VIVID

Educational **V**ideos to Address Racial Disparities in **I**mplantable Cardioverter Defibrillator Therapy **V**ia **I**nnovative **D**esigns

STUDY STATISTICAL ANALYSIS PLAN

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1. Overview

This is the statistical analysis plan (SAP) for Educational **V**ideos to Address Racial Disparities in **I**mplantable Cardioverter Defibrillator Therapy **V**ia **I**nnovative **D**esigns (**VIVID**) study. The purpose of this document is to provide an overview of the study design and study objectives, and outline the types of analyses and data presentations relevant to the study objectives. This plan is a supplement to the materials provided in the VIVID protocol (version date: February 27, 2020).

1.1 Primary Objective

VIVID is a prospective randomized controlled clinical trial that will evaluate in black patients:

- Whether a video decision support intervention compared with clinician counseling i.e. usual care (UC), will increase the proportions of patients accepting ICD implantation.

1.2 Secondary Objectives

- Whether the proportions of patients accepting ICD in concordant video group is higher relative to discordant video group.
- To evaluate whether change (i.e. pre to post intervention improvement) in patients' knowledge of SCD and ICDs in the educational video intervention group is larger compared to change in the UC group.
- To evaluate whether change in decisional conflict from baseline to one-week follow up in the educational video intervention group is different than for the UC group. This change will also be evaluated comparing the racially concordant vs. racially discordant video.
- To evaluate whether proportion of patients with an ICD implanted within 90 days of study enrollment in the educational video intervention group is higher compared to the UC group. This proportion will be also evaluated comparing the racially concordant vs. racially discordant video.
- To determine if the time (minutes) spent with the clinician is different in the intervention compared with UC arms.

1.3 Patient Eligibility and Consent

Inclusion criteria:

1) Non-hospitalized patients with ejection fraction ≤35%
2) New York Heart Association class I-III heart failure,
3) Age >21
4) Eligible for an implantable cardioverter defibrillator (ICD) for the primary prevention of sudden cardiac death
5) Self-identified race as black
6) Provision of informed consent to participate in the study.

Exclusion criteria:

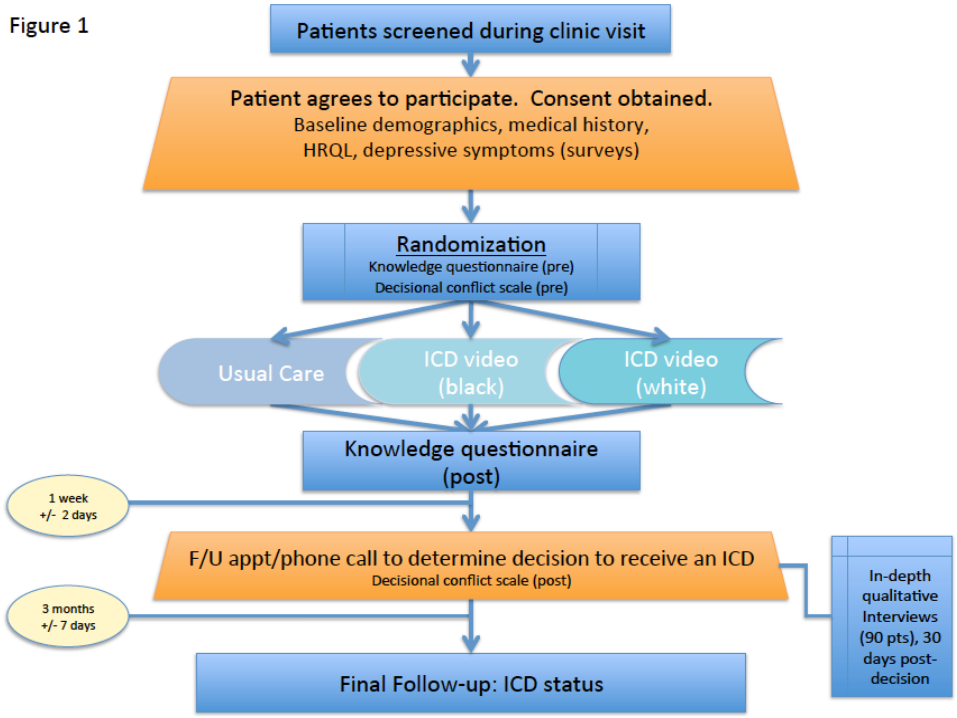
1) Life expectancy <12 months

2) Listed for Orthotopic Heart Transplantation (OHT)
3) Transplant (OHT) or OHT imminent within 12 months,
4) History of ventricular fibrillation or sustained ventricular tachycardia without reversible causes (secondary prevention indication)
5) ICD already implanted (pacemaker upgrade that met other criteria would be eligible)
6) Myocardial infarction within the last 40 days,
7) Coronary revascularization within the last 3 months,
8) Patients who are unable to understand the study procedures due to cognitive or language barriers.
9) Inpatients will be excluded from the study because decision-making processes are thought to be appreciably different in inpatients as compared with outpatients.
10) Plan a priori for subcutaneous ICD (Sub-Q ICD) (dialysis patients etc..)

