have a profound and favorable impact on our educational programming.

New for 2003 - for your audio visual needs, LCD projection will be available upon request in free communication and clinical case sessions. Please review, complete and return the AV form by March 14, 2003. To assist in the preparation of your session, we have developed recommendations for presentations with slides. Both of these forms can be found in the Speaker Section of the ACSM website <http://www.acsm.org/meetings/pdf/speaker.pdf>.

In the event an emergency arises that prohibits you from presenting your material, please immediately inform the Education Department at ACSM in writing. The Board of Trustees has a long-standing policy that speakers who fail to provide notice of a reason acceptable to the Program Committee for not delivering an accepted paper will be prohibited from presenting at future annual meetings. Also be advised per Program Committee policy, only the first author may withdraw the abstract.

Meeting Registration: The Program Committee requests all speakers pre-register for the meeting by April 15, 2003. (**NOTE:** should you pre-register by March 14th, you can take advantage of the first early bird price break.) Pre-registering for the meeting allows ACSM the opportunity to ensure all speakers have registered for the meeting and gives you the advantage of avoiding long lines in the registration area. Registration form and housing information can be found in the Annual Meeting Preview in the Speaker Section of the ACSM website <http://www.acsm.org/meetings/pdf/speaker.pdf>.

Audio Visual Needs: Please submit your audio-visual needs by completing the AV Equipment Order Form which can be found in the Speaker Section of the ACSM website <http://www.acsm.org/meetings/pdf/speaker.pdf>. Please return this form per specific instructions.

Thank you for your contribution to the program - we look forward to your presentation.

Sincerely,
2003 ACSM Program Committee
50th Annual Meeting of the American College of Sports Medicine

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format on preceding page for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Carlos J. Crespo	Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Inter American University of Puerto Rico	B.S.	1980	Chemistry
Texas Tech University, Lubbock, Texas	M.S.	1986	Sports Health
Loma Linda University, Loma Linda, California	Dr.P.H.	1989	Preventive Care

A. Positions and Honors.**Positions and Employment**

1980-1982 Respiratory Therapy Technician, Bella Vista Hospital, Mayaguez, Puerto Rico
 1982-1984 Chemist, Spectron International, Inc., San Juan, Puerto Rico
 1984-1986 Research Assistant, Human Performance Laboratory, Texas Tech University, Lubbock, Texas
 1986-1989 Research Assistant, Dept of Nutrition and Center for Health Promotion, Loma Linda, California
 1989-1991 Assistant Professor/Chair, Dept of Physical Education, Univ. Sagrado Corazon, San Juan, PR
 1991-1995 Health Statistician, National Center for Health Statistics, CDC, Hyattsville, Maryland
 1995-1996 Public Health Analyst, National Heart, Lung, and Blood Institute, NIH, Bethesda, Maryland
 1993-1997 Adjunct Assistant Professor, Morgan State University, Baltimore, Maryland
 1995-1997 Assistant Professor, Dept Health and Fitness, American University, Washington, DC
 2000-present Associate Professor, Dept Social Preventive Medicine, University at Buffalo, Buffalo, NY
 2001-present Adjunct Research Associate Professor, Roswell Park Cancer Institute, Buffalo, NY

Professional Activities

1988-present American College of Sports Medicine, (fellow), President, Regional Chapter (2000-02)
 1992-present American Public Health Association, member
 1999-present Montgomery County Latino Health Initiative, Maryland, Technical Advisor
 2000-present American College of Epidemiology, member
 2001-present American Council on Exercise, member Board of Directors
 2001-present American Heart Association, Council on Epidemiology and Prevention, member
 2002-present Minority Organ Donation Education Program, Board of Directors
 2001-present Minority Health Coalition of Buffalo, member
 2002-present Commission on Nutrition and Physical Activity, Commonwealth of Puerto Rico, member
 2002-present NIH Epidemiology and Disease Control (EDC-2) Study Section, member (2002-2004)

Honors

1980 Outstanding College Graduate, Inter American University, San German, PR
 1986 Outstanding Academic Achievement, Certificate of Scholarship, Texas Tech University, Lubbock, TX
 1986-9 Public Health Traineeship, Loma Linda University, School of Public Health, Loma Linda, CA
 1990 Meritorious Service Award, Asociacion Puertorriquena del Corazon, San Juan, PR
 1995 Elected Fellow, American College of Sports Medicine, Indianapolis, IN
 1997 Secretary's Award for Distinguished Service, U.S. Dept of Health and Human Services, Washington, DC
 1999 NIH/NIA, Best Presentation on Aging Research, NIA Technical Assistance Workshop, San Francisco, CA
 2002 Montgomery County, Maryland. Leadership Award for Latino Health Initiative

B. Selected peer-reviewed publications (out of 35)

1. **Crespo CJ**, Keteyian SJ, Heath GW, Sempos CT. Prevalence of leisure time physical activity among U.S. adults. *Archives of Internal Medicine* 1996;156:93-98.
2. Fulwood R, Johnson M, **Crespo C**, Blount A; Building a national network to confront heart disease and stroke in African American communities. *Urban Cardiology* 1996;March/April:9-14.
3. **Crespo CJ**, Loria CM, Burt VL; Hypertension and other cardiovascular risk factors among Mexican Americans, Cuban Americans and mainland Puerto Ricans from the Hispanic Health and Nutrition Examination Survey. *Public Health Reports*. 1996;Vol III, Supplement 2:7-10.
4. Loria CM, **Crespo CJ**, Burt VL; Hypertension among Hispanic children, *Public Health Reports*, 1996;Volume III, Supplement 2:22-24.
5. Shankar S, Huerta EE, Gutierrez-Mohamed M, **Crespo CJ**; Cancer prevention behaviors and access to health care among Salvadorean living in Washington, D.C. Area. *Ethnicity and Disease*, 1998 Winter;8(1):1-9.
6. Seagal D, **Crespo CJ**, Smit E. Active Seniors, Protect Them, Don't Neglect Them. *Public Health Reports*, March/April, 1998, Vol 113, 137-139.
7. Andersen RE, **Crespo CJ**, Bartlett SJ, Cheskin LJ, Pratt M. Vigorous physical activity and television watching habits among US children and their relation to body weight and level of fatness. *Journal of the American Medical Association*, 1998;279:938-942.
8. **Crespo CJ**, Ainsworth B, Keteyian SJ, Heath GW, Smit E. Prevalence of no leisure-time physical activity and its relation to social class in US adults: Results from the Third National Health and Nutrition Examination Survey, 1988-1994. *Medicine and Science in Sports and Exercise*, 1999, 31:1821-1827.
9. **Crespo CJ**, Smit E, Andersen R, Carter-Pokras O, Ainsworth B. Race/ethnicity, social class and their relationship to physical inactivity during leisure-time in U.S. adults. *American Journal of Preventive Medicine*, 2000,18:46-53.
10. **Crespo CJ**, Physical Inactivity in racial and ethnic minorities in the United States: The National Health Objectives. *The Physician and Sports Medicine*, 2000,28:36-51.
11. Snelling AS, **Crespo CJ**, Schaeffer M, Walburn L, Smith S. Non-modifiable and modifiable factors correlated to osteoporosis in post-menopausal women. *Journal of Women's Health and Gender Based Medicine*. 2001;10:57-65.
12. **Crespo CJ**, Smit E, Andersen RE, Troiano RT, Bartlett S, Macera C. Television Watching, Energy Intake, and Severe Overweight in US children. Results from the Third National Health and Nutrition Examination Survey. *Archives of Pediatric and Adolescent Medicine*, 2001;155:360-365.
13. Andersen RE, **Crespo CJ**, Franckowiak S, Christmas C, Walston J. Obesity and reports of no-leisure time physical activity among older Americans. *Educational Gerontology*. 2001;27:297-306.
14. **Crespo CJ**, Smit E. Acculturation and physical inactivity during leisure-time among Mexican Americans. *American Journal of Public Health*, 2001;91(8):1254-1257.
15. Bassett DR, Fitzhugh G, **Crespo CJ**, King GA, McLaughlin JE, Nelson D. Physical activity and ethnic differences in hypertension prevalence in the United States. *Preventive Medicine*, 2002;34:179-86.
16. Friedman D, **Crespo CJ**, Bellantoni M, Andersen RE. Race/ethnicity, social class, and their relationship to hormone replacement therapy. Results from the Third National Health and Nutrition Examination Survey. *Menopause*. 2002 Jul-Aug;9(4):264-72.
17. **Crespo CJ**, Smit E, Snelling AS, Sempos CT, Andersen RE. Hormone replacement therapy and its relationship to lipid and glucose metabolism in diabetic and nondiabetic postmenopausal women: results from the third national health and nutrition examination survey. *Diabetes Care*. 2002;10:1675-80.
18. Nolte, R, Franckowiak S, **Crespo CJ**, Andersen RE. U.S. Military Weight Standards: What Percent of U.S. Young Adults Make the Grade?. *American Journal of Medicine*. 2002;13(6):486-490.
19. **Crespo CJ**, Garcia-Palmieri M, Sorlie P, Perez-Perdomo Rosa, McGee DL, Smit E, Sempos C, Lee IM. The relationship between physical inactivity, body weight, and all cause mortality in Puerto Rican men: Results from the Puerto Rico Heart Health Program. *Annals of Epidemiology*. 2002;12:543-552.
20. Sempos CT, Rehm J, Wu T, **Crespo CJ**, Trevisan M. Average volume of drinking and all-cause mortality in African Americans. The NHEFS cohort. *Alcohol: Clinical and Experimental Research*. Jan, 2003;27.

Contributions to government reports:

1. *Surgeon General Report on Physical Activity and Health*; U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, July 1996.
2. *Sixth Report of the Joint National Committee on Detection, Evaluation, and Control of High Blood Pressure*. National High Blood Pressure Education Program. November, 1997.
3. *Salud para su Corazon: Bringing Heart Health to Latinos*. A guide for building community programs. Office of Prevention, Education and Control, National Heart, Lung, and Blood Institute, December, 1998.

C. Research Support

Ongoing Research Support

R01 ES11368 Vena (PI) 09/01/01-8/31/06
NIEHS

Community Based Research of Autoimmune Disease and Asthma

This project proposes to continue community participatory research projects currently underway in two targeted minority communities in Buffalo: 1) a community on Buffalo's east side concerned with pollution from toxic waste sites and point sources of pollution and a cluster of autoimmune disease, and 2) a west-side community of Buffalo near a high-traffic corridor with elevated exposures to diesel exhaust and documented higher prevalence of asthma.

Role: Co-Investigator

DAMD17-02-1-0252 Crespo (PI) 02/01/02-01/31/05
USAMRDC

Prostate Cancer Mortality in Puerto Rican Men: The Effect of Body Habitus and Physical Activity

This proposal will study prospectively the effect of excess body weight, body fat and physical inactivity on prostate cancer mortality in Puerto Rican Men from the Puerto Rico Heart Health Program Study.

Role: PI

5 T32 CA 09051-21A1 Vena (PI) 09/29/97-07/31/03
NIH/NCI

Medical Sociology, Epidemiology, and Control of Cancer

Objective: This is a training grant for pre-doctoral and postdoctoral fellows in cancer epidemiology.

Role: Co-Investigator

Completed Research Support:

NIH Crespo (PI) 09/01/99-08/30/00

Puerto Rico Cancer Mortality Feasibility Study

Objective: To assess the feasibility of obtaining cancer mortality using the Puerto Rico Demographic Registry, Puerto Rico Cancer Registry, and the US National Death Index in men from the Puerto Rico Heart Health Program.

