Healthcare Delivery Systems: Increasing Diversity of Clinical Trials

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Number of Words: 2,218
Number of Figures and Tables: 9
Number of Equations: 0
Number of Supplements: 1
Number of References: 11

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Abstract

Healthcare systems need to adapt to changing demands quickly to incorporate new services, new delivery mechanisms for existing services, and potentially increased capacity requirements to meet patient demand. Modeling will help strategic decision-makers maximize the performance of the healthcare system. This study aims to select a test case where a specific existing healthcare delivery service does not align with patient demand, design and develop a mathematical model to address the selected health care service, conduct data analysis and recommendations to evaluate and improve changes to the service. To this end, I utilized a meta-analysis model to assess the potential of new recruitment techniques in increasing the diversity of clinical trial pools. The production of this model was created by the acquisition of clinical trial data from publicly-available resources that was filtered by the inclusion of data on race and ethnic participation in clinical trials. From this model, I was able to generate the odds ratio to determine the potential of implementation of new recruitment strategies in increasing the diversity of clinical trial participants, in comparison to standard recruitment strategies. The resulting meta-analyses determined that the majority of the comparison between the utilization of new recruitment strategies to standard practice did not increase the likelihood of success in increasing diverse participation amongst racial and ethnic minority groups.

Keywords: Healthcare delivery systems, clinical trials, increasing diversity, meta-analysis

Introduction

A health care delivery system is an organization of people, institutions, and resources that deliver health care services to meet the health needs of a target population, whether that be a single-provider practice or a large health care system[1]. Many aspects in the management of healthcare delivery systems are quantitative. Due to immense the amount of changing data within health care, healthcare systems find it difficult to identify insights that are most valuable to patients. Data-driven approaches to health outcome assessment are the core of effective healthcare system management [2]. Healthcare systems need to adapt to the changing demands of patient populations by incorporating new services, new delivery mechanisms for existing services, and potentially increasing capacity requirements to meet patient demand. Furthermore, a predictive modeling framework is needed to quickly assess how a new service delivery would improve current conditions or how many more resources (providers, staff, and rooms) are needed to handle the influx of patient demand. Mathematical modeling is an important tool for evidence synthesis and informs clinical and public health decision-making, such that these models can provide evidence to support recommendations to maximize the performance of health care systems. The aims of this capstone are to select a use case where a specific existing healthcare service of clinical trials does not align with patient demand and/or new delivery mechanisms are being considered that may help to improve patient experience and outcomes, design and develop a mathematical model to address the selected health care service, and conduct data analysis and recommendations to evaluate and improve changes to the healthcare service.

Determine the Test Case

The test case serves the purpose to determine if different features within a system are performing as expected and to confirm that the system satisfies all related standards, guidelines and customer requirements. In addition, the test case can also help reveal errors or defects within the system[3]. The test case chosen for this project was to focus on increasing diversity amongst clinical trial participants.

Clinical trials are conducted to are conducted to evaluate the safety, effectiveness, and efficacy of clinical treatments and devices. Clinical Trials are conducted through 4 phases: Preclinical, Phase I, Phase II, and Phase III[4]. The preclinical phase identifies the potential of a new product tor treatment that is likely to be safe and will work in people, demonstrated through animal testing. Phase I determines the highest thresholds of the new treatment that can be given safely without causing severe side effects. Phase II obtains data on whether the product or treatment actually works in treating a disease or indication. Finally, Phase III compares the safety and effectiveness of the new treatment against the current standard treatment.

Increasing diversity of clinical trials was primarily chosen due to underrepresentation of minority and ethnic groups in the conduction of clinical trials in the United States (US). As reported in 2011, African Americans and Hispanics comprised 12% and 16% of the US population, respectively, but only 5% and 1% of trial participants were African Americans and Hispanics, respectively. The underrepresentation of racial and ethnic minority in clinical research presents concerns due to people of different ages, races, and ethnicities may react differently to certain medical products and treatments. This shortcoming has created gaps in our understanding of diseases and conditions, preventive factors, and treatment effectiveness across populations. These gaps in knowledge can impede the quality of health care decision making, ability to counsel people on ways to reduce their risk, optimal treatment responses, and even the development of more effective medications or interventions.

