Official Title:

Evaluating the Impact of Financial Navigation on Financial Catastrophe and Distress for Cancer Care: A Randomized Control Trial- COST-FIN

NCT number:

Not Yet Assigned

Document Date:

June 6, 2024

4.3 Statistical Design and Power Plan

Introduction

The aim of this study is to test the effectiveness of a financial navigation program (FNP) in reducing catastrophic health expenditure and financial distress among cancer patients in Nigeria though a two-site randomized clinical trial (RCT).

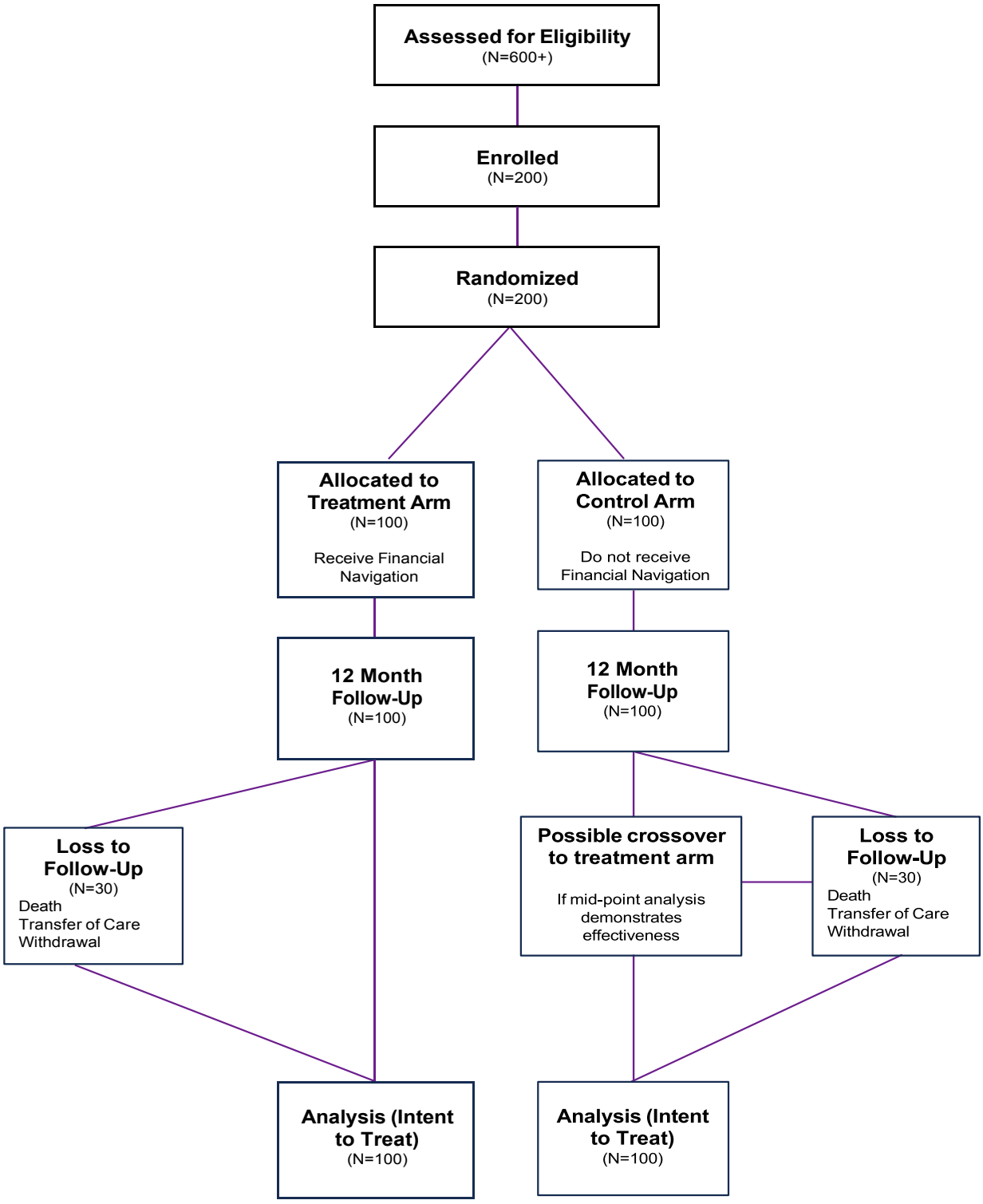
Study Design

We will conduct a prospective RCT of 200 patients with newly diagnosed breast, colon, rectal, or prostate cancer at two cancer care facilities in Nigeria. Inclusion will be limited to patients over the age of 18, those that are treatment naïve, and those that received their diagnosis within 6 weeks of presentation to the sites. It is estimated that over 400 patients between the two sites will be eligible. Recruitment will take between 9-12 months, though it is expected that this target may be reached sooner.