Role: PI

Pending Support

NIH Crespo (PI) 04/01/03-03/31/06

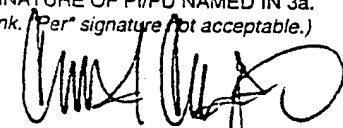
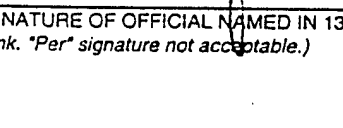
University of Puerto Rico-Roswell Park Cancer Partnership

Role: PI

Principal Investigator/Program Director (Last, first, middle): _____

NIH Freudenheim (PI) 06/15/02-06/14/06
Minority Supplement to Methylation and Oxidation in Breast Cancer Epidemiology
Role: PI

NIH Crespo (PI) 09/01/03-08/30/05
Diet and Cancer in Puerto Rican Men
Role: PI

Department of Health and Human Services Public Health Service		LEAVE BLANK--FOR PHS USE ONLY.	
Grant Application Follow instructions carefully. Do not exceed 56-character length restrictions, including spaces.			
1. TITLE OF PROJECT Diet and Cancer in Puerto Rican Men			
2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION <input type="checkbox"/> No <input checked="" type="checkbox"/> Yes (If "Yes," state number and title) Number: PA-01-021 Title: Small Grants Program for Cancer Epidemiology			
3. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR		New Investigator <input type="checkbox"/> No <input checked="" type="checkbox"/> Yes	
3a. NAME (Last, first, middle) Crespo, Carlos. Juan		3b. DEGREE(S) Dr.P.H., M.S.	
3d. POSITION TITLE Associate Professor		3e. MAILING ADDRESS (Street, city, state, zip code) 3435 Main Street 270 Farber Hall Buffalo, New York 14214	
3f. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT Social and Preventive Medicine			
3g. MAJOR SUBDIVISION Medicine and Biomedical Sciences			
3h. TELEPHONE AND FAX (Area code, number and extension) TEL: (716) 829-2975 x641 FAX: (716) 829-2979		E-MAIL ADDRESS: ccrespo@buffalo.edu	
4. HUMAN SUBJECTS <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes		5. VERTEBRATE ANIMALS <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes	
4a. Research Exempt <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If "Yes," Exemption Number		5a. If "Yes," IACUC approval Date	
4b. Human Subjects Assurance No. pending		5b. Animal welfare assurance no.	
4c. NIH-defined Phase III Clinical Trial <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes			
6. DATES OF PROPOSED PERIOD OF SUPPORT (month, day, year-MM/DD/YY) From 09/01/03 Through 08/30/05		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD 7a. Direct Costs (\$) 50,000. 7b. Total Costs (\$) 78,500.	
		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT 8a. Direct Costs (\$) 100,000. 8b. Total Costs (\$) 157,000.	
9. APPLICANT ORGANIZATION Name The Research Foundation of State University of New York Address on behalf of University at Buffalo The UB Commons, Suite 211 520 Lee Entrance Amherst, NY 14228-2567		10. TYPE OF ORGANIZATION Public: <input type="checkbox"/> Federal <input type="checkbox"/> State <input type="checkbox"/> Local Private: <input checked="" type="checkbox"/> Private Nonprofit Forprofit: <input type="checkbox"/> General <input type="checkbox"/> Small Business <input type="checkbox"/> Women-owned <input type="checkbox"/> Socially and Economically Disadvantaged	
Institutional Profile File Number (if known):		11. ENTITY IDENTIFICATION NUMBER 1146013200F6 DUNS NO. (if available) 02-06-57151 Congressional District 27th	
12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE Name Dr. Charles Kuars Title Assistant Vice President Address Sponsored Programs Administration The UB Commons, Suite 211 520 Lee Entrance Amherst, NY 14228-2567 Telephone (716) 645-2977 FAX (716) 645-3730 E-Mail awards@research.buffalo.edu		13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION Name Title Grant & Contract Administrator Address Sponsored Programs Administration The UB Commons, Suite 211 520 Lee Entrance Amherst, NY 14228-2567 Phone (716) 645-2977 FAX (716) 645-3730 E-Mail @research.buffalo.edu	
15. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.		SIGNATURE OF PI/PO NAMED IN 3a. (In ink. "Per" signature not acceptable.) 	
16. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Service terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.		SIGNATURE OF OFFICIAL NAMED IN 13. (In ink. "Per" signature not acceptable.) 	
		DATE 12/19/02	

DESCRIPTION: State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Describe concisely the research design and methods for achieving these goals. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary/confidential information. **DO NOT EXCEED THE SPACE PROVIDED.**

This is a small grant to study prospectively diet and prostate cancer among Puerto Rican men who took part in the Puerto Rico Heart Health Program (PRHHP). Few studies have been able to study the relationship of diet with prostate cancer mortality longitudinally among Hispanics or any other minority group in the United States. Although cancer mortality rates have decreased in the past 20 years in the general population, it has increased in the Hispanic population. Cancer mortality rates among Hispanics are lower than those observed among non-Hispanic whites; however, for Puerto Ricans both in the United States and in Puerto Rico, cancer mortality rates are greater than those observed for all Hispanics combined. Moreover, the number one cancer killer among Puerto Rican men is prostate cancer, not lung cancer. The reason for this inter- and intra-ethnic variation in cancer rates remains unclear. Established and emerging risk factors associated with prostate cancer include age, race, diet, obesity, physical inactivity, smoking, alcohol intake and sexually transmitted diseases, among others. The PRHHP collected information on these risk factors during four examinations between 1964 and 1980 with enormous potential for increasing our understanding of the etiology of this disease in US minority population.

Most of the published information on legumes and prostate cancer are based on findings from soy legumes with limited applicability to the US diet, since non-soy legumes are the most commonly eaten type of legumes in the Western diet. We found only one published epidemiological study that examined the relationship of non-soy legumes with prostate cancer. Consumption per capita of legumes in Puerto Rico is double that of the US. The specific aim of this small grant is to examine the relationship of dietary consumption of non-soy legumes with prostate cancer mortality in Puerto Rican men.

For this grant we plan to ascertain and characterize prostate cancer mortality in the cohort of men from the PRHHP using information from the Puerto Rico Demographic Registry, Puerto Rico Cancer Registry and the National Death Index Plus. This proposal is innovative because (a) it takes advantage of an established cohort to investigate cancer mortality in an under-studied Hispanic subgroup with higher cancer mortality rates than other Hispanic subgroups; (b) has the potential to study other exposures such as skin color, sexually transmitted disease, alcohol, smoking and other emerging risk factors with prostate and other cancers; and (c) will contribute new knowledge regarding the relationship between intake of non-soy legumes and prostate cancer mortality.

PERFORMANCE SITE(S) (organization, city, state)

University at Buffalo, State University of New York, Buffalo, NY

KEY PERSONNEL. See instructions. Use continuation pages as needed to provide the required information in the format shown below. Start with Principal Investigator. List all other key personnel in alphabetical order, last name first.

Name	Organization	Role on Project
Carlos J. Crespo, DrPH, MS	University at Buffalo	Principal Investigator
Ellen Smit, PhD, RD	University at Buffalo	Co-Investigator
Christopher Sempos, PhD	University at Buffalo	Co-Investigator
Jo Freudenheim, PhD, RD	University at Buffalo	Co-Investigator
Paola Muti, MD, MS	University at Buffalo	Co-Investigator
Susan McCann, PhD, RD	University at Buffalo	Co-Investigator
Rosa Perez Perdomo, MD, PhD, MPH	University of Puerto Rico	Consultant
Mario R. Garcia Palmieri, MD	University of Puerto Rico	Consultant
Mark Messina, PhD	Nutrition Matters, Inc.	Consultant

Disclosure Permission Statement. Applicable to SBIR/STTR Only. See instructions. ☐ Yes ☐ No

A. Specific Aims:

This is a small grant to examine the potential for conducting cancer epidemiological research longitudinally among Hispanics using an established cohort of Puerto Rican men. For this R03 we plan to study diet as an exposure and fatal prostate cancer as an outcome in a cohort of men from the Puerto Rico Heart Health Program (PRHHP). This proposal is innovative because (a) it takes advantage of an established cohort to investigate cancer mortality in an under-studied Hispanic subgroup with higher cancer mortality rates than other Hispanic subgroups; (b) has the potential to study other exposures such as skin color, sexually transmitted disease, alcohol, smoking and other emerging risk factors with other cancers; and (c) will contribute new knowledge regarding the relationship between intake of non-soy legumes and prostate cancer mortality.

Few studies have been able to study the relationship of diet with prostate cancer mortality longitudinally among Hispanics or any other minority group in the United States. Although cancer mortality rates have decreased in the past 20 years in the general population, there is great variability in cancer mortality across racial and ethnic populations in the United States. Cancer mortality rates among Hispanics are lower than those observed among non-Hispanic whites; however, substantial differences exist among Hispanic subgroups. For example, for Puerto Ricans both in the United States and in Puerto Rico, cancer mortality rates are greater than those observed for all Hispanics combined. Moreover, the primary cancer killers among Puerto Ricans are different than those observed for other Hispanics. The number one cancer killer among Puerto Rican men is prostate cancer, not lung cancer. The reason for this inter- and intra-ethnic variation in cancer rates remains unclear. Established and emerging risk factors associated with prostate cancer include age, race, diet, obesity, physical inactivity, smoking, alcohol intake and sexually transmitted diseases, among others. A prospective study on Puerto Rican men collected information on these risk factors during four examinations between 1964 and 1980 with enormous potential for increasing our understanding of the etiology of this disease in US minority population. The specific aim of this small grant is:

Aim 1. To examine the relationship of dietary consumption of legumes with prostate cancer mortality in Puerto Rican men.

B. Background and Significance**B.1. Introduction**

Prostate cancer is not only a major public health problem in the United States, but worldwide¹. We have selected prostate cancer as the primary outcome of this pilot study because prostate cancer is the number one cancer killer among Puerto Rican men. Racial differences in cancer mortality may provide important clues to the etiology of the disease and a better understanding of environmental influences. Moreover, the identification of specific risk factors within cohorts of high, moderate, and low risk can significantly increase our understanding of carcinogenesis². Epidemiological studies have provided evidence regarding the role of diet and other lifestyle factors in the etiology and prevention of site-specific cancers. It is not clear if diet, alcohol consumption, cigarette smoking, obesity and other cultural/lifestyle factors influence cancer mortality differently among culturally diverse populations. Because populations from different cultures experience different rates of prostate cancer, it is possible that certain environmental and lifestyle factors can be modified to ultimately reduce prostate cancer mortality within populations. This is confirmed

Table 1. Age adjusted cancer death rates (per 100,000) in Puerto Rico and in the United States, 1986-1987*

Cancer site	Men	
	U.S.	P.R.
All sites	163.2	121.7
Lung	56.9	17.9
Prostate	15.7	16.1
Colorectal	17.2	9.0
Stomach	5.3	12.4
Oral cavity	3.8	9.0

* rates are age adjusted to the World Health Organization standard world population, 1986-87. Source: NCI/NIH Pub 96-691