The overall aim of this paper is to determine the potential of new recruitment strategies that could be implemented into clinical trials, in order to increase diverse participation amongst clinical trial pools.

Materials and Methods

For the conduction of this project, I researched through publicly available data from government databases, primarily those of ClinicalTrial.gov[5] and PubMed.gov. Through this research, I found a single zip file containing all study records available on ClinicalTrials.gov that had 403,640 studies with their own unique National Clinical Trial (NCT) number. On PubMed.gov, I searched for research papers that utilized specific, targeted recruitment techniques for clinical trials. I found three specific studies that used new recruitment techniques and had documented data to support the targeted the patient populations of those who suffer from fibromyalgia[6] and Parkinson's Disease[7]. The final study's patient population was those of cancer survivors[8]. I utilized the combination of this resources to gather data that would form the foundation for my results.

After finding the data, I conducted a literature review of possible methods of analysis. I decided to utilize the methods of meta-analysis. Meta-analysis is a research process used to merge the findings of single, independent studies, using statistical methods to calculate an overall or 'absolute' effect[9]. This type of analysis has three steps: Identification, Screening, and Included. Identification finds the studies through database searching. Screening identifies studies that meet baseline measurements. Eligibility identifies the studies that meet the eligibility criteria. Finally, Included accounts for the studies represented in the final analysis.

To conduct the statistical analysis for the meta-analysis, I utilized the odds ratio to determine the strength of the association between two events, the exposure and outcome. The exposure being that of participants receiving the new or the standard recruitment strategy. The outcome being the composition of the clinical trial pools. This ratio will allow for the comparison between the odds that the patient population was given the new recruitment strategy to the odds that the patient population was given the standard recruitment strategy (Fig. 1). If the odd ratio calculated is higher than 1, the more likely the that the relationship between the exposure and event, or outcome, is causal. Therefore, if the odds ratio is calculated to be over 1, the odds that the inclusion of new recruitment in the clinical trial design will have a higher likelihood of success of increasing diversity of participants in comparison to the standard recruitment strategy[10,11]. In addition, after the calculation of the odds ratio, the data was inputted into a forest plot.

		Event	
		Yes	No
Exposure	Yes	a	b
	No	c	d

$$\text{Odds Ratio} = \frac{\text{odds of the event in exposed group}}{\text{odds of the event in non-exposed group}}$$

$$\text{Odds Ratio} = \frac{a/b}{c/d} = \frac{ad}{bc}$$

Fig. 1. Odds Ratio. The figure demonstrates the calculation of the odds ratio. The exposure is represented by the treatment of either the new or standard recruitment strategy. The event, or outcome, is represented by the clinical trial composition.

Results

Characteristics of Studies included in Analysis

My search results for clinical trial data yielded 404, 640 studies. The studies were screened to determine the number of studies that had an overall status of completion, this yielded 216,726 studies. The studies were then processed to determine which studies were processed without error, this yielded 216, 618. The studies sought for retrieval that reported baseline measurements as expected yielded 44,303. The eligibility criteria determined that 18 studies met the criteria for inclusion (Fig. 2).