Eligible patients will be enrolled and randomized to an intervention arm (receive financial navigation) or the control arm (do not receive financial navigation) at a 1:1 allocation rate. We will utilize blocked randomization with stratifications for study site, cancer type, and cancer stage (early vs late). Those in the financial navigation arm will receive support through education and assistance in financial literacy, insurance enrollment, and charitable solutions to finance care.

Follow-up visits for both arms will take place at 3 months, 6 months, and 12 months. Participants in both arms will also be contacted regularly via telephone to report external costs incurred. The study design is visualized in the figure below.

Figure 1. CONSORT Flow Diagram for RCT



Outcomes

Primary Outcomes

Financial Catastrophe (FC). Following WHO and World Bank definitions, financial catastrophe will be defined as health expenditures that exceed 10% of the household income, 25% of household expenditure, or 40% of non-subsistence household expenditure[1]. To assess FC, we will sum all direct and indirect out-of-pocket (OOP) cost related to cancer treatments and represent this as a proportion of their household Income, household expenditure, and non-subsistence expenditure. To reduce bias from informative censoring, we will also calculate the risk of FC for those that stop treatment due to their inability to pay.

Financial Distress (FD). We will use the FACIT-COST tool, which is specifically designed and validated for cancer patients, to measure financial distress[2]. The questionnaire consists of 12 Likert-scale questions and has a total score range of 0-44.

Secondary Outcomes

Cost-related non-adherence. We will collect data on delays in presentation, treatment initiation, and deviation from recommended treatment via structured interview of the patients and the treating medical oncologist by the research assistant at 6 months. For each treatment modality, we will calculate the proportion of patients that were prescribed the treatment but did not pursue it. We also will capture whether it was not pursued due to cost.

Population and Subgroups

Populations

Intention-to-treat (ITT). Includes all randomized study subjects. This will be the population analyzed for financial catastrophe.

Modified Intention-to-treat (mITT). Includes all randomized study subjects that completed at least 3 months of follow-up. This will be the population analyzed financial distress as 3 months is the first timepoint after baseline that the outcome is measured.

Subgroups

Subgroups will be analyzed for both primary outcomes for the following characteristics: study site, cancer type, cancer stage, age, sex, and household wealth.

Analyses

All analyses will be done at alpha = .05 and under normal assumptions unless otherwise stated.

Primary Outcomes

Financial Catastrophe. To assess the impact of the financial navigation program on financial catastrophe, we will use two-sample tests for difference in proportions, at a one-sided alpha level of 5%. Additionally, we will perform multiple logistic regression with LASSO variable selection to identify factors associated with financial catastrophe. The pool of independent variables will include treatment arm, cancer type, cancer stage, age, sex, site, and SES.

Financial Distress. To assess for the effect of the financial navigation program on financial distress, we will perform a one-sided two-sample t-test for difference of means on the FACIT- COST scores between the treatment and control groups. For this calculation, we plan to compare scores reported at 6 months. However, if the most recent score for a participant is at 3 months, we will use that instead. Additionally, we will perform multiple linear regression with LASSO variable selection, with predictors selected among treatment arm, cancer type, cancer stage, age, sex, and SES.

Secondary Outcomes

Cost-related non-adherence. We will compare the proportions of patients that did not pursue prescribed treatments between the control and treatment groups for each treatment type.

Proportions will be calculated with 95% confidence intervals. To capture the effects of multiple factors on non-adherence we will use multivariable logistic regression modeling.

Landmark Analysis

An interim analysis will be conducted once 50% of the recruitment target (100 participants total) have completed at least 6-months of follow-up, which is estimated to occur around 1 year from study start. Applying our power calculations for 100 participants, we would need to observe a 23% difference in incidence of FC and a 5.6-point difference in FD scores between trial arms at one-sided 5% significance. If these significant differences are observed, this will be sufficient evidence for the effectiveness of the FNP and all enrolled participants in the control arm will be given access to the FNP. We would continue to collect endpoint-related data until study completion (1 year follow-up for all enrolled participants).

Sample Size and Power Calculations

The primary outcome measures for the sample size calculations are 1) financial catastrophe, and 2) financial distress.

Financial Catastrophe

Financial catastrophe (FC) will be a binary outcome for all participants. It will be defined as total health expenditure reported on the study that exceeds 10% of the participants' household income, 25% of total household expenditure, or 40% of non-subsistence expenditure, or loss- to-follow-up due to inability to pay for treatment.

To estimate rates of financial catastrophe in our control and treatment groups, we considered 1) estimated income of the participants, 2) estimated cost of cancer treatment, and 3) estimated cost savings between the two arms. Estimates for FC rate was calculated based on a normal distribution. Income was used in the estimate rather than household expenditure as this data is more prevalent in the literature.

