Obesity and Cancer in ARIC: Findings for prostate cancer and future opportunities

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Atherosclerosis Risk in Communities (ARIC) Study

- ARIC originated as a study of atherosclerosis, 1987-1989.
- ~16,000 men and women (~27% Black) from 4 field centers
  - ~4,000 participants from Washington County
- 4 consecutive clinic visits, a 5th visit completed in 2013, 6th in 2017, 7th visit underway
- Repeated, clinically evaluated anthropometric measures and associated metabolic, lipid, and inflammatory markers
- ~30 years of follow-up
- U01 – enhance the infrastructure of ARIC for cancer epidemiology research
  - Linking with state registries to capture up-to-date incidence
  - Collecting medical records to capture characterizing information
  - Obtaining consent for tissue collection

Obesity and Prostate Cancer

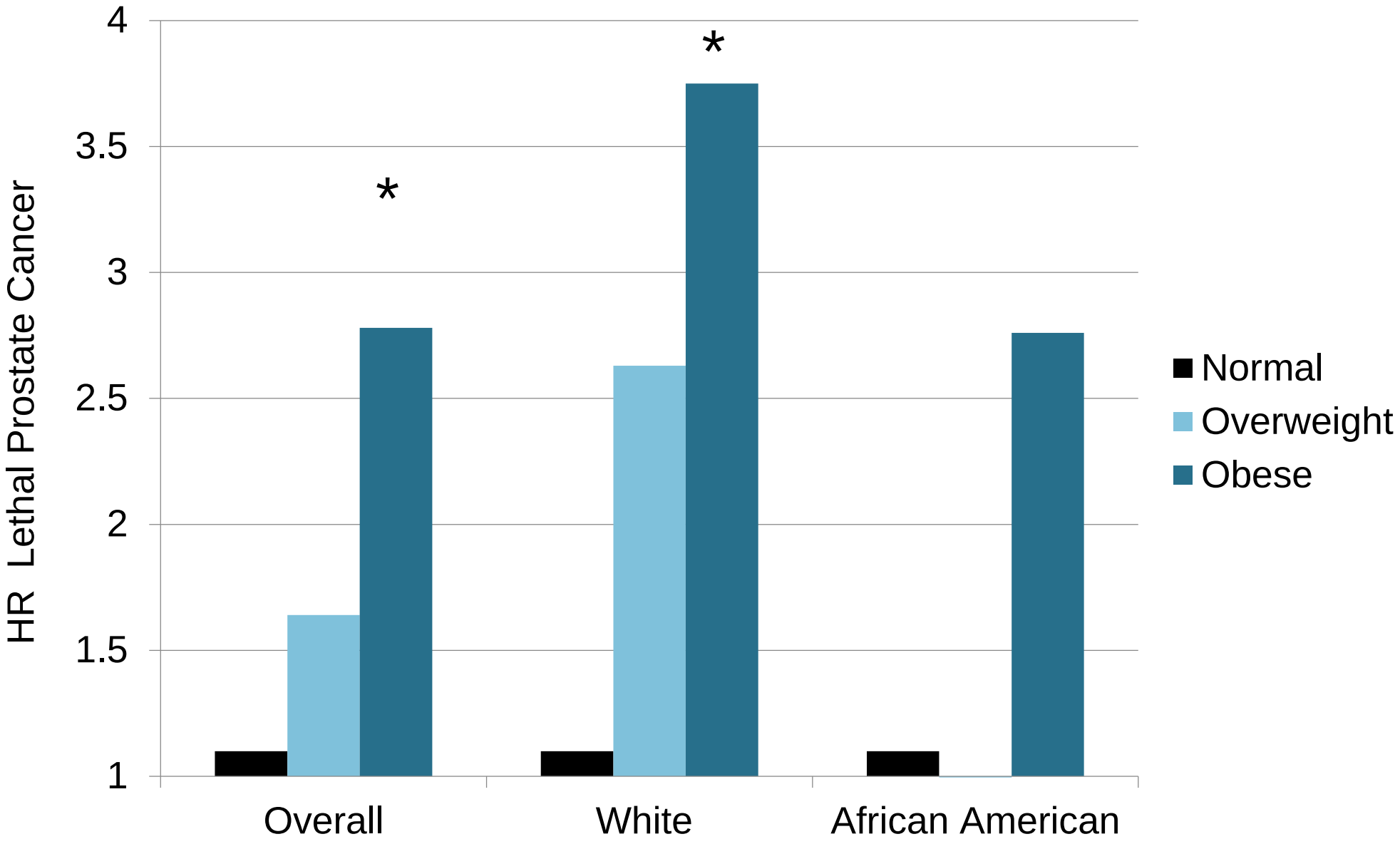
- Obesity is a risk factor for poor prostate cancer outcomes.
- Most cohorts use self-reported height and weight to calculate body mass index.
- Studies have reported inconsistent findings for the association between obesity and prostate cancer among Black men.
- We evaluated the association between obesity and prostate cancer using updated, clinically measured clinically measured body mass index, overall and stratified by race.