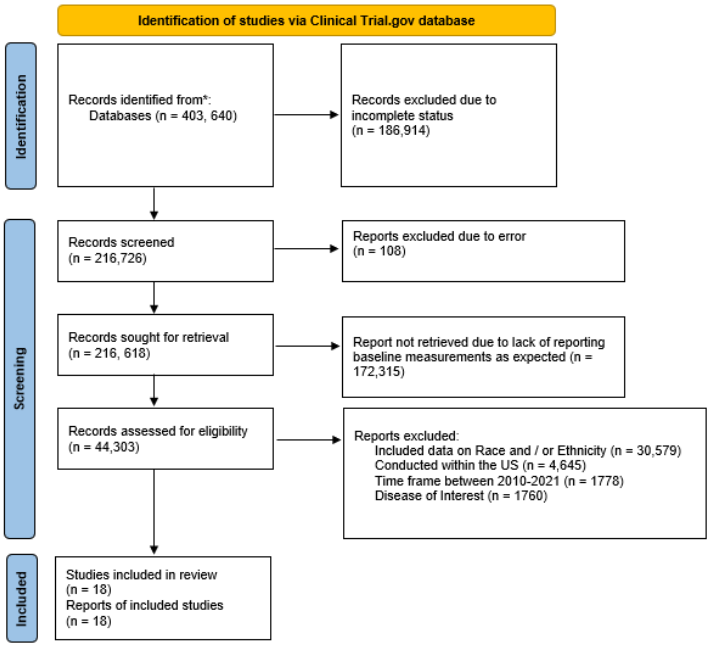

Fig. 2. PRISMA flow diagram of records/studies included at each stage of meta-analysis. The figure demonstrates the process of meta-analysis for determining which studies, acquired from ClinicalTrial.gov, would be utilized for the statistical analysis.

Table 1 shows the detailed characteristics of the included studies from PubMed that will be utilized for comparison for the clinical trial pool that received the new recruitment strategy. The 18 studies from ClinicalTrial.gov were utilized as the clinical trial pool that received the standard recruitment strategy. Supplemental Table 1 shows the detailed characteristics of the included studies from ClinicalTrials.gov that were determined in Figure 2. According to ClinicalTrial.gov, ethnicity data relates only to those who categorize themselves as Hispanic or Not-Hispanic. In terms of race, ClinicalTrial.gov had the categories of American Indian/ Alaska Native, Asian, Native Hawaiian or Other Pacific, Black or African American, White, and More than one race. However, based on the parameters of the racial and ethnic breakdown of the clinical pools, some races were added together to represent the Non-White participants. This was completely dependent on the racial and ethnic groups documented in the data for the PubMed studies (Table 1).

Table 1: Contextual and Clinical Trial Characteristics of PubMed Studies

Study	Intervention	Patient Population	Recruitment Technique	Participants
Park et al, 2021	Evaluating effective recruitment strategies in an exercise trial	Fibromyalgia	Web-based advertisements	Total: 16 White: 8 Black: 4 Other:4
Dobkin et al, 2020	Evaluating novel designs for recruitment and retention	Parkinson's Disease	Targeted Ad Campaigns through Facebook and Google	Total: 4689 Non-White: 199 Hispanic: 231
Arnobit et al, 2021	Exploring Online and Face to Face Recruitment Strategies	Cancer Survivor	Web-based (email, social media)	Total: 77 White: 56 Non-White: 21

Table 1. Contextual and clinical trial characteristics of studies included in the meta-analysis of PubMed studies. This table displays the name, intervention method of the study, target patient population, recruitment strategy, and the racial and ethnic composition of the clinical trials. These studies will be utilized as the data for the new recruitment strategy in the meta-analysis

Main Meta-analysis

I separated out the studies based on the population and/ or disease of interest. Then, I proceeded to calculate the odds ratio. I pooled the data and conducted the following analysis: the odds ratio of Black and White participants of fibromyalgia studies (Fig. 3 and Fig 4), the odds ratio of Non-White and Hispanic of Parkinson's Disease studies (Fig. 5 and Fig.6), and the odd ratio of Non-White participants of Cancer Survivor studies (Fig.7). The 95% confidence intervals (CI) were calculated as well. Finally, the total odd ratio was calculated by adding the total number of participants exposed to the new recruitment strategy and the standard recruitment strategy. After conducting the analysis on the five sets of data, I found that the majority of the studies (80%) concluded that the intervention of new recruitment strategies did not signficantly increase the odds of increasing diverse participation amongst racial and ethnic minority groups in comparison to the standard recruitment strategies and were found to be statistically significance (alpha = 0.05) (Table 2). The one data set that did not produce that result was the odds ratio calculated for the Non-White participants who received the new recruitment strategy of the Arnobilt et al, 2021 (Table 1). The odd ratio was reported over one, however the p-value statistic returned a value greater than alpha, therefore this relationship was determined to be statistically insignificant (Table 2).