Estimated income: Because income in Nigeria is highly variable, we repeated the sample size calculation for multiple income estimates that are based on Lagos state specifically ($6,614)[3], the average mean income across three studies of cancer patients in the southwest region ($3,469)[4-6], and the 2022 GDP per capita of Nigeria ($2,163)[7].

Estimated cost: To estimate the OOP cost of cancer care, we considered findings from two recent comprehensive studies on the cost of cancer care (all types) in Southwest Nigeria with large sample sizes ($n > 200$ in each study). The average cost between the two studies ($5,307 and $4,200) was $4,754[4,8]. The second study did not report a standard deviation, so this was pulled solely from the first study.

Estimated savings: Studies in the United States have demonstrated that financial navigation has reduced patient costs primarily through insurance enrollment. In our study, the financial navigator will aim to enroll every patient in the treatment arm in an insurance plan. Based on the services covered and the coverage limits of existing private insurance plans in Nigeria, we expect that patients will save about $2500 on average from insurance coverage and charitable funding that will be facilitated through financial navigation. This was calculated by subtracting annual premiums from annual coverage limits for cancer care. We applied this estimated $2500 in savings to the estimated cost of cancer care for patients in the treatment group. It is expected that nearly 100% of patients in the control group will not be insured based on nationwide coverage rates and data from our study sites.

Calculations for minimum sample size are done for a one-sided difference of proportions test at 95% significance and 80% power. We decided to use a one-sided test as we only expect the navigation to reduce costs.

Income estimate source	Income	CHE Threshold	Control: Est OOP (SD)	Control: Est FC rate	Treatment: Est OOP (SD)	Treatment: Est FC Rate	Minimum sample size per group
GDP per capita- Lagos State	$6,614	$661.4	$4,754 ($5,046)	79.1%	$2,254 ($5,046)	62.4%	91
SW Region Studies	$3,469	$346.9		80.9%		64.7%	93
GDP per Capita - Nigeria	$2,163	$216.3		81.6%		65.7%	95

Estimates for the rate of FC in the control group are slightly higher than our retrospective analysis on breast (74%) and colorectal patients (67%), which is expected as our retrospective data did not include indirect costs.

All enrolled participants will be included in this intent-to-treat analysis, regardless of loss-to- follow-up. Based on the sample size calculations from scenarios above, this subaim would require a minimum sample size of 100 patients per group (200 patient total).

Financial Distress

Financial distress (FD) will be a continuous outcome for all participants. The scores will be obtained from the FACIT – COST questionnaire (range 0-44).

A previous study on prostate cancer patients in Nigeria[9] found a mean (SD) score of 26.5 (10.08). Studies on the impact of financial navigation on this measure have not been done in Nigeria or sub-Saharan Africa. Studies in the United States on the impact of financial navigation on this outcome have demonstrated an average difference of 7 points but had lower baseline/control scores[10-12]. Therefore, we predict a more conservative difference in group averages at 5 points. That is, we expect the mean (SD) score to be 26.5 (10.08) in the control group and 31.5 (10.08) in the treatment group.

To detect this difference with a one-sided difference of means test at 95% confidence and 80% power, this would require a minimum sample of 50 participants per group (100 total). Assuming a 20% attrition rate prior to collection of this outcome at 3 months, the target recruitment size would be 60 participants per group (120 total).

Aim 2. Activities of the navigator and cost-benefit analysis. This analysis will be descriptive and will not include hypothesis testing.

Taking the largest sample size from the above calculations, we will aim to recruit 200 participants for this study.

Loss-to-Follow-up and Missing Data

We estimate that 20% of the enrolled patients will die from their cancer within the 1-year follow-up period based on studies on cancer survival in Nigeria[13-15]. Loss-to-follow-up for reasons other than death (stopped treatment, transfer of care, or withdrawal) is estimated to be about 10% over the 1-year study period[14-16], resulting a in a completion rate of 70%. Given the minimal risk of the intervention and the perceived benefits to the patients undergoing treatment, we expect that the drop-out rate in the intervention arm will be minimal.

Furthermore, the timeline of our outcome assessment in line with the timeline of follow-up and treatment for colorectal cancer, prostate cancer, and breast cancer, which will facilitate follow-up. However, we will design a statistical plan to address the possibility of non-response or attrition. We will first determine the proportion of missing data in the trial. We will explore attrition across trial arms as a basic step to assess bias. We will provide cross-tabulations of the proportions of missing values on all baseline characteristics, as well as on the primary outcome measures. To assess whether there are systematic differences between those lost-to-follow-up and those not – and thus whether these factors should be included in analysis – we will model missingness at follow-up as a function of baseline covariates, including the intervention.

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