Clarke et al. In process.

Obesity and Lethal Prostate Cancer

- Updated measures of body mass index and waist circumference
- Cox proportional hazards regression to estimate the hazard ratios and 95% confidence intervals of lethal prostate cancer adjusting for race, age, education level, field center, and updated smoking status, waist circumference, insulin and glucose.
- Lethal prostate cancer: a first primary diagnosis of prostate cancer this has an advanced stage (T4 or N1 or M1) at diagnosis or that later leads to death from prostate cancer in a cohort of males without prostate cancer at baseline.
- 97 lethal prostate cancer cases in 120,623 person-years overall
- 59 prostate cancer deaths in 94,895 person years in white men; 38 prostate cancer deaths in 25,727 person-years among black men

Obesity and Lethal Prostate Cancer, ARIC

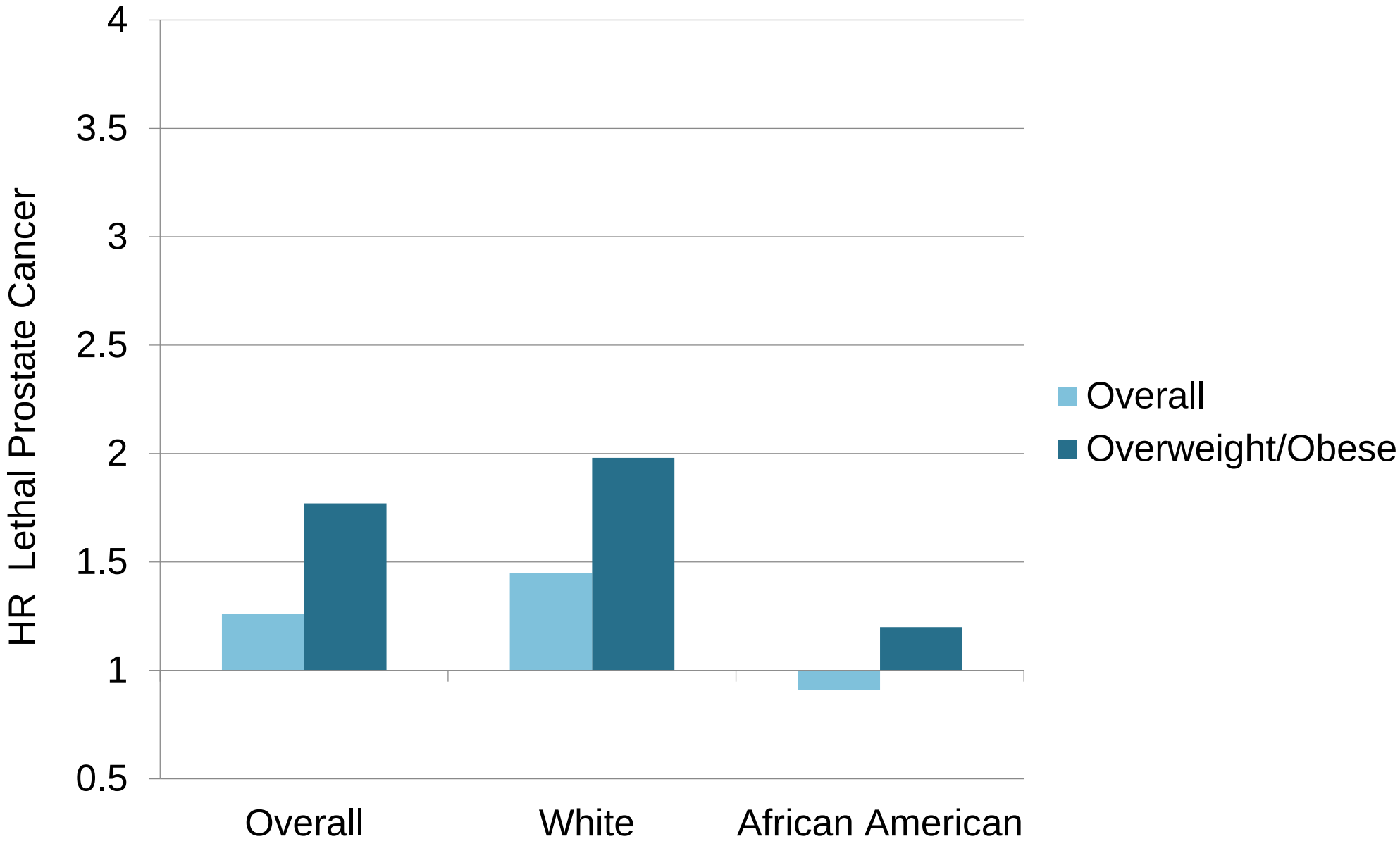


* P < 0.05

Weight Gain and Lethal Prostate Cancer

- Weight gained during mid to later life is unlikely due to increases in muscle mass
- Calculated the average annual weight change over the 12 year period between Visit 1 and Visit 4 using linear regression
- Cox proportional hazards regression to estimate the hazard ratios and 95% confidence intervals of lethal prostate cancer adjusting for race, age, education level, field center, and updated smoking status, updated waist circumference, baseline BMI.
- Overall and among men who were overweight or obese at baseline.