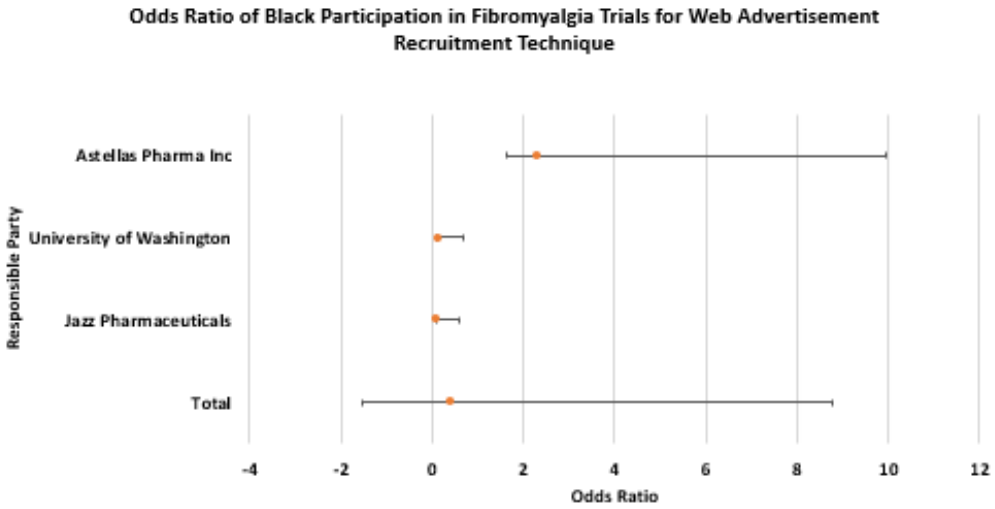

Fig. 3. Odds Ratio of Black Participation in Fibromyalgia Trials for Web Advertisement Recruitment Technique. This figure demonstrates the odds ratio between the Black participants in the standard and recruitment trials. The total odds ratio of 0.402, indicating that group that received the new recruitment strategy has odds 0.402 times lower compared to the standard recruitment group in terms of the success of increasing diversity of participants.

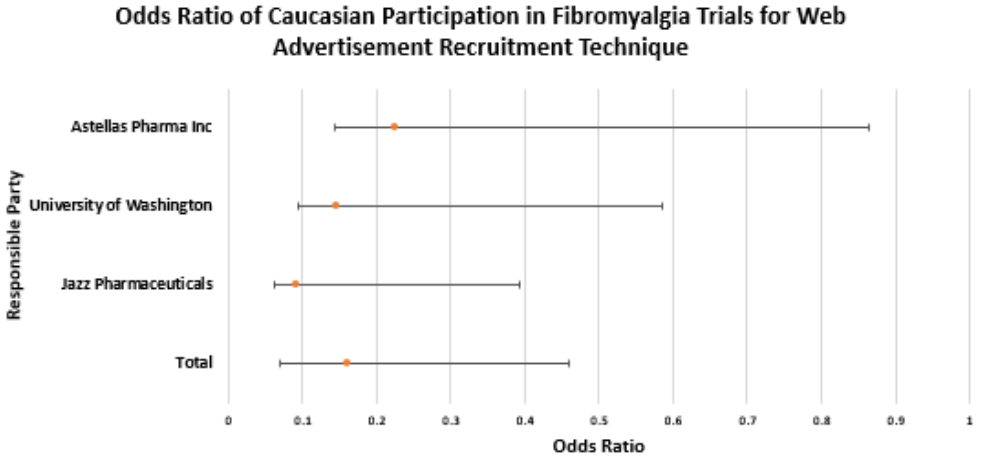

Fig. 4. Odds Ratio of Caucasian Participation in Fibromyalgia Trials for Web Advertisement Recruitment Technique. This figure demonstrates the odds ratio between the Caucasian participants in the standard and recruitment trials. The total odds ratio of 0.160, indicating that group that received the new recruitment strategy has odds 0.160 times lower compared to the standard recruitment group in terms of the success of increasing diversity of participants.