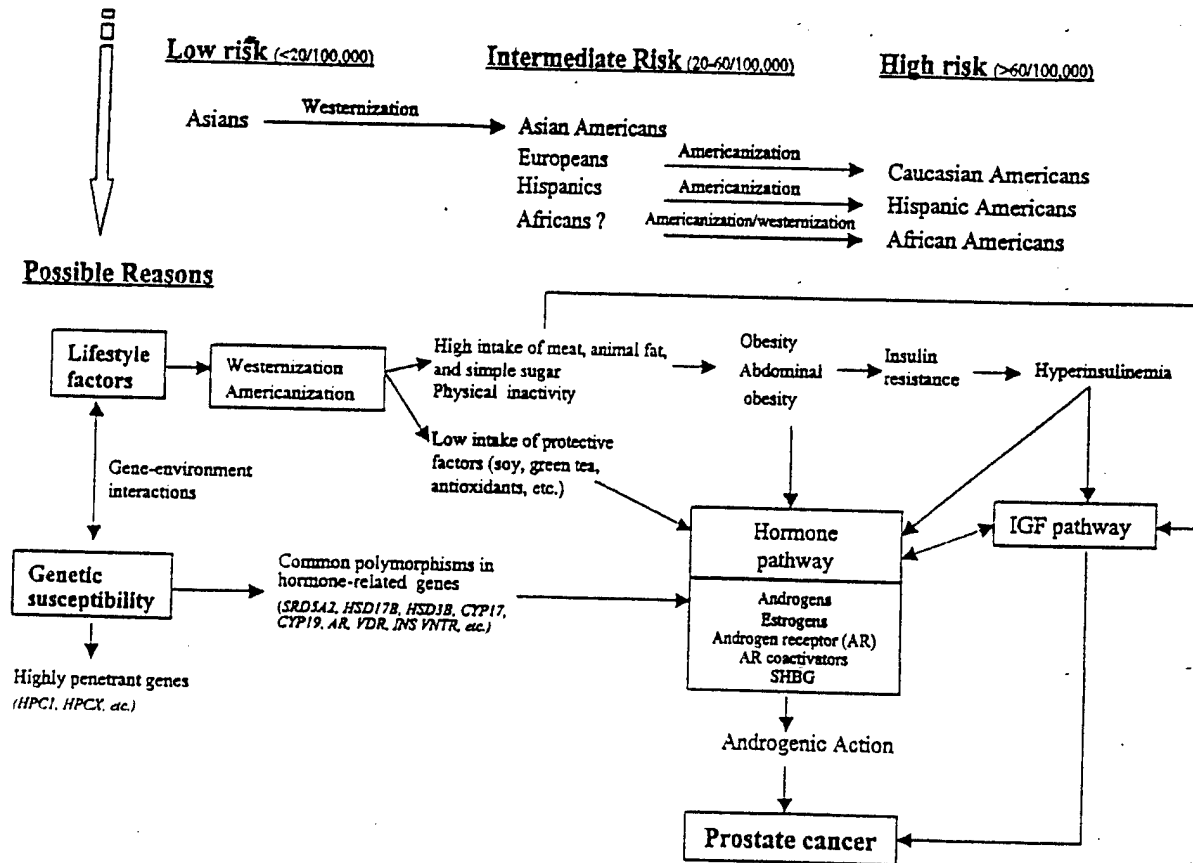
by the increased incidence and cancer mortality observed in migrants from low-risk countries to high-risk countries^{2,3}.

B.2. Race/ethnic differences in prostate cancer risk.

Figure 1 illustrate the possible environmental and genetic reasons for the differences in prostate cancer risk observed among diverse populations.

Figure 1.

Racial/Ethnic Differences in Prostate Cancer Risk



Putative relations: westernization and racial/ethnic differences in prostate cancer risk.

(Adapted from Hsing and Devesa. Epidemiologic Reviews, 2001;23:3-13)

International comparisons of cancer trends and patterns have helped identify lifestyles associated with prostate cancer risks. Although microscopic (latent) prostate tumors in most populations are similar, striking differences in the incidence rates among racial/ethnic groups exist. Between 1988-1992, the highest reported rates (age-adjusted world standard), exceeding 30,000 per 100,000 man years, were observed among US blacks, in contrast to the very lowest rates, less than 3 per 100,000 man years, observed among men in China. Rates in Black Caribbean men, especially from Jamaica, are also among the highest in the world. In Europe, incidence rates were higher in France, but notably lower in the United Kingdom, Italy, and Spain, yet prostate cancer mortality was similar in Italy and Spain (11.2/100,000 and 13.5/100,000, respectively) and higher in France and United Kingdom (16.3/100,000 and 17.1/100,000, respectively). Differences in quality of health care and diagnosis of cancer, completeness and accuracy of cancer reporting may play a role in the ethnic variations of prostate cancer risk. However, an increase in incidence of prostate cancer is not necessarily related to an increase of new cases but to improvements in diagnosis. Fatal prostate cancer, however, is more representative of the aggressive prostate cancers that have shown to be difficult to treat and prevent³. As part of this grant we propose to assess prostate cancer mortality using a cohort of Puerto Rican men.

The possibility that there are modifiable risk factors than can be altered in cancer prevention is enhanced by the strong variation in risk across ethnic groups. In figure 1 Hsing et al., show that dietary factors associated with prostate cancer include high intake of meat consumption, animal fat, simple sugars and low intakes of soy, green tea and antioxidants. More epidemiological data is needed to elucidate the role of other dietary components such as non-soy legumes ³⁻⁸.

B.2.1. Prostate cancer in Puerto Rican men

Puerto Ricans are the second largest group of Hispanics in the United States and have higher cancer mortality rates than all other Hispanic groups combined. Approximately 3.9 million Puerto Ricans live on the island of Puerto Rico and approximately 3 million more live in the continental United States, mostly in urban areas on the East coast ⁹. Puerto Ricans are US citizens and can travel freely between Puerto Rico and the United States. The age-adjusted prostate cancer mortality rates among men from Puerto Rico and the United States are somewhat similar (16.1/100,000 and 15.7/100,000 respectively). Table 1 shows the different cancer mortality rates in Puerto Rico and in the United States. To what extent diet, or any other environmental or genetic exposure are related to any of these disparities remains a high priority within the US Public Health Service, the National Cancer Institute and the National Center for Research on Health Disparities ¹⁰⁻¹⁶. Although, we propose to study the relationship of a specific dietary component with prostate cancer in this pilot study, future research of other dietary factors and lifestyles in this cohort can provide additional information for this and other cancer sites.

Figure 2 shows the leading causes of death in Puerto Rico, with cancer accounting for 15 percent of total mortality. A report of National Cancer Data Base among Hispanics, consistently reports higher percent mortality from prostate cancer among Puerto Ricans than among non-Hispanic whites, Mexican Americans, Cuban Americans and all other Hispanics in the United States ¹⁷. Net migration in Puerto Rico in fiscal year 1980 was -16,101, yet in 1994 it was +26,853. This constant exchange of population from continental US to the island denotes a migration pattern that is very unique to this Hispanic subgroup ¹⁵. Thus, the findings from this proposal has the potential to benefit not only island Puerto Ricans, but also Puerto Ricans living in the US.

The major large epidemiological studies conducted on Puerto Ricans were the Hispanic Health and Nutrition Examination Survey (HHANES), and the Puerto Rico Heart Health Program (PRHHP). The HHANES was a cross sectional survey conducted by National Center for Health Statistics (NCHS) 1982-1984, and included only Puerto Ricans from the New York City metropolitan area ¹⁸.

The PRHHP began in the early 1960's and included a random sample of

Figure 2 Percent distribution of deaths, PR, 1996

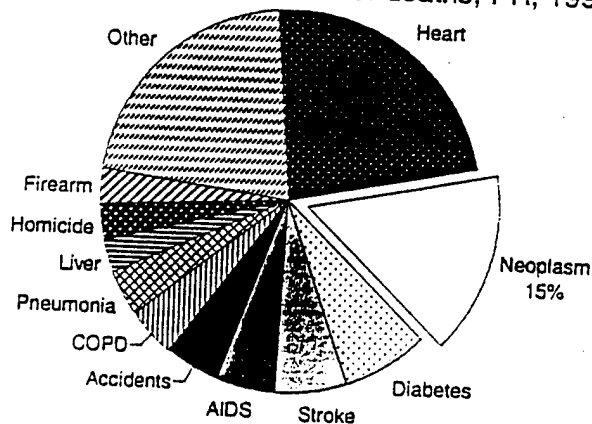
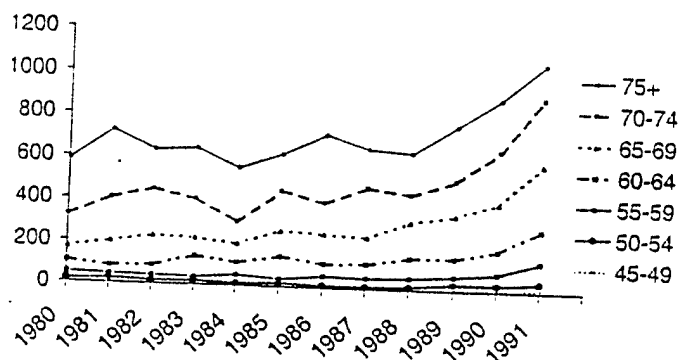


Figure 3. Trend in age-specific incidence rates (per 100,000) of prostate cancer in Puerto Rico, 1980-91



Source: Puerto Rico Cancer Registry, Personal Communication,

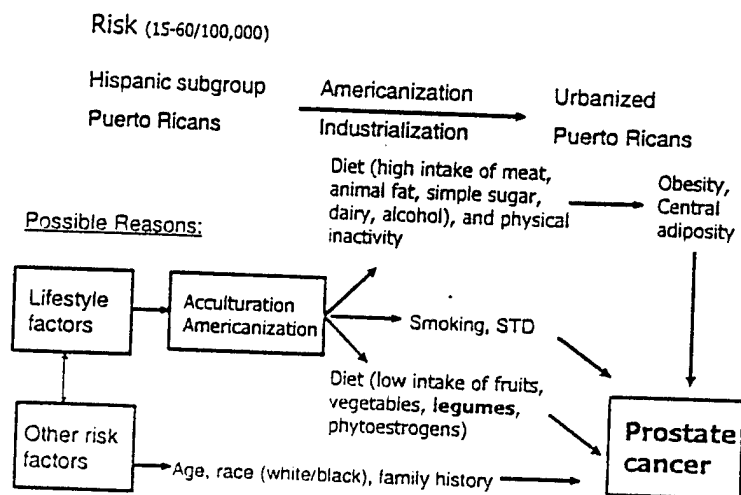
9,824 men, 35-79 years of age at baseline, from both urban and rural areas on the island in order to study risk factors for coronary heart disease incidence and mortality. The last of the four examinations occurred in 1974-1977^{19,20}. The PRHHP offers considerable potential for providing insight into the risk factors for cancer mortality in one of the largest minority groups in the US. In addition to diet and lifestyle information pertinent to prostate cancer, this study also collected information on skin color using standardized methods developed at the Smithsonian Institute that can be used to further study the effect of race on prostate cancer risk²¹.

While prostate cancer mortality has decreased in the general population, prostate cancer mortality rates continue to increase in certain ethnic groups. Prostate cancer is the second leading cause of all male cancer deaths in the US, following lung cancer. In 1994, however, prostate cancer became the leading cause of all cancer deaths (11.7%) among Puerto Rican men, followed by cancer of the trachea, bronchus and lung (9%)^{22,23}. The median age of the surviving participants in the PRHHP is approximately 90 years (projected age range 72-99 years), an age where substantial increases in prostate cancer mortality are observed^{11,24,25}. Figure 3 shows that the age-specific incidence of prostate cancer has increased in every age group in Puerto Rico. Prostate cancer mortality has also increased. Again, prostate cancer is the most lethal cancer among Puerto Rican men. Of the 2,516 deaths due to malignant neoplasms among Puerto Rican men in 1994, 505 were due to prostate cancer (11.7%), making this the most frequent cause of cancer deaths in Puerto Rican men²³. As with other migrant populations, the cancer mortality rates of Puerto Ricans living in US are intermediate between those observed for Puerto Rico and the United States^{12,17,26-28}.

B.3. Diet and prostate cancer.

The most extensively studied risk factors for prostate cancer include age, race/ethnicity, family history, dietary intakes, body weight, alcohol, physical activity, androgen production and metabolism, occupation, and living in the United States. Of these, age, race and family history are well documented but the underlying mechanism of action is not entirely understood. For the other factors some studies show a positive association while others show a negative association or no association at all²⁹⁻⁴⁰. Although little is known about specific biological pathways, it is likely that endogenous androgen metabolism plays a role in the etiology of prostate cancer. Androgens, especially dihydrotestosterone, controls cell growth in the prostate. The fact that prostate cancer rates change in migrant populations and vary dramatically in ethnically similar populations residing in different geographic locations strongly suggest that environmental factors can greatly influence the risk of this cancer. Figure 4, is an adaptation of Figure 1 with specific exposures that can be studied among the Puerto Rican population. In 1998, the Prostate Cancer Progress Review Group recommended extending research efforts to include nonwhite ethnic groups. "An important priority is the establishment of cohort of African American, Hispanic and Asian American men to be studied for genetic and lifestyle factors in relation to prostate cancer."² The National Cancer Institute has also identified the importance of cohort studies as outlined on program announcement PAS-02-009.

Figure 4. Characterizing prostate cancer risk in Puerto Rican men



One of the strengths of longitudinal studies is that the time-sequence in which the nutritional exposure precedes the disease can be established. Moreover, if the longitudinal studies acquired baseline information on other possible risk factors such as smoking, alcohol, obesity and physical inactivity, then there is an increased confidence in the observed absolute estimate of risk and the ability

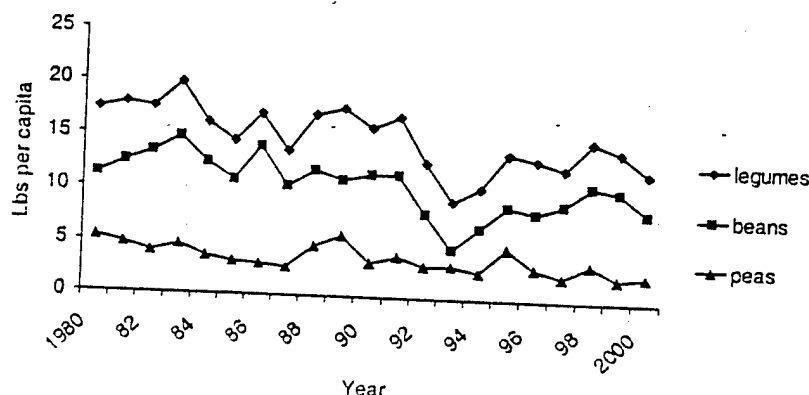
to control for confounding, especially as the cohort becomes older. Dr. Freudenheim and Dr. Paola Muti, co-investigators in this grant, have published extensively on the role of diet and breast cancer in pre- and post-menopausal women and on gene and environmental exposures with prostate cancer. Findings on the relationship between diet and breast cancer in pre- and post-menopausal women may be useful in generating additional hypothesis to better understand the role of diet in prostate cancer in younger and older men ^{6,40-50}.

B.3.1. Legumes and prostate cancer

Plant foods have been associated with a protective risk for prostate cancer in several studies ^{45,51}. Reduced prostate cancer risks have been associated with higher intakes of carotenoid-rich vegetables and soy products in Japan, higher intakes of beans, lentils, peas, and dried fruits among Seventh Day Adventist men, and among Japanese men in Hawaii consuming tofu ⁵²⁻⁵⁴. Similarly, reduced mortality from prostate cancer has been reported for men with higher intakes of cereals (which contain lignans) ^{25,55}.

Legumes include peas, beans, lentils, and peanuts. Beans and peas are staple foods of the Puerto Rican diet, particularly, pinto, kidney, small white, black-eye and black beans, and green pigeon peas and chick-peas ^{56,57}. Figure 5 shows the per capita consumption of total legumes, beans and peas (gandules) in Puerto Rico for the last 20 years. In contrast to the US, beans play a significant role in the Puerto Rican diet. In fact, consumption of legumes in Puerto Rico (14 pounds/capita) is double that of the US (7 pounds/capita) in 2000. Tucker, et al., found rice and beans, and dried beans to be major sources of energy in the Puerto Rican diet ⁵⁸. They are a rich source of plant-based protein, dietary fiber and phytoestrogens. Beans have long been recognized for their protein content and more recently have been noted for their soluble-fiber content, but in general there has been relatively little research and discussion about the nutritional attributes of legumes, especially non-soy legumes ⁴. The most commonly eaten beans in Puerto Rico are shown in Figure 6. Soy beans are not a commonly consumed product in Puerto Rico, as in the US.

Figure 5. Trend in yearly consumption of total legumes per capita in Puerto Rico, 1980-2000.



Source: Puerto Rico Agricultural Statistics, Commonwealth of Puerto Rico
Personal communication: Ana Cruz, Director of Agricultural Statistics, Dec. 10, 2002

The relationship between prostate cancer and the dietary properties of beans, e.g., dietary protein, dietary fiber and phytoestrogens is not well established ^{4,5,5,59}. Strom et al found a lower risk of prostate cancer associated with higher phytoestrogen intakes, but was limited by a small sample ⁶⁰. In a meta-analysis of case-control studies in Canada, Jain et al reported reduced risks of prostate cancer associated with beans, lentils and nuts (OR=0.69, 95% CI=0.53-0.91) ⁵¹.

In a multi-center case control study that included African-Americans, Whites, Japanese and Chinese populations the relationship of prostate cancer with legumes from soy and non-soy products were studied separately. An inverse association between prostate cancer risk and non-soy legumes was found for African Americans, but not for Whites, Japanese or Chinese. On the other hand, soy foods were not significantly related to prostate cancer risk for any of the groups studied. Combining all legumes into one category yielded significant protection against prostate cancer for African Americans and Chinese men ⁵⁹. Our proposal is innovative in that we will examine the relationship of intake of non-

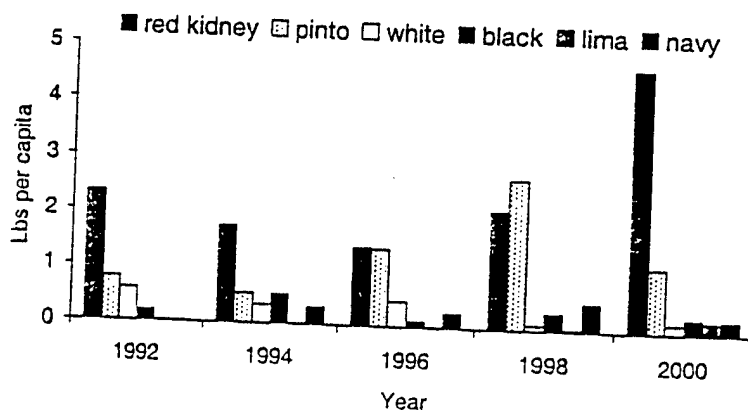
soy legumes (the most widely consumed type of legume in the US and by Hispanics) with prostate cancer prospectively and with the ability to control for confounders such as skin-color, alcohol intake, smoking, physical activity, body weight, energy intake and dietary fat.

Phytoestrogens (plant estrogens) are plant compounds with estrogen-like biologic activity. Phytoestrogens may prevent prostate cancer because of a dose-dependent reduction in serum 17β -estradiol and testosterone levels. Estrogen receptors β in the prostate binds with isoflavones genistein which has an affinity similar to that of 17β estradiol mediating their anti-cancer effect through this target. Other mechanism of actions may also be through induction of p21 by a p53 independent pathway; inhibition of the serum prostate-specific antigen; inhibition of epidermal growth factor autophosphorylation; and inhibition of NF- κ B activation. It is not clear if all these mechanisms operate *in vivo*, however^{50,61}. The three main classes of phytoestrogens are isoflavones, coumestans, and lignans. These compounds are structurally similar to estrogen, and have demonstrated estrogenic activity *in vitro*, in animal models, and to some extent in human studies⁶¹. Isoflavones are part of the broader class of bioflavonoids found in most plants, and are largely restricted to tropical legumes. Lignans are found abundantly in legumes, cereals, fruit, and vegetables, with the highest concentration in flaxseed and bread products made with flax⁶¹. Although present in smaller relative amounts, several foods and beverages such as coffee and orange juice are also significant contributors to total dietary intake of lignans due to the amounts of those foods consumed each day⁶². Among non-Asian populations, lignans provide the largest contribution to total phytoestrogen intake⁵. Research in non-Asian populations with high, moderate and low intakes of legumes (e.g., beans, peas and lentils), are needed to more clearly understand their relationship to prostate cancer in diverse populations who typically consume less soy^{50,63}. More importantly, to be able to assess the preventive impact of non-soy legumes on prostate cancer is of high public health significance, as these are more commonly eaten in the Western world. Although there are specific ethnic groups (i.e., Puerto Ricans, Mexican-Americans, Cuban-Americans) who consume high levels of non-soy legumes, there are no establish longitudinal cohort to test this hypothesis yet. Most, if not all, of the epidemiological

evidence has hinted at an association between soy phytoestrogens and reduction of prostate cancer. The lack of published reports on the effect of non-soy legumes on prostate cancer may be due to the lack of studies that have enough participants consuming varying levels of non-soy legumes. We have a unique opportunity to examine this using data from the PRHHP.

Lignans have been related to cancer risk. *In vitro* investigations have demonstrated a number of physiologic actions by enterolactone which could affect prostate cancer risk, such as synthesis of sex hormone binding globulin and alteration of 17β -hydroxysteroid dehydrogenase type 5, which is involved in estrogen and androgen metabolism^{64,65}. Diet has been clearly shown to have the ability to affect circulating hormone levels through changes in androgen production rates or impacting metabolism and clearance of circulating hormones⁶⁶. Dorgan demonstrated that both total testosterone and sex hormone binding globulin could be changed through controlled dietary changes of fat and fiber. In this study, total testosterone and bound testosterone was increased 13% and 15%, respectively, in response to a high fat, low fiber diet in men⁵⁸. The lignan precursors, secoisolariciresinol and matairesinol, are

Figure 6. Trend in per capita consumption of the most commonly eaten type of beans in Puerto Rico, 1992-2001.



Source: Puerto Rico Agricultural Statistics, Commonwealth of Puerto Rico
Personal communication: Ana Cruz, Director of Agricultural Statistics, Dec. 10, 2002

metabolized in the gut to form the estrogenically active compounds enterodiol and enterolactone; these compounds are structurally similar to endogenous estrogens⁶⁷⁻⁶⁹. Epidemiologic evidence suggests that cancer risk is lower among populations with higher intakes of lignans (usually measured by urinary excretion)⁷⁰⁻⁷², unfortunately few studies have examined dietary lignan or legume intakes (especially non-soy legumes) and prostate cancer risk.

B.4. Significance

An increase in the life-expectancy and the unexpected increase of the Hispanic population during the last decennial census highlight the significance of improving our understanding of the relationship of age and other risk factors such as diet with prostate cancer among Hispanics and Hispanic subgroups. Establishment of cohorts of diverse population with varying risk has also been identified as priority by the Prostate Cancer Research Group and the National Cancer Institute. Prostate cancer is the number one cancer killer of Puerto Rican men; it is more lethal than lung cancer. Different aspect of the diet may play a role in the etiology of prostate cancer, but more importantly few studies have collected information on this and other confounders prospectively to make a strong case for a relationship, if there is one. Although Hispanics are one of the largest minority groups in the US, there are no published report on the longitudinal relationship between diet and prostate cancer among Hispanic subgroups. Most prostate cancer studies have been conducted in Europe, North America, Japan, and Hawaii. Puerto Ricans are the second largest group of Hispanics in the US and the proportion of people over the age of 75 years have increased dramatically since 1960 population estimates. As previously illustrated, prostate cancer and overall cancer mortality among Puerto Ricans is somewhat different than other Hispanics. We also know that the annual percent change of prostate cancer mortality from 1990 to 1995 increased among Hispanics, but decreased for Whites, Blacks and Asian and Pacific Islanders⁷³. We have a unique opportunity to learn more about the relationship between diet and lifestyles that are related to prostate cancer in a cohort of men that were examined for 12 years with standardized formats. Moreover, this cohort provides the unique opportunity to study the relationship of non-soy legumes with prostate cancer.