- Expressed as risk associated with 2 lb gain per year.

Weight Gain, 2lb/year, and Lethal Prostate Cancer, ARIC



Hyperglycemia and Prostate Cancer

- Diabetes has a consistent inverse association with prostate cancer incidence, but findings for hyperglycemia have been inconsistent.
- Less is known about the association with prostate cancer mortality.
- Differences in the measurement of glycemia (biomarker, fasting status), the selection of the reference group, and handling of those with diagnosed and undiagnosed diabetes across studies.
- There are several biomarkers of glycemia with good clinical use for diabetes: identifying those at high risk, diagnosis of diabetes, monitoring glycemic control among those with diabetes.
- Capturing glycemia for etiological prostate cancer questions is challenging

Hyperglycemia and Prostate Cancer

- Fasting glucose (FG), glycated hemoglobin (HbA1c), and glycated albumin (GA) available in all participants at visit 2. Men were classified as:
  - Low: FG ≤ 3.8* mmol/L; HbA1c ≤ 4.9%, GA ≤ 10%
  - Normal: FG 3.9 to 5.5 mmol/L; HbA1c 5.0 to 5.6%, GA 11 to 16%
  - High: FG ≥ 5.6 mmol/L; HbA1c ≥ 5.7%, GA ≥ 17%
  - Diabetes: Self-reported diagnosis; diabetes medication use

- For the joint classification, men were categorized as:
  - Low on any biomarker (n=753)
  - Normal on all 3 biomarkers (n=1,075)
  - High on any biomarker (n=2,925)
  - Diabetes (n=409)

Marrone et al. Under Review.