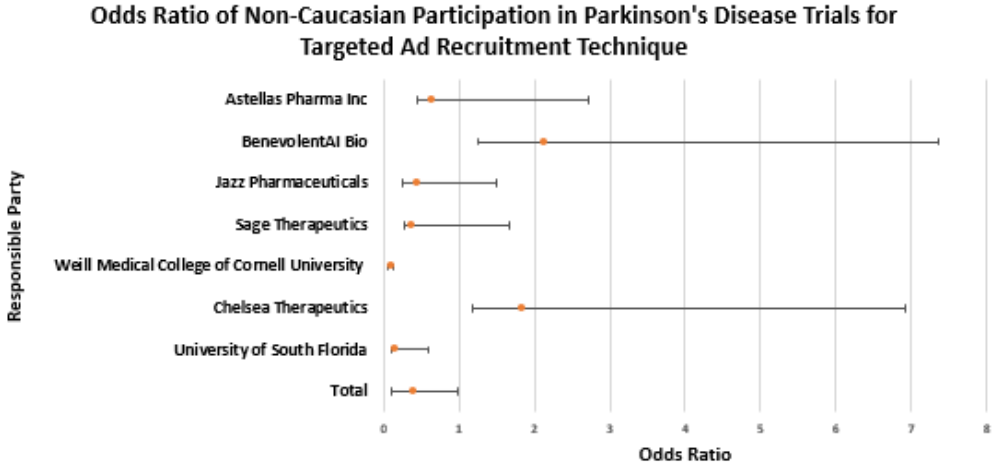

Fig. 5. Odds Ratio of Non-Caucasian Participation in Parkinson's Disease Trials for Targeted Ad Recruitment Technique. This figure demonstrates the odds ratio between the non-Caucasian participants in the standard and recruitment trials. The total odds ratio of 0.407, indicating that group that received the new recruitment strategy has odds 0.407 times lower compared to the standard recruitment group in terms of the success of increasing diversity of participants.

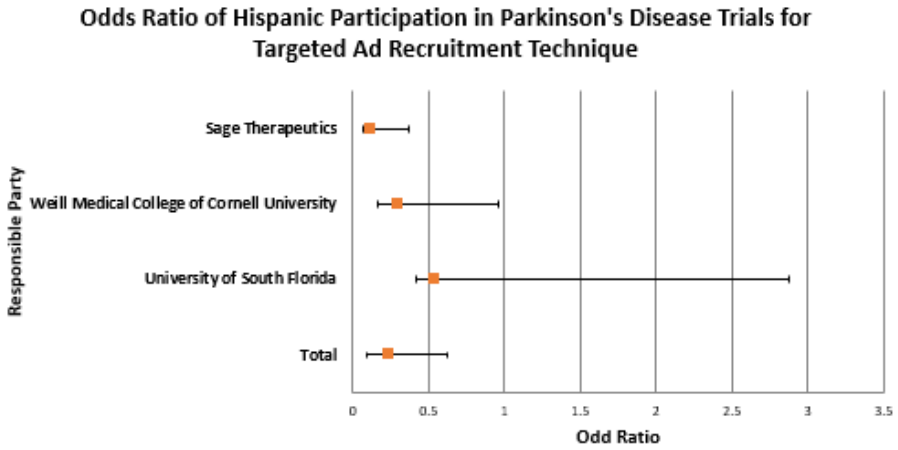

Fig. 6. Odds Ratio of Hispanic Participation in Parkinson's Disease Trials for Targeted Ad Recruitment Technique. This figure demonstrates the odds ratio between the non-Caucasian participants in the standard and recruitment trials. The total odds ratio of 0.233, indicating that group that received the new recruitment strategy has odds 0.233 times lower compared to the standard recruitment group in terms of the success of increasing diversity of participants.