1.4 Study Design

Study processes are outlined in Fig. 1.

Figure 1



The Research Assistant (RA) will screen patients for participation/eligibility, prior to the patients scheduled visit to the electrophysiology clinic. When possible an introductory letter will be sent to potential patients by mail from their provider and research team. At the electrophysiology clinic visit, the RA will approach the patient about participation in the study. At that time (baseline visit), the RA will review study procedures and begin the consenting process. The consent process will include a full explanation of the research protocol and aims, as well as use of the iPad technology for the patient to review and sign the consent. The patient will also review and sign a medical release form, to facilitate patient follow-up, if the patient is not

available via phone. In certain U.S. states, the patient will also review and sign a bill of rights statement. Following the consent and other document(s) signature process, the patient will provide baseline demographics (age, gender, payer status, household income, education, distance from health care facility, method of transportation, current employment status and a number of other social determinants), followed by administration of the Health Related Quality of Life Survey (HRQOL) SF-12v2, a depression assessment PHQ- 2, knowledge questionnaire and the decisional conflict scale (DCS), on the iPad. The patient will then be randomized on the iPad to one of the three study arms: A) video with black participants, B) video with white participants, or C) usual care (UC), i.e. clinician counseling. The patient will view a video (per randomization) or consult with their clinician to discuss the ICD procedure. After exposure to their assigned arm (video or usual care), but prior to the conclusion of the visit, patients will be administered on the iPad the same knowledge questionnaire as before the randomization. Using the iPad at the end of the visit, the RA will note the length of time the patient spent with the provider using an iPAD based timer.

Following consent and other processes on the iPad, the RA will collect baseline visit data from the patient's medical record, including medical history, heart failure classification (NYHA), etc. The baseline data will be entered into the Data Collection Form (DCF). For each patient enrolled, the RA will be responsible for submitting the iPad data and entering the baseline visit data via the DCF within a short time.

Following the baseline visit, the DCRI Outcomes Call Center interviewing team will contact patients at two intervals: one-week post intervention and 90-days post-intervention to ascertain information regarding ICD decision/implantation and to administer questionnaire(s). Medical record abstraction will be performed to determine ICD implantation among patients who cannot be reached at 90-days. For those individuals who did not receive an ICD we will seek to understand reasons for no ICD implantation utilizing chart review and telephone interview.

1.5 Sample Size Justification

Note: The primary outcome sample size computations were originally based on two co-primary comparisons (video vs. usual care and concordant vs. discordant video) with the Bonferroni adjustment for type I error by specifying two-tailed 0.025 type I error (0.025=0.05/2) for each of the two above comparisons. Due to challenges with enrollment, prior to data lock and unbinding, a single primary comparison of video vs. usual care was chosen and type I error of 0.05 will be used.

The primary outcome is proportions of patients accepting ICD implantation in video vs. usual care (UC) groups at 1 week after baseline visit. The sample size has been determined to provide a reasonable level of confidence for detecting clinically important differences in decision of ICD implantation between groups if such differences indeed exist. *In the pilot study **60%** of black patients in the video group indicated yes for ICD placement compared with **43%** in the UC arm.* We estimated a 15-20% increase in the proportion of patients indicating yes for ICD implantation in the video group could change practice patterns. Considering the above UC proportion of 43%, with total of 309 analyzable subjects with equal spread into the UC, concordant video, and discordant video groups (i.e. 103 patients in each of the three randomized groups) there is 91% power to detect 20% absolute increase in the combined video group, and 80% power to detect 17% absolute increase.

2. Statistical Analysis

All analyses will be conducted using SAS version 9.4 or higher software (SAS Institute Inc., Cary, NC) and R version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria). A p-value <0.05 will be considered as statistically significant.

2.1 Demographics and Baseline Characteristics

Frequency distribution and summary statistics for demographic and baseline variables will be presented by educational video and usual care. Continuous variables will be summarized as mean (±SD), median and inter-quartiles, categorical variables will be presented as counts and percentages.