Although prostate cancer is now more detectable, prostate cancer mortality continues to increase. Thus, early detection is not necessarily being translated into reduced prostate cancer mortality. The findings from this small grant will contribute to gain substantial new knowledge in subsequent studies to better understand how established and emerging risk factors (e.g., diet, lifestyles, STD, and familial aggregation) relate to fatal prostate cancer. Also, information obtained through this small grant can be used to better understand the etiology of other cancers that are more common among Puerto Ricans than among other populations, (i.e, stomach and oral cancers) and how potential risk factors for these cancers relate to each other.

C. Preliminary Studies

C.1. The Puerto Rico Heart Health Program

The PRHHP included a random sample of 9,824 men, 35-79 years of age at baseline. The sample was randomly selected from four rural municipalities (Naranjito, Comerio, Barranquitas, and Corozal), and three urban municipalities (Bayamon, Guaynabo, and Carolina). The baseline exam was conducted during the years 1965-1968. There were three subsequent exams, which took place during the years 1968-71, 1971-75, and 1974-77. Currently, follow-up data is available for vital status and cause of death for the twelve-year period subsequent to a participant's initial examination date for the 9,815 men. Only **nine** of the original sample of 9,824 men were lost to follow-up over the twelve-year period. No cancer incidence data are available from the original study. The only incidence data collected were for coronary heart disease and those data are for eight years of follow-up⁷⁴⁻⁷⁹.

Early in the 1960's the National Heart, Lung, and Blood Institute funded the PRHHP to confirm the lower CHD mortality rates observed in island Puerto Ricans and to study prospectively a group of rural and urban Puerto Rican men who were free from heart disease. The majority of the participants were between the ages of 45-64 years, which was the original target age range. To prevent delay in scheduling and to promote good community relations, approximately 1,000 men less than 45 years or greater than 64 years were examined as well^{75,80,81}. The design and methods used in the PRHHP were adapted from the Framingham Heart Study and validated by the National Institutes of Health for use in

other population-based, observational, longitudinal cohorts such as the Honolulu Heart Study, The Israel Ischemic Heart Disease Project, and the Yugoslavia Cardiovascular Disease Study. The National Institutes of Health was directly involved in every phase of the implementation of the PRHHP and oversaw the data collection and data analysis^{74,75}. Findings from the PRHHP helped establish physical inactivity, high blood cholesterol and high blood pressure as independent risk factors for heart disease. Other contributions include a better understanding of the relationship of other correlates with heart disease such as skin color, hematocrit, calcium intake, and highlighted the association between low cholesterol levels and cancer^{20,75-78,82,83}.

The PRHHP provides a unique epidemiological cohort of men who took part in multiple examinations including extensive information on lifestyle, diet, body composition, exercise, and smoking habits. Table 2 describes the examination dates and response rates of participants in the PRHHP. The response rate to the initial examination was 81 percent (9,824 out of 12,167). A detailed investigation of all deaths and cardiovascular end-points were obtained using hospital and physician records, clinical information from the study examination, autopsy reports, and information from family and next of kin⁷⁶.

Thus, the PRHHP was designed to examine the natural progression of heart disease in a culturally and ethnically homogenous population, and these principles can be equally applied to study prostate cancer. The PRHHP has not examined the association of any characteristics with cancer incidence or mortality. Our preliminary analysis from the 12-year mortality follow up (up to 1981) shows that 382 of this cohort of men died of cancer (approximately 22 percent of all deaths) (Table 3). The large racial differences in prostate cancer highlights the need for the establishment of cohorts of men at high, moderate, and low risk to be studied for genetic and lifestyle factors in relation to future prostate cancer occurrence, and for progression of disease once it occurs².

Table 2. Description of exam dates, number of participants alive, deceased and taking the exam, and response rates.

Exam No.	Dates of Exam	Alive	Deceased	Taking Exam	Percent Taking Exam
Exam 1	1965 - 1968	9,824	0	9,824	
Exam 2	1968 - 1971	9,618	206	8,746	90.9%
Exam 3	1971 - 1975	9,236	382	7,940	86.0%
Exam 4	1974 - 1977	8,828	408	7,910	89.6%
12 yr mortality	1979 - 1980	-----	741	-----	
Total	1965 - 1980	-----	1737	9,815	

mortality follow-up only

C.2. Published manuscripts on diet, lifestyle and heart disease.

Several manuscripts on physical activity, obesity and diet have been published using data from the Puerto Rico Heart Health Program. First in 1966, Blanton et al., published a dietary study of men residing in urban and rural areas of Puerto Rico. Later in 1972, Garcia-Palmieri published an article in *Circulation* about the interrelationship of serum lipids with relative body weight and physical activity in Puerto Rican men. These earlier studies were mostly cross-sectional relationships using data from the first examination of the PRHHP. In 1977, the *American Journal of Clinical Nutrition* published a report establishing the association of serum cholesterol with intakes of total fat, saturated fatty acids, polyunsaturated fatty acids, total carbohydrate and starch (all measured as percent of calories). These associations were mostly noted in urban dwellers after adjusting for relative body weight and other covariates. Using two and half year incidence of CHD, the PRHHP study confirmed the role of physical inactivity as an independent risk factor for CHD. In 1980 the *American Journal of Clinical Nutrition* published an article linking intakes of legumes with lower CHD incidence. A multivariate analysis confirmed that the beneficial effects of legume intake was independent of body weight, hematocrit, blood pressure, serum cholesterol, alcohol intake, cigarette smoking, urban/rural residence and age. Milk consumption and calcium intake were later associated with reduced hypertension. Gordon et al., found that the inverse relationship between starch intake and incidence of heart disease in Puerto Rico was an

indirect result of differences in fat intake. Other studies identified racial differences in the left ventricular hypertrophy and coronary heart disease risk factors in light and dark skin Puerto Rican men^{19,21,74,76-78,84-87}. These findings were later confirmed in other studies using different methodological assessment tools (i.e., 24-hr recall vs food frequency questionnaire) and in other racially diverse populations.

The above publications represent the potential to use the data collected on diet, physical activity, body weight and other lifestyles to conduct cancer research. Other publications from the PRHHP have also investigated other exposures such as alcohol, skin color, socioeconomic status, urban/rural residency with CHD as the outcome^{77,83,88-90}.

Table 3. Number of *Observed* (1965-1978) and *Expected* (1979-2001) deaths from all causes, all cancers, and prostate cancer

Year of Death	Number alive at the beginning of the period	All causes mortality (N)	Cancer Death (N)	Prostate Cancer Deaths (N)	Proportion of all deaths due to cancer (%)
Observed					
1965-1968	9,824*	142	29	6	20.4
1969-1978	9,682	1,452	325	65	22.4
Expected**					
1979-2001	8,230	3,088	618	124	20.0
Total					
Deaths 1965-2005	NA**	5,124	1,060	212	20.7

* Initial sample from exam 1 which was conducted during the years, 1965-1968 ** see section C.3 for methods used to estimate the numbers of expected events.

C.3. PRHHP Probability of Death

The number of observed and anticipated or expected deaths in the PRHHP cohort due to all causes and cancer are shown in Table 3. Using the mean probability of death for the years 1976-78, 0.200, the expected number of deaths due to all causes was calculated using a life table approach with the probability of death assumed to increase by factor of 1.001 each year from 1979-2005. Using those assumptions, a total of 5,124 deaths and 1,060 cancer deaths are expected through 2005. The number of deaths due to cancer was calculated using a similar approach and also represents a cancer mortality rate of around 22%. This is somewhat larger than the 15 percent of deaths due to cancer in Puerto Rico in 1996 presented in Figure 1, which includes men and women, and persons of all ages. The expected number of deaths and probability of death in this table are comparable to data from the Framingham Heart Study⁹¹. Using 32 years of mortality follow-up data from the Framingham Study we found 43% (2222/5209) of the cohort had died. In our calculations approximately 47% (4682/9824) are expected to be dead by 2001, nearly 35 years after the midpoint of first examination (1965-1968). These estimates have been confirmed using a subsample of this cohort in a cancer mortality feasibility study with a 46% mortality as of 2001, (681/1477). The estimated numbers of prostate cancer deaths were calculated based on our cancer mortality feasibility study, described below, and recognizing that 20% of all cancer deaths in Puerto Rico are due to prostate cancer^{23,92}.

C.4. Puerto Rico Cancer Mortality Feasibility Study

We conducted a cancer mortality feasibility study using 1477 participants from the original cohort who were pairs of brothers. This means at least two members of the same biological family were part of the cohort. Table 4 provides a description of the participants used for the feasibility study. The main

objective was to assess the feasibility of ascertaining cancer mortality in a group of Puerto Rican men using more than one approach: (1) The Puerto Rico Demographic Registry; (2) The Puerto Rico Cancer Registry and (3) The National Death Index (NDI). The Puerto Rico Cancer Registry permitted us to confirm cancer mortality and provided us with a cancer registry number for further validation of time of diagnosis. The NDI Plus provided us with possible matches using two-part last names, in conjunction with the causes of death and dates of deaths among participants dying either in Puerto Rico or in any of the 50 states plus the District of Columbia.

The first step in our cancer mortality feasibility study was to use the Puerto Rico Demographic Registry to assess vital status and cause of death on approximately 1,500 participants. Of these 1,477 participants had complete records to be submitted to the Puerto Rico Demographic Registry for confirmation of vital status. We found the percent of cancer deaths to be 17%, (115/ 681). Using the confirmed vital status and cause of death from the PR Demographic Registry, we selected 100 participants who died from cancer (including all those for whom prostate cancer was the underlying cause of death), and randomly selected 100 participants considered alive and 100 participants who died of non-cancer causes.

Thus, we created a sub-sample of 300 names to confirm cancer mortality using the Puerto Rico Cancer Registry and the US NDI. Results from our feasibility study found that the Puerto Rico Cancer Registry identified 5 cases out of a 100 where a cancer diagnosis had been reported but final underlying cause of death was not cancer. Regarding the NDI, we did not find any participant dying outside of Puerto Rico, at least out of the 300 names submitted. Although the NDI could have identified subjects who died outside of Puerto Rico, in our small sample all of our matches ended up being from the Commonwealth of Puerto Rico. This is supported by migration studies in the Puerto Rican aging population⁹. We propose to conduct NDI matches, only on those for whom we do not find a death certificate from the Puerto Rico Demographic Registry or for whom we do not have a match using the Puerto Rico Cancer Registry. If we find an NDI match outside of Puerto Rico, we will then contact the state specific Cancer Registry for time of diagnosis and any other pertinent

information regarding that case. The most important cancer registries for this component are those from New York City, New York, New Jersey, Florida, Massachusetts, Connecticut, Pennsylvania and Illinois. This represents where most of the Puerto Rican population lives in the continental US (Contact names and addresses are provided in the appendix).

Table 4. Comparison of participants in the Puerto Rico Cancer Mortality Feasibility Study and the original cohort of the PRHHP.

	Feasibility		Original	
	N	%	N	%
Age, years				
35-44 y	73	4.9	364	3.7
45-54 y	785	53.1	5030	51.2
55-64 y	536	36.3	3792	38.6
65 y+	83	5.6	638	6.5
Body size (BMI)				
Underweight (<18.5)	49	4.9	292	3.2
Normal wt. (18.5-24.9)	670	53.1	4304	47.1
Overweight (25-29.9)	566	38.3	3435	37.6
Obese (30+)	192	13.0	1105	12.1
Urban living	948	64.2	6843	69.6
Education				
No schooling	143	9.7	912	10.0
Grades 1-4	469	31.8	3209	35.2
Grades 5-8	462	31.4	2625	28.8
Grades 9-12	292	19.8	1632	17.9
College	107	7.3	738	8.1
Smoking status:				
Non-smokers	406	27.5	3125	34.2
Ex-smokers	355	24.1	2020	22.1
Current smokers	715	48.4	3992	43.7

C.5. Body weight, physical activity and all cause mortality in Puerto Rican Men.

We published a paper studying the effect of physical activity, body weight and all cause mortality using the 12-year mortality follow-up data: Crespo CJ, Garcia-Palmieri M, Sorlie P, Perez-Perdomo Rosa, McGee DL, Smit E, Sempos C, Lee IM. The relationship between physical inactivity, body weight, and all cause mortality in Puerto Rican men: Results from the Puerto Rico Heart Health Program. *Annals of Epidemiology*. 2002, 12:543-552⁹³. Our results also show that Puerto Rican men who were overweight, but who were physically active were protected from premature mortality compared to overweight men who were not physically active. Figure 7 shows the percent of deaths, crude death rate by body weight categories. Figure 8 shows the cumulative survival rate by quartiles of physical activity. After adjusting for age, overweight status and other known CVD risk factors, we found physically inactive Puerto Rican men (those in quartile 1) had a statistically significant higher all cause mortality than those who were more active (men in quartiles 2, 3 and 4, OR=0.68, 0.64, and 0.57, respectively). We also found that physically active (Q2-Q4) overweight (BMI \geq 25-29.9) men had significant lower all-cause mortality than sedentary (Q1) overweight men. Consistent with public health recommendation, our findings support the view that participation in physical activity of at least moderate-intensity is protective against all cause mortality, and that this protection is also of benefit to overweight men⁹⁴. It is unclear if similar benefits can be observed for site-specific cancer mortality.

Figure 7. Number of deaths and crude death rates according to body weight in Puerto Rican men from the Puerto Rico Heart Health Program

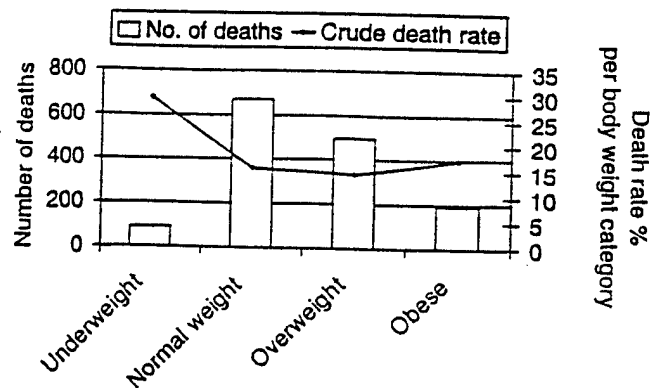
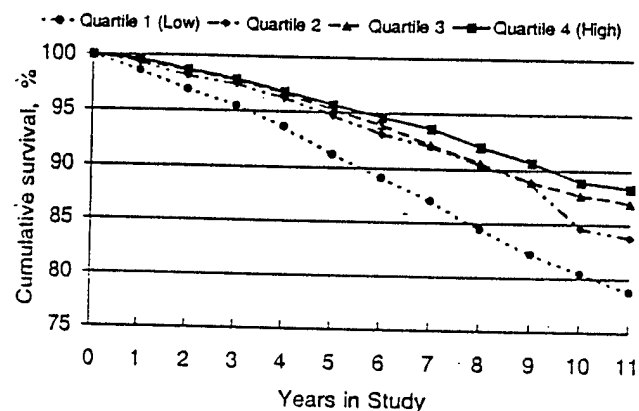


Figure 8. Cumulative survival (per 100) among Puerto Rican men aged 35-79 years at baseline by quartiles of physical activity. (12 yr follow up)



Survival is based on men who did not have any pre-existing heart disease at baseline and who were alive 3 years after the study started.

We are currently funded to examine the role of physical activity, body weight changes and prostate cancer mortality in this cohort. Prostate cancer mortality is being collected through death certificates. We propose in this small grant proposal to further characterize prostate cancer mortality using linkages with the Puerto Rico Cancer Registry such as time of diagnosis and stage of cancer. As a result of these efforts we will be able to examine if exposure to legume consumption is related to prostate cancer and in what direction, if any, is this relation. There are other exposures in relation to other cancer that can be studied subsequent to this pilot project. For example, as part of the PRHHP there is laboratory confirmed sexually transmitted disease that were measured during the first examination on 9,753 participants to study syphilitic heart disease. Skin color was collected under the arm using standardized tiles from the Smithsonian Institute to classify participants in a gradient of skin color from 1 to 30, this was done during the third examination. Smoking history was obtained, with detailed information on tobacco use that included cigarette, pipe, cigar smoking and tobacco chewing. Alcohol consumption was obtained as part of a 24-hour recall in the first examination and as part of limited food

frequency questionnaire conducted during the second examination. These exposures are of high public health significance given that Puerto Ricans have one of the highest rates of oral cancers in the US and probably the world. Again, for this small proposal our primary aim is to ascertain prostate cancer mortality in this cohort and to examine its association with an established dietary exposure not well studied (non-soy legume). Future proposal could include nested case-control study of prostate and other cancers. Another important feature of the PRHHP is that close to 2000 of the members of the cohort were pairs of brothers. This lends itself to further study familial aggregation of potential risk factors.

C.6. Baseline dietary data

In 1965, a 24-hour dietary recall was incorporated in the standardized examinations given to men in the Puerto Rico Heart Health Program, and subsequently in the Framingham Study and the Honolulu Heart Study. Each study was designed according to the special research interests, but comparable data collection systems were sought. These studies provided some of the earliest epidemiological findings linking diet to coronary heart disease. The methods used to obtain dietary recalls, train interviewers, and quality control procedures in the PRHHP have been published previously⁹⁵. These earlier dietary findings on diet (e.g., saturated fat intake) and heart disease have been confirmed in other studies. Food models and standard-sized utensils were used to obtain a quantitative assessment from participants during a 24-hour dietary recall. Intake of energy and nutrients was

Table 5. Dietary intake at baseline in Puerto Rican Men from the Puerto Rico Heart Health Program.

	Mean	SD
Beans and peas, ¼ cups	2.3	2.2
Fruits, in 100 gm servings	1.2	1.8
Starchy vegetables in 50 g	2.7	3.3
Cooked vegetable ¼ cup	.30	.91
Milk, 1 oz serving	4.0	2.8
Total carbohydrates, g	276.2	107.9
Meat (beef, veal, pork, ham) oz	2.6	2.9
Dairy protein, g	24.4	15.4
Plant protein, g	24.1	12.1
Animal protein, g	28.2	23.4
Total protein, g	84.5	34.7
Fish protein, g	7.9	15.9
Animal fat, g	73.1	38.5
Vegetable fat, g	19.7	21.7
Saturated fat, g	34.9	17.2
Polyunsaturated fat, g	14.2	11.7
Monounsaturated fat, g	36.6	18.6
Dietary cholesterol, mg	410.7	313.3
Total fat, g	93.5	43.9

calculated using the United States Department of Agriculture Handbook #8 food composition tables or other more direct sources of nutrients analysis for foods special to Puerto Rico. Previous dietary studies in Puerto Rico, including a pilot study before the implementation of the PRHHP had revealed that relatively few food items account for a major part of the total calorie intake^{13,96}. This situation facilitated the preparation of a pre-coded dietary interview form listing the most commonly eaten foods among participants of the PRHHP. Additionally, during the PRHHP subjects were asked if the previous day's diet was a good representation of their usual intake, and 80% reported that their 24-hour recall was representative of their usual intake. Those foods considered to be most commonly consumed by the participants were listed in a pre-coded form for the 24-hour recall, based on information from the pilot study. Inclusion of 39 common foods in addition to the 24-hour recall served to take into account their separate contribution to the usual dietary intake of the participants⁹⁵. For this proposal we want to examine foods that are readily available and consumed year round such as legumes. For commonly used dishes a standard recipe was determined and dietary analysis took into account their separate components.

The 24-hour recall has been used in other large-scale dietary studies conducted in the United States in recent years by the USDA and the National Health and Nutrition Examination Survey (NHANES) of the National Center for Health Statistics. Several of the co-investigators in this proposal have used dietary data from the 24-hour recall from PRHHP, NHANES I Epidemiological Follow-up and more recently the NHANES II longitudinal follow up to assess relationships between exposure to

nutritional factors and chronic diseases^{74,97-104}. Table 5 presents a partial list of some of the dietary variables already cleaned and available in electronic format. Dr. Freudenheim, a co-investigator in this grant, has studied extensively the relationship of fruits and vegetables, types of dietary fats, and other environmental and genetic exposures with hormone-related cancers^{42,43,105}. Moreover, we are including as part of the team Dr. Mark Messina, an expert on soy legumes, to assist us in understanding methodological issues in legume research that may be related to prostate cancer. Moreover, his assistance in the preparation of this grant and interpretation of the data has been and will be very valuable.

D. EXPERIMENTAL DESIGN AND METHODS

D.1. Overview

The study population consists of Puerto Rican men who took part in the PRHHP and participated in four examinations (1964-1979) and a mortality follow up study between 1979 and 1981. Subsequently a feasibility study conducted in 1998-2000 (N=1477), assessed vital status and found 681 deaths all in the island of Puerto Rico. Currently, vital status has not been investigated in the remainder of the cohort (N=7,406). In our feasibility study we found prostate cancer to be a contributing cause of death on 29 cases. From our projected estimates in Table 3 we expect to have 212 cases of prostate cancer deaths. For this grant we plan to re-establish this cohort of Puerto Rican men to investigate the relationship of diet with prostate cancer, but subsequent analysis can include other exposures. We will first organize a database with time of diagnosis and mortality from prostate cancer. Further analytical research will include a study of the relationship of legume consumption with prostate cancer mortality in Puerto Rican men. Our first goal, therefore, is to finalize the assessment of prostate cancer mortality using data from the Puerto Rico Demographic Registry, the National Death Index (NDI) and the Puerto Rico Cancer Registry. Results from our feasibility study showed that it is more cost effective to first assess vital status and multiple cause of death using the Puerto Rico Demographic Registry than the NDI.

D.2. Ascertainment of prostate cancer mortality

Prostate cancer mortality will be established using a combination of data sets from the Puerto Rico Demographic Registry and the Puerto Rico Cancer Registry. The National Death Index Plus will be utilized for participants found not dead in the Puerto Rico data bases. The Puerto Rico Cancer Registry permitted us to ascertain when prostate cancer was not the underlying cause of death, but a contributing cause. It also allowed us to identify time of diagnosis among the cases to more clearly determine the fast aggressive cancers. Our earlier feasibility study found the Demographic Registry to provide the fastest and most cost-effective mechanism for determining cause of death. The NDI showed that the use of two-part last names, common among Hispanics, is not as commonly used in other states, as it is in Puerto Rico. The use of one last name, especially among common Hispanic surnames, produced many false positives (over 50%). In addition, we did not find any NDI match from this cohort in any state outside of Puerto Rico. Table 6 describes the information needed for searches in the above registries and the available data in the PRHHP.

D.2.1. The Puerto Rico Demographic Registry

The Puerto Rico Demographic Registry is the repository of all the death certificates of persons deceased in the commonwealth of Puerto Rico. According to the Pan-American Health Organization (PAHO, 1999), death registries in Puerto Rico are very complete, and causes of death are certified by physicians: 52% by family doctors, 37% by physicians who base their certification on the results of autopsies and medical records or other tests, and remaining 11% by physicians who utilize other sources of information. All deaths that occur in Puerto Rico are registered at local offices of the Population Registry located throughout the island in both the rural and urban areas. Each death certificate has the full name of the deceased, with the father's and mother's last names; names of the parents of the deceased; underlying and other significant conditions contributing to death but not related to cause given; date of death; place of death; social security number; death certificate registration number; and if applicable, the hospital where the death occurred and funeral home processing the deceased. To obtain a death certificate the investigator needs to submit a written request with the full name of the deceased, mother's and father's last name, date of birth, and social security number (if SSN available).

After confirming vital status using the Puerto Rico Demographic Registry, we will submit names to the National Death Index only for those participants who are classified as alive from PR Demographic Registry. In our feasibility study we submitted 300 names to the National Death Index, of which 100 were considered alive. We did not find a match in the NDI; however, our sample (N=100) was too small for us to feel confident that no member of the cohort died in the US. During the fourth examination (1974-1977) there was one person out of the 7,919 participants who had relocated to live in the United States. Thus, in the event that any member of the cohort died in any of the 50 states, the District of Columbia, or the Virgin Islands, we expect to find him using the NDI. Dr. Sempos, Dr. Crespo, and Dr. Freudenheim have utilized the NDI in previous studies and are familiar with its methods.

D.2.2. The National Death Index Plus:

The National Death Index is a central, computerized index of death record information compiled from magnetic tapes submitted under contractual arrangement to the National Center for Health Statistics (NCHS) by State vital statistics offices. These tapes, beginning with deaths occurring in 1979, contain a standard set of identifying data for each decedent. The NDI enables investigators to determine if persons in their studies have died; if so, the Index provides the names of the States where the death occurred, the corresponding death certificate numbers, and the dates of death. The NDI file contains death record information for all 50 states, the District of Columbia, Puerto Rico, and the Virgin Islands. The "NDI Plus Coded Causes of Death" is a new optional service, which provides the underlying and multiple causes of death for deceased subjects. The causes of death are available in coded form (using ICD-9 codes) for deaths occurring from 1979 through the most recent year. Sathiakumar et al. compared 509 deaths that occurred after 1979 to ascertain the completeness of the NDI Plus. Three nosologists evaluated ICD codes calculated from death certificates against those of the NDI Plus and found few discrepancies. Moreover, the discrepancy rates for selecting the appropriate cancer death site were approximately one percent

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Table 6. Data needed for the National Death Index, Puerto Rico Demographic Registry, and the Puerto Rico Cancer Registry to report cancer incidence and multiple causes of deaths

Variable	NDI	PR Office Registry	PR Cancer Registry	PRHHP
Name of person	✓	✓	✓	✓
Last name	✓	✓	✓	✓
First name	✓	✓	✓	✓
Middle Initial	✓	✓	✓	✓
Father's surname	✓	✓	✓	✓
Mother's last name		✓	✓	✓
SSN	✓	✓	✓	✓*
Date of birth	✓	✓	✓	✓
Month	✓	✓	✓	✓
Day	✓	✓	✓	✓
Year	✓	✓	✓	✓
Age at death	✓	✓	✓	✓
Date of death, year	Opt.			✓
Sex	✓	✓	✓	✓
Race	✓			skin color*
Marital status	✓			✓
State of residence	✓	✓	✓	✓
State of birth	✓			✓
Sequence number	Opt.			✓
Optional user data	Opt.			
Place of death				✓
Cause of death				✓
Hospital of death				✓ (Opt.)
Physician				✓ (Opt.)

* available on approximately 20% of participants

* collected during the third exam White, Black

NDI matching algorithms require that the user's data agree with the NDI data according to one of the following: 1) Social Security Number (SSN) and either first or last name; 2) SSN and father's last name; 3) month and year of birth and first and last name; 4) month and year of birth, first name, and either father's or mother's surname. Agreement on names may be either exact spelling matches or "soundex" matches to account for certain spelling errors¹⁰⁷. The effectiveness of the NDI matching

process is dependent on the completeness and quality of the death certificates submitted to NCHS by the states, the completeness and quality of the data provided by the NDI user, and the effectiveness of the NDI matching ¹⁰⁸. When SSN are available the NDI has sensitivities that are greater than 97 percent. In a study of Vietnam-era veterans, the NDI had a greater sensitivity than the Social Security Administration files, the Veterans Administration files, and the Internal Revenue Service files ¹⁰⁹. Edlavitch and Baxter made direct comparisons of mortality data from a single state (Minnesota) death certificate search against those of the NDI using a cohort of 2,925 hospitalized patients and found a 97.8 percent agreement ¹¹⁰. The NDI had a 97 percent sensitivity among participants of the American Cancer Society's Cancer Prevention Study. These studies shows that the NDI has a very high sensitivity ascertaining cause of death with cohort studies, with state specific mortality requests, and when ascertaining cancer mortality in longitudinal studies ¹¹¹⁻¹¹³.

In our preliminary analysis we found that the SSN of participants in the Puerto Rico Heart Health Program Study were collected as part of Exam 3 (1971-1975) with 7940 taking the exam, and of these many did not know their SSN. Thus, we expect that SSN to be missing for approximately half of the participants. This phenomenon is not unusual and researchers have reported successful matches in mortality studies with missing SSN. For example, Stampfer et al. studied 346 members of the Nurses' Health Study who had died between 1979-1980 with missing SSN ¹¹⁴. They used name and month and year of birth as the matching variables and found a sensitivity of 96.5 percent and a specificity of 100 percent. Wentworth, Neaton and Rasmussen (1983) used data from the Multiple Risk Factor Intervention Trial (MRFIT), and submitted 194 known death cases for the years of 1979-1980 ¹¹⁵. The NDI correctly identified 98.4 percent of deceased persons with a SSN and 91.1 percent of the deceased persons without a SSN. Williams, et al. (1992) found a sensitivity of 97 percent when the SSN was included and 92 percent without SSN. Thus, the NDI is a very good source of vital status information for researchers who do not have access to SSN ¹¹⁶.

D.2.3. The Puerto Rico Cancer Registry

The Puerto Rico Cancer Registry was part of the National Cancer Institute Surveillance, Epidemiology and End Results Program (SEER) until 1991. The Puerto Rico Cancer Registry now works in collaboration with the Centers for Disease Control and Prevention Cancer Registries. The mandate of the Puerto Rico Cancer Registry has not changed and the main goal continues to be to collect, analyze and disseminate data useful in the prevention, diagnosis and treatment of cancer. We used data from the Puerto Rico Cancer Registry to produce figure 1 and present the trend in age-specific prostate cancer rates in Puerto Rican men from 1980 to 1991. Other information on the prevalence, incidence and cancer mortality in Puerto Rico was collected with the cooperation of the Director of the Puerto Rico Cancer Registry. The Puerto Rico Cancer Registry monitors the impact of cancer in the population of Puerto Rico and maintains surveillance of new cases and mortality from all cancers.

One of the main aims of this small grant is to better characterize prostate cancer mortality, using the Puerto Rico Cancer Registry; however, if data on prostate cancer incidence is readily available we will incorporate it in the database for future analysis. Earlier this summer, we submitted a planning grant between the University of Puerto Rico and the Roswell Park Cancer Institute with Dr. Crespo as the PI, to establish a partnership between these two institutions to conduct multidisciplinary cancer research. For this partnership agreement, Dr. Crespo and Dr. Figueroa-Valles (Director of the Puerto Rico Cancer Registry) have started working in other cancer training and research projects. Multiple meetings and discussion have taken place and there is agreement to use the resources of the Cancer Registry to better ascertain (i.e., time of diagnosis) and characterize (i.e., stage) cancer mortality in this cohort.

D.3. Data analysis:

Table 4 shows the baseline percent distribution by age group of the original sample and those in the pilot feasibility study. Additional measures of exposures and other dietary confounders can be found on Table 5. What is critical at this point is that as the median age continues to increase the expected number of prostate cancer cases is also expected to increase. We will follow standard statistical methods in epidemiology to analyze the data as detailed below ⁹².

D.3.1. Dietary data analysis

In prospective studies a broad assessment of diet is desirable because many dietary exposures and many disease end-points ultimately will be investigated. To relate diet at baseline to the eventual occurrence of disease, a measure of the usual intake of foods by participants is preferred. Currently, no dietary assessment method is likely to measure the true intake for an individual^{99,117-123}. At baseline men from the PRHHP completed a 24-hour recall and 80% reported it to be representative of their usual intake. The current database includes 67 dietary variables for the baseline visit.

The strengths of the 24 hour recall include less reliance on memory since the period of recall is immediate. The literacy of the participant is less important since the tool is interviewer administered¹¹⁸. For this particular study, the key strength is the flexibility to analyze diet by nutrient, food group, meal patterns and for specific foods. Because of the complex ways in which diet and nutrition may affect prostate cancer, it is important to have as much dietary intake information as possible. This is of particular importance when the diet of the study population is different from the general US population. To illustrate this, a typical Puerto Rican diet contains as staple foods mixed dishes such as rice and beans and the use of "sofrito" or "recaito." "Sofrito" is a cooked condiment; literally it means

something lightly fried. The "sofrito" in Puerto Rico is a sauce composed of plant or animal fat, and garlic, onion, tomatoes, green peppers, cilantro, oregano, pepper, salt and tomato sauce. These are all cooked together until the flavors blend well. It is used in relatively large amounts in stews, braises and in stewed beans. "Recaito" refers to a combination (usually in a blender, or chopped) of fresh cilantro leaves, sweet chili pepper, cooking tomato, Italian frying pepper, garlic and onion, to be used in the "sofrito." Capturing some of these foods in a pre-coded food frequency questionnaire is difficult, unless specifically designed for the population being studied.

The weaknesses of the 24 hour recall include that participants may not report their intake accurately due to cognitive issues and difficulty estimating portion sizes, and the availability of only a single 24 hour recall¹¹⁸. With a single 24-hour recall, a high degree of intra and inter-individual variation is likely as such it may not represent an individual's usual intake. This could result in misclassification of an individual's intake and may bias the results towards the null. On the other hand, previous studies that used the 24 hour recall to examine diet and cancer associations compared their results to the magnitude of risk found by other studies that used a food frequency questionnaire. They found that the magnitude of the risk was similar, suggesting that the degree of misclassification may be similar in both methods¹²⁴⁻¹²⁶. For this feasibility study we are looking at foods that older men are more likely to consume on a regular basis such as legumes that may have lower within-person variability and that are routinely consumed in the Puerto Rican diet. From personal experience growing up in Puerto Rico, and to this day, rice and beans are served daily.