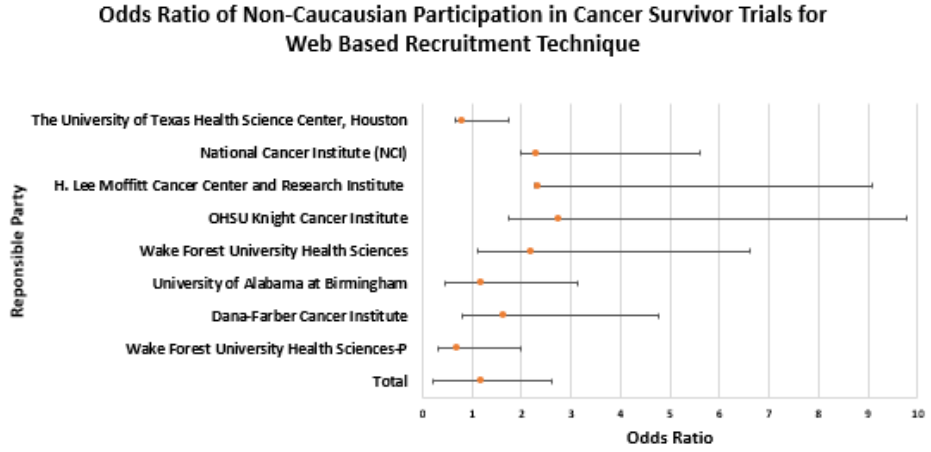

Fig. 7. Odds Ratio of Non-Caucasian Participation in Cancer Survivor Trials for Web-Based Recruitment Technique. This figure demonstrates the odds ratio between the non-Caucasian participants in the standard and recruitment trials. The total odds ratio of 1.180, indicating that group that received the new recruitment strategy has odds 1.180 times higher compared to the standard recruitment group in terms of the success of increasing diversity of participants.

Disease	Demographics	Odds Ratio	Low 95% CI	High 95% CI	P- value
Fibromyalgia	Black	0.402	1.93	8.36	0.0000999
Fibromyalgia	Caucasian	0.160	0.09	0.3	0
Parkinson's Disease	Non-Caucasian	0.407	0.29	0.57	0
Parkinson's Disease	Hispanic/ Latino	0.233	0.14	0.39	0
Cancer	Non-Caucasian	1.180	0.96	1.44	0.06

Table 3. The average results of the total odds ratios between the new recruitment strategy and the standard recruitment strategy in increasing the likelihood of success in increasing the diversity of clinical trial pool. This table displays the results of the average of all the data sets. 80% of the data produced an odd ratio of below one, indicating that the implementation of the new recruitment strategy has a lower chance of success of increasing clinical trial diversity, in comparison to the standard recruitment strategy. These conclusions were determined to be statistically significant. One data set did produce an odds ratio higher than one, indicating that the implementation of the new recruitment strategy has a higher chance of success of increasing clinical trial diversity, in comparison to the standard recruitment strategy. However, this conclusion was determined to be statistically insignificant.

Discussion

As a result of this project, I was able to met the aims of the project, such that I was able to determine a test case, design and develop a mathematical model, and perform data analysis.

The meta-analysis identified potential new recruitment strategies that could be implemented into clinical trial design, in order to decrease the diversity of clinical trial participant pools. However, the introduction of the new recruitment strategy across the majority of the trials demonstrated that it lowered chances of success at increasing the diversity of clinical trials. The trials that demonstrated this finding were found to be statistically significant. Therefore, the study determined that the implementation of these new recruitment strategies would not increase diverse participation. This may be indicative of different recruitment strategies being more effective across specific racial and ethnic minority groups.

Limitations

The most pervasive limitation was the lack of data availability. Initially, it was difficult to find studies that evaluated and documented data on their findings of the use of new recruitment strategies. Most of the literature that I initially found on new recruitment strategies was in the format of a review nature and did not include specific documentation of data, however they did highlight the potential for the strategies to increase diversity in the composition of clinical trials. In addition, I found three documented recruitment strategies with supporting data (PubMed), therefore it limited the racial and ethnic minority groups to the racial and ethnic minority groups included in new recruitment trials. In addition, the limited sample size has a high change of having a lower statistical power. Therefore, it would be difficult to determine conclusive results in terms of recruitment strategies.

Future

For future iterations of this work, I would enhance this model by incorporating that factors that relate to the reasons why those of racial and ethnic minority groups do not participate in clinical trial conduction. In addition, I would target studies that provide specific data. In addition, I would aim to develop an enhance estimation tool to determine the what the composition of the clinical trials pool would be expected given the inclusion of the new recruitment strategies and ways to reduce barriers to racial and ethnic minority participation in clinical trial conduction. Furthermore, I would want to incorporate other factors, such as age and sex, in to the model, in order to determine if the new recruitment strategies have the potential of increasing the diversity of those factors. In addition, I would expand the model to encompass retention rates, since retention is a contributing factor to the time frame of clinical trial conduction.

End Matter

Author Contributions and Notes

Patricia Edouard collected, filtered, and analyzed the data for conduction of this project. In addition, I wrote the paper

The author declares no conflict of interest.

Acