Expanding an Active Surveillance Cohort to Improve Survivorship for Men With Favorable Risk Prostate Cancer

NCT Number: NCT05424783

Approval Date: May 27, 2022

Statistical Analysis Methods

To evaluate the **primary objective**, assessing the association between the degree of confirmatory testing (i.e., ENACT Control, ENACT GPS Intervention vs. MAGIC GPS + MRI +/- Confirmatory PB) and completion of the AS PB, bivariate analysis will be done using Chi-squared tests. Group completion rates will be estimated using 95% confidence intervals, and group differences will be tested using pooled Z-Tests. Multivariate logistic regression models will be employed to estimate the group differences in completion using odds ratios (OR) and their confidence intervals, adjusted for potential confounders, such as race, age, NCCN risk group, marital status, insurance status, health literacy, etc. Stepwise model selection will be performed prior to the estimations of ORs. In multivariate models, indicator variables will be created for the ENACT GPS and MAGIC groups to compare to the ENACT control group.

Due to the non-randomized nature of the cohorts, propensity score methods will be used to balance the characteristics of the non-randomized three groups on factors associated with adherence to prostate biopsy based on the literature. The factors include age, comorbidities, health literacy, education, socioeconomic status (insurance, income, employment), prostate cancer family history, Gleason grade group 1 vs. 2, tumor volume, and fear of progression/side effects (MAX-PC), marital status, social support, site, and provider. We will investigate different propensity score methods, such as matching or stratifications on the propensity score, weighted models using the probabilities of groups using the propensity score, and propensity score adjustment. The balance diagnostics for the adequacy of the propensity score methods will be examined. Inferences about differences among the 3 groups from using propensity score methods will be reported.

Similar bivariate, multivariate, and propensity score methods will be employed for the analyses of the secondary objectives. Specifically, multivariate logistic regression models with propensity score methods will be employed to evaluate the group differences in biopsy reclassification, **secondary endpoint #1**. We will use multinomial logistic regression to establish the propensity scores, i.e., the probabilities of being in the 3 groups (outcome variable is ENACT GPS, MAGIC vs. ENACT Control) for each individual. The factors to be considered in the multinomial logistic regression models include age, Charlson comorbidity index, health literacy (3-8 = low literacy/9-15 = adequate literacy) , education, socioeconomic status (insurance, income, employment), first degree prostate cancer family history, Gleason grade group 1 vs. 2, tumor volume, and fear of progression/side effects (MAX-PC), marital status (married vs. other marital statuses), social support (below median perceived support), and study site (VA/County/UIC).

We will explore 3 different propensity score methods: 1) matching or stratifications on the propensity score; 2) weighted models that include the probabilities of group membership based on their propensity score; and 3) propensity score adjustment. The balance diagnostics for the adequacy of the propensity score methods will be examined using standardized bias as defined in Harder, Stuart, and Anthony (2010). Each method will have a standardized bias estimate and the method that produces the least bias will be preferred. We will report the least biased

versions that provide clinically meaningful inferences and compare to the pre-propensity score analyses.

For **secondary objective #3**, racial differences in completion rates within each group will be first described using confidence interval estimates within each group. Multivariate logistic regression models using propensity score methods will then be employed to estimate the OR for AA versus non-AA patients. Similar methods will be used to assess the racial differences in adherence (**exploratory objective #1**) and biopsy reclassification/Gleason grade group increase (**exploratory objective #2**). Interactions between race and group effects will be tested for the formal identification of race as a group effect modifier in the multivariate models.

For the identification and description of factors associated with treatment choice (**secondary objective #2**), frequencies of patient endorsed factors will be displayed and ranked. Since this data is only available for the MAGIC cohort, we do not expect to have statistical power for formal inference on the effect of top ranked factors on patient treatment choices. However, such effect will be explored using multinomial logistic regressions for treatment choices using top endorsed factors as predictors, adjusted for patient and disease related factors.

For **exploratory objective #3**, race and group effect on time-to-biopsy reclassification or Gleason grade group increase will be explored using Kaplan Meier plots, log-rank tests, and multivariate Cox proportional hazard models. Although not powered, such analyses will inform future studies using time-to-event type of endpoint for similar research.

For **exploratory objective #4**, differences in AS PB completion rates by insurance status within each group will be first described using confidence interval estimates within each group. Multivariate logistic regression models using propensity score methods will then be employed to estimate the OR for uninsured versus publicly insured versus privately insured. In ENACT, uninsured status was negatively associated with choosing active treatment instead of active surveillance, which allowed us to make insurance a binary variable; we will assess for this as well. The analysis will use similar methods to those used in secondary objective #3. Interactions between insurance status and group effects will be tested for the formal identification of insurance status as a group effect modifier in the multivariate models.

Accrual and Feasibility

Per the table below, in ENACT we recruited 200 men from the same sites and thus have two sub-cohorts already recruited. We were without a coordinator at Stroger for 6 months and did not open enrollment at Jesse Brown VA until Year 2 of ENACT. Moreover, we had a Control Group that did not receive the GPS, whereas all men will get mp-MRI and GPS in MAGIC. We believe that recruitment of 250 is feasible under this protocol, but we preserve funding for assay and mp-MRI costs. If these funds are not used, we will extend recruitment. We estimate an accrual rate of 11 participants per month for 18 months.

	Year 1				Year 2				Year 3				
	Q1	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**TOTAL**
UIC (n = 40)	4	9	9	9	7	2	-	-	-	-	-	-	40
Stroger (n = 89)	7	17	17	17	17	14	-	-	-	-	-	-	89
JBVA (n = 93)	9	18	18	18	18	12	-	-	-	-	-	-	93
Quarterly enrollment	20	44	44	44	42	28	0	0	0	0	0	0	222
Cumulative enrollment	20	64	108	152	194	222	222	222	222	222	222	222	222