Hyperglycemia and Prostate Cancer

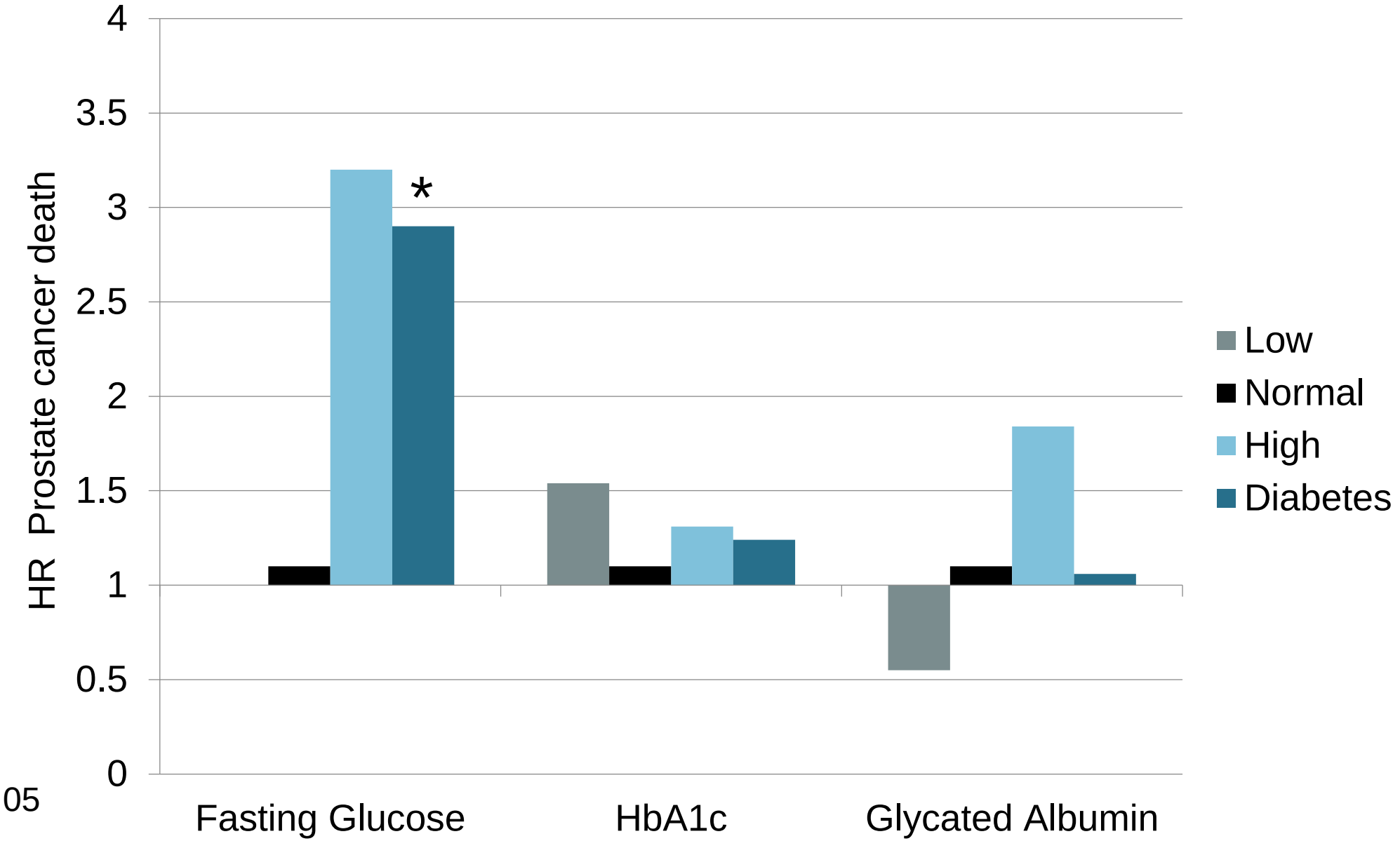
- Evaluated the association of individual biomarkers, and joint categories of biomarkers, with fatal prostate cancer
  - Fatal prostate cancer
  - Overall and by race
  - Fructosamine
  - No insulin measure at V2

- Cox proportional hazards regression to estimate the estimate hazard ratios and 95% confidence adjusting for race, age, education level, field center, updated smoking status, and updated body mass index and waist circumference.

- 64 prostate cancer deaths in 94,908 person-years

Marrone et al. Under review.

Association between each glycemia biomarker and fatal prostate cancer



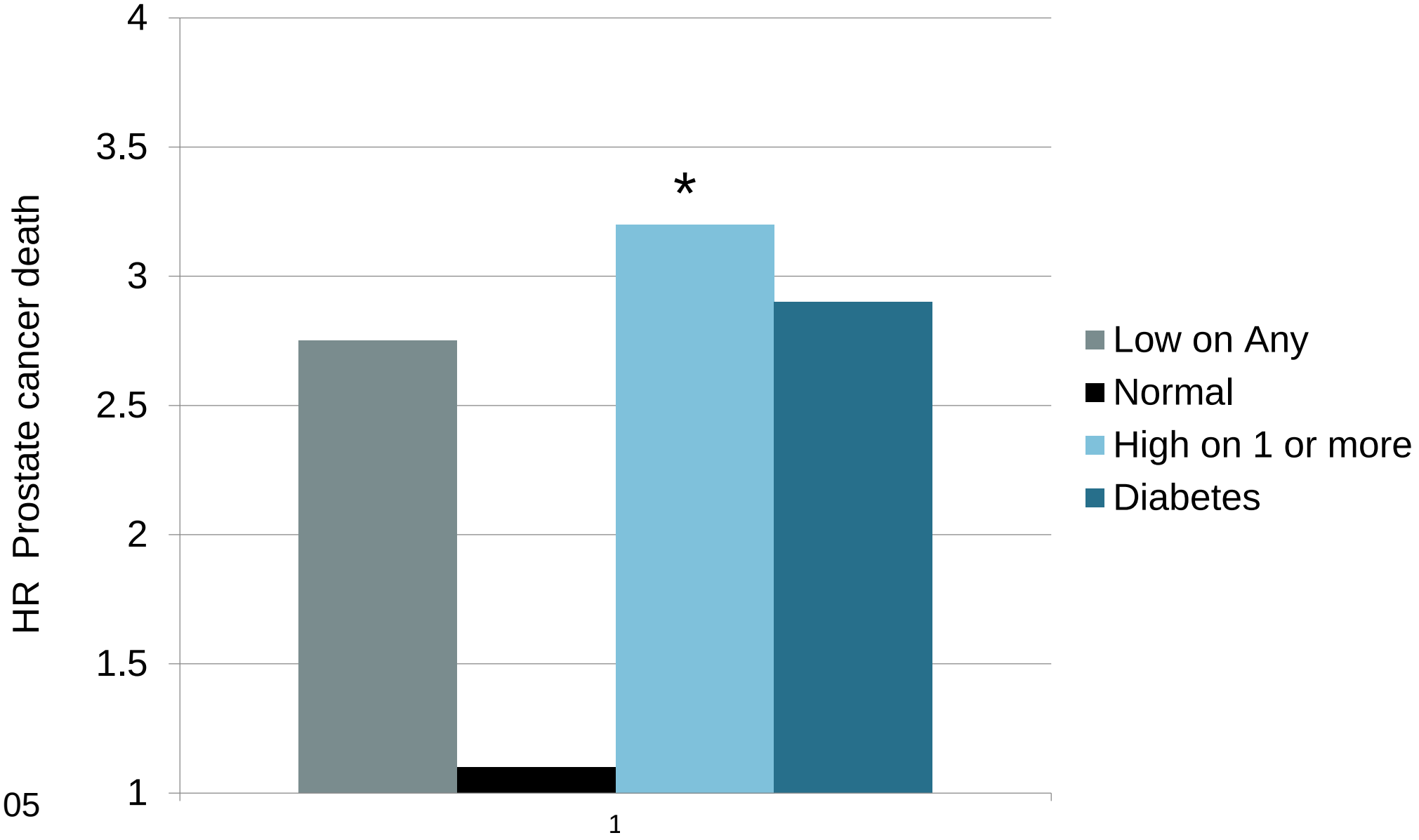
* P < 0.05

Classification of Glycemia by Multiple Biomarkers

	Normal Fasting Glucose				High Fasting Glucose		
		HbA1c				HbA1c	
	Low	Normal	High		Low	Normal	High
GA				GA			
Low	30 (1.7%)	129 (7.4%)	18 (1.0%)	Low	28 (0.9%)	123 (4.1%)	59 (2.0%)
Normal	200 (11.5%)	**1,075 (61.8 %)**	280 (16.1 %)	Normal	170 (5.6%)	1,511 (50.1 %)	1,026 (33.9 %)
High	0	4 (0.2 %)	2 (0.1)	High	0	8 (0.3 %)	**100 (3.3%)**

Marrone et al. Under review.

Association between joint categories of three glycemia biomarkers and fatal prostate cancer



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Comstock Center

- Home to the Washington County ARIC field center
- CLUE
  - CLUE I: 26,147 participants (23,951 Wash Co residents) in 1974
  - CLUE II: 32,894 participants (25,076 Wash Co residents) in 1989
  - ~30% of adult residents participated; highest participation from women, Caucasians, higher education, age 45-70
  - Baseline blood, questionnaire, FFQ (II)
  - Ongoing, detailed follow-up for cancer outcomes

Meritus Hospital

- Main treating hospital for ARIC and CLUE members
- Head pathologist supportive of JHU collaborations
- JHU IRB and Meritus IRB approved repository
  - Deceased participants – Immediate access to ALL tissue >10 years
  - Living participants – Sequester ALL tissue >10 years; access with participant permission or when participant dies
- Meritus IT linked all CLUE and ARIC participants to pathology record database (1998-2015)
- Identify specimen from cohort member, but no diagnostic information

Washington County Tissue Repository

- With the support of the Cigarette Restitution Fund, established a storage facility next to the Meritus Hospital pathology storage facility

- Meritus pathology technician sequesters and stores cohort member specimens

- 1998-2005 specimens
  - CLUE: 16,939 specimens from 9,351 participants
  - ARIC: 3,595 specimens from 1,776 participants

- Comstock center staff members retrieve and abstract pathology records for specimens in the repository

Washington County Tissue Repository

- ARIC Inventory
- 382 cancer cases
  - 78 breast, 40 prostate, 53 colorectal, 37 lung, 41 bladder
- 287 non-melanoma skin cancer cases
- 2,925 non-cancer tissues
  - 83 breast biopsies and surgeries, 45 prostate biopsies and TURPs, and 1,009 colorectal adenomas, hyperplastic polyps, and biopsies
- Specimens can be linked to existing cohort data
- Specimens can be accessed via standard cohort procedures

Conclusions

- The ARIC cohort, which includes ~4,000 Maryland residents, has been expanded for cancer epidemiology research.

- The diverse study population, repeated clinical visits, and ongoing participant contacts provides the opportunity to address research questions that may not be possible in other cohorts.

- In ARIC, we are addressing important questions around obesity and prostate cancer in White and Black men.

- ARIC is poised to address research questions around aging and cancer in the near future.

Conclusions

- With support from the CRF, we are developing a tissue repository for cohort members in Washington County
- Tissue specimens can be linked to existing cohort data
- Building the inventory for 1998-2005
  - ARIC, 1998-2005: ~11% cancer, ~8% non-melanoma skin cancer, ~81% non-cancer tissue
  - CLUE, 1998-2005: ~1800 cancer specimens
- Repository is continuously updated

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Prostate Cancer Foundation

Comstock Center

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