D.3.2. Analysis of the baseline 24 hour recall data

We propose to examine the association of dietary intake and prostate cancer using 2 analytical approaches. These approaches are similar to those used in other analysis of the PRHHP and in analysis of 24-hour recall data and cancer in the NHANES follow-up studies^{74,124-126}. The first approach will entail the comparison of intake among prostate cancer deaths and non-prostate cancer deaths. The crude mean level of the nutrients at baseline (before the development of prostate cancer) will be calculated for those who die of prostate cancer and those who do not, and the difference between the means will be tested. Thus, any measurement error is very likely to be homogeneously distributed among both groups. We will adjust nutrient intake for potential confounders, including energy intake, and obtain adjusted means using generalized linear regression models (e.g. nutrient intake = intercept + b.* prostate cancer

Table 7. Variability of legume intake

Serving (1/4 cup)	
0 servings	28%
1 servings	14%
2 servings	21%
3 servings	15%
4 servings	22%
Total	100%
Mean	2.30
Median	2.00
Standard Deviation	2.16
Coefficient of variation	4.70
Range	0-20
Interquartile range	3

deaths (binary) + $b_2 \cdot \text{age}$; where b_1 is the change in nutrient for prostate cancer deaths, while holding age constant and; where b_2 is the change nutrient for every unit change age, after adjusting for prostate cancer deaths). If interactions of the diet and prostate cancer death association are present, means will be calculated stratified.

We expect to have a 90% power to detect a 0.5 differences in servings between prostate cancer cases (N=212) and non-cases (N=9,200), assuming equal variance, a mean intake of 2.2 servings (1/4 cup = 1 serving) in non-cases and an alpha of 0.05 with a 2 sided t-test. Additional calculation of power and differences are illustrated on Table 8.

The second approach will entail estimating the risk of prostate cancer deaths according to intake. Based on the distribution of the analytical cohort, the men will be categorized into quartiles of each measure of legume intake. The highest quartile will represent the highest intake and the lowest quartile will represent the referent category for each nutrient. Estimates of prostate cancer deaths will be calculated comparing each of the 3 upper quartiles to the referent category. We will use Cox proportional hazard model to estimate the relative risk and compute 95% confidence intervals. One of the key advantages of this analytic approach is the ability to examine dose response. Tests for trends will be performed by treating the quartiles of intake as continuous variables. Potential confounders will be examined and included in the model. Interactions of the dietary factors and prostate cancer death association will be examined and if deemed significant, an interaction term will be included in the model and or stratified analysis will be done. For those dietary intake variables that are correlated with energy intake, analysis will include both unadjusted and calorie adjusted dietary intake. The residual method of energy adjustment will be used¹¹⁷. This method calculates residuals for the nutrient based on a model where the dietary variable is the dependent variable and caloric intake is the independent variable. The resulting residual nutrient estimates are then used in the disease model (i.e. disease = intercept + $b_1 \cdot$ residual nutrient; where b_1 is the change in the log odds for every unit change in energy adjusted nutrient intake). If we observe that energy intake is associated with prostate cancer independent of the nutrient than the model will also include energy intake (i.e. disease = intercept + $b_1 \cdot$ residual nutrient + $b_2 \cdot$ energy; where b_1 is the change in the log odds for every unit change in energy adjusted nutrient intake, while holding energy intake constant and, where b_2 is the change in the log odds for every unit change in energy, after adjusting for nutrient intake). This method of adjustment will address the question of whether there is an association of legumes, independent of energy intake, with prostate cancer deaths and also addresses the question of whether there is an association of energy intake, independent of legume intake, with prostate cancer deaths. Using a Cox proportional Hazards model with prostate cancer mortality as the outcome and legume intake as the covariate (assuming a standard deviation of 2.2) will achieve 90% power to detect a hazards ratio of 1.12 (alpha 0.05), based on 212 cases and 9,200 non-cases.

Table 8. Power calculation for a two sample t-test on mean intake of legume

Difference	Power
.1	0.10
.2	0.26
.3	0.50
.4	0.74
.5	0.90
.6	0.98

D.4. Limitations:

Cohort studies, such as the PRHHP, usually obtain their dietary information at a single point in the adult life of the participants. One assumption in prospective studies is that diet is constant. For cohort studies conducted during the 1950's, 1960's and 1970's, and among older men this may be a reasonable assumption⁹⁹. Errors, however, can be introduced if dietary habits change over time and are not recorded in the study. A related concern is that the relevant time period for exposure to consumption of non-soy legumes in relation to prostate cancer risk has not been established either. The PRHHP collected a 24-hour recall at baseline and a food frequency questionnaire in a subsample during the second examination. The foods that the participants reported eating in 1960-1970 may not be the same reported during the baseline period. The Hispanic Health and Nutrition Examination Survey, compared eating patterns among more acculturated Puerto Ricans from the New York City metropolitan area and

those of the US general population⁵⁸. The results from this study confirmed that rice and beans, and dried beans were major contributors of energy to the Puerto Rican diet. In our cohort of older men, we believe that variations in consumption of staple foods such as beans and peas have remained somewhat constant, especially among older men and if they continued to live in Puerto Rico. The foods we are proposing to study have been readily available and consumed in Puerto Rico without major changes in the market as demonstrated in Figure 5.

Measurement errors in dietary assessment and relationships between dietary components may lead to confounding of the study results. However, certain epidemiological data linking dietary factors and cancer are somewhat consistent regardless of their method of assessment. For example, evidence consistently supports an inverse relationship between colon cancer risk and intake of vegetables and fruits. Other relationships that have been observed include whole grains, dietary fiber, and animal fat. Important risk factors not to be ignored include physical inactivity, obesity alcohol, and smoking. Although health assessment methods are not perfect, the above variables are not extremely sophisticated or complicated variables to assess. Assessments of other confounders or effect modifiers such as body mass index, smoking, and physical inactivity during the PRHHP are considered very adequate and similar to other large epidemiological studies, e.g., Framingham Study, Honolulu Heart Study, NHANES I and II Epidemiological Follow Up.

D.5. Strengths

This is a unique opportunity to assess the feasibility to establish a cohort of Hispanics to study cancer. If we can ascertain cancer mortality in this cohort, there are several exposure variables for which there is little longitudinal data and many unanswered questions. This small grant has the potential to identify off-springs for the establishment of a more complete cohort that will study gene and gene-environment interactions. Dietary data was obtained at baseline, and a food frequency was obtained in a subsample (N<2,000) during the second examination, physical activity obtained at three different examinations, and body size was obtained four different times in a span of 10 years. Smoking history was obtained at each examination, inclusive of cigarettes, pipe and cigars. Laboratory confirmed sexually transmitted disease was obtained at baseline. Moreover, at 12 year follow up, only nine of the original cohort had been lost to follow up. Additionally, the PRHHP had a rigorous quality control in data collection second to none at the time of implementation. We have access to the original files and these files can be used to re-enter some of the dietary data using more up to date nutrients tables from dietary software such as the University of Minnesota Nutritional Dietary Systems to calculate dietary fiber, vitamins and other nutrients to conduct a nested case control study using the prostate cancer cases obtained as part of this proposal. **This study is innovative in that it is a very cost-effective way to assess prospectively unanswered questions about non-soy legumes and prostate cancer risk in an established cohort of an understudied population.** In our review of the literature we found only one published article that examined the relationship of non-soy legumes with prostate cancer risk by Kolonel, et al., 2000, (reference 59). To establish a cohort of Hispanics and to follow them over the next 30 years would cost substantially more.

A very important strength of the study is the personnel involved. Dr. Crespo is well experienced in data analysis of large data bases (HHANES, NHANES III, and PRHHP) and has had experience in working with the Puerto Rico Demographic Registry, the National Death Index and the Puerto Rico Cancer Registry. Dr. Crespo received an R03 grant from NIA to conduct a cancer mortality feasibility study using the PRHHP cohort, and familiar with the strength and limitations of each of the databases to be used, especially the Puerto Rico Cancer Registry. The original primary investigator and project officer of the PRHHP are integral parts of the research team (Dr. Mario R. Garcia Palmieri and Dr. Paul Sorlie). We also include a former project officer of the NHANES I, II follow up, Framingham Study and the Jackson Heart Study (Dr. Christopher Sempos). Dr. Jo Freudenheim, is one of the foremost knowledgeable persons studying the relationship between diet and cancer. Dr. Paola Muti has extensive experience investigating diet and hormone metabolism, with breast and prostate cancer in diverse populations, and Dr. Ellen Smit has collaborated with Dr. Crespo in multiple other projects related to diet and chronic disease. Dr. McCann has a K07 to study cancer and diet, specifically phytoestrogens. Dr. Rosa Perez Perdomo, works extensively with the Puerto Rico Demographic Registry in other projects at the University of Puerto Rico, and is experienced working with participants from the PRHHP. The

research team includes an excellent and experienced group of nutritionists and epidemiologists, listed in alphabetical order: Dr. Freudenheim, Dr. McCann, Dr. Messina, Dr. Sempos, and Dr. Smit.

D.6. Timetable:

Timetable Years 01-02	Year 1 (Months)											
Tasks	1	2	3	4	5	6	7	8	9	10	11	12
Meeting of collaborators and representatives from Puerto Rico Demographic Registry (PRDR) and PR Cancer Registry (PRCR)	✓											
Finalize details of data needed to obtain cancer mortality	✓	✓										
Merge personal identifiers with data to create electronic file		✓	✓									
Submit request to the PRDR and PRCR			✓	✓								
Obtain preliminary death certificate data from PRDR and PRCR					✓	✓	✓					
Verify information received from PRDR & PRCR is what is needed					✓	✓	✓					
Verify matches with original files of PRHHP								✓	✓			
Extract data from Death Certificates (causes of death & SSN)							✓	✓	✓	✓		
Enter data on underlying and multiple causes of death & SSN								✓	✓	✓	✓	✓
	Year 2											
Meeting of collaborators to assess progress, changes in protocol, and future steps	✓											
Apply for NDI number	✓											
Obtain approval from states requiring pre-approval for use of NDI and Cancer Registries (New York, New Jersey, Pennsylvania, Connecticut, Massachusetts, Illinois, Florida)		✓										
Meeting with PRDR and PRCR to finalize data collection		✓	✓	✓	✓							
Decide on criteria for submission of multiple names of cohort for submission to NDI			✓									
Prepare electronic file to NDI with established criteria			✓									
Begin analyzing dietary analysis and other covariates				✓	✓	✓	✓					
Collect information from NDI and update cause of death					✓	✓	✓	✓	✓			
Convert final dataset on cancer incidence and mortality into SAS and merge with original cohort file								✓	✓			
Finalize assessment of cancer mortality using PRDR and NDI								✓	✓	✓		
Analyze data on legume consumption and prostate cancer									✓	✓	✓	
Prepare final report to NIH												✓

E. HUMAN SUBJECTS

Research will include human subjects although no individual will be contacted directly. All data is in the form of secondary data analyses from sources of mandatory reporting and other studies in which subject consent was obtained. No subject will be contacted as part of this proposal.

1. All individuals who have information contributing to the data sources described in the Methods section will be included. Individuals will not be identified in anyway. Any identifying information on these data sets will be kept confidential. No information is available to identify pregnant women, prisoners, or institutionalized individuals.
2. All information will be obtained from already existing databases specifically for reporting purposes. The use of this data for any other reason will have to go through the established process to request data by the organization in which it is housed.
3. The databases will be used to maintain this research consist of information that is required on all participants i.e., death certificates, cancer registry.
4. An IRB request will be submitted through the State University of New York at Buffalo.
5. There are no potential risks to the individuals included in the study. No identifying information will be released and will be kept confidential. All original documents will be kept at the original site of data collection under the statues described with the IRB specific to the project.
6. All information from any data source will be reported in aggregate.
7. Inclusion of women: This study is about prostate cancer, thus, women will not be part of the analytic sample
8. Inclusion of children: The study is based on adult men, thus, no children are included in this study
9. Inclusion of minorities: The participants in this study are ALL minorities of Hispanic ethnicity.
10. Data and safety monitoring plan: Not applicable.

F. VERTEBRATE ANIMALS

Not applicable