2.2 Primary Outcome – ICD acceptance at 7 days in video vs. usual care

The proportions of patients accepting ICD implantation at 7 days between educational video intervention and usual care will be compared. The white ICD educational video (discordant) and black ICD educational video (concordant) will be combined. Pearson chi-square test will be used to test whether there is a difference in the proportion of patients accepting ICD implantation between combined video intervention group and usual care group. We do not expect small counts in light of the pilot study results but, if necessary, the Fisher Exact Test will be used. In addition to a p-value, we will provide the estimate of difference in proportions and 95% confidence interval (CI). **We will also evaluate whether the ICD acceptance treatment effect differed prior to and after introduction of the CMS regulations regarding shared decision process (February 15, 2018).**

2.3 Secondary Outcomes

Due to the secondary nature of the analyses, there will be no adjustment for type I error. However, it is important to note that all these comparisons are pre-specified and results of all the performed comparisons will be reported.

2.3.1 ICD acceptance at 7 days in the racially concordant vs. discordant video.

Pearson chi-square test will be used to test whether there is a difference in the proportion of patients accepting ICD implantation (yes vs. no/unsure) between concordant video group and discordant video group. The Fisher Exact Test will be used if necessary. In addition to a p-value, we will provide the estimate of difference in proportions and 95% confidence interval (CI).

2.3.2 Changes in knowledge score.

Outcome definition: To test the hypothesis that a patient centered educational video can improve patients' knowledge of SCD and ICDs, a 13-item questionnaire is developed to assess knowledge of SCA and ICD therapy. This short questionnaire comprises true/false statements designed to measure participants' comprehension of SCD, associated risk factors, and treatment options including ICD therapy. Possible scores vary from 0 to 13, with a higher score indicating better knowledge. To assess the change in knowledge, the same questionnaire will be administered immediately before (pre) and after (post) the exposure to the video or UC. Additionally, participants will be contacted at 7 days post enrollment, and the same questionnaire will be administered to assess retention of information.

Analysis method: To determine the effect of the video on knowledge of SCD and ICDs, two-tailed t-test (or Wilcoxon rank sum test if substantial departure from normality is noted) will be used to test whether there is a difference in the mean changes in knowledge score pre- and post-exposure between combined video group and usual care group. In addition to p-value we will provide the estimate and 95% confidence intervals of the difference in the changes in knowledge score (after minus before exposure) between combined video group and usual care group. We will also compare within groups the pre- and post-values, as well as 7-day values.

2.3.3 Changes in decisional conflict scale (DCS).

Outcome definition: We will use the DCS to measure decisional conflict. The scale measures a person's perception of the difficulty in making a decision, the extent to which they feel uncertain about treatment options, are knowledgeable about the risks and benefits of options, clear about personal values, and supported in decision making. Higher scores indicate greater decisional conflict and patients experiencing decisional conflict are more likely to change their minds, delay decisions, express regret, and fail knowledge tests. Patients will be administered the DCS **pre-** intervention at the baseline enrollment visit and **post** intervention at 7 days post enrollment. Respondents will be asked to reflect on their decision and respond to the DCS questions using a 5-point Likert scale. Responses to each statement are scored 0 (strongly agree) to 4 (strongly disagree). Total scores range from 0 to 100, with higher scores indicating greater decisional conflict.

Analysis method: **We will compare change in DCS from baseline to 7-days (post minus pre)** between the video intervention and usual care groups using independent samples t -test or Wilcoxon rank sum test if substantial departure from normality is noted. In addition to p-values, we will provide the estimate and 95% confidence intervals of the difference in DCS pre- and post-exposure for the both groups. We will also compare across treatment groups the pre- and post-exposure DCS values. The DCS change will also be compared between the racially concordant and discordant video groups.

2.3.4 Comparison of ICD implantation status at 90 days from study enrollment.

To determine the differences in implantation rates in the video intervention versus UC arms, the difference in the proportion of patients with an ICD implanted within 90 days of study enrollment between combined video intervention arm and UC arm will be compared using the Pearson chi-square test. If necessary, the Fisher Exact Test will be used. In addition to a p-value, we will provide the estimate of difference in proportions and the 95% confidence interval (CI).
We will also compare ICD acceptance at 7 days and implantation status at 90 days, overall and within randomized groups. We will use the McNemar test due to correlation of the ICD acceptance and implantation status within a patient. The above analyses will be repeated for comparison of the racially concordant and discordant video groups as well.

2.3.6 Patient-Provider time comparison.

Patient-Provider time (in minutes) will be compared between the video intervention and usual care groups, as well as between concordant and discordant video groups. We will use independent samples t -test or Wilcoxon rank sum test if substantial departure from normality is noted. In addition to p-values, we will provide the estimate and 95% confidence intervals of the patient-provider time in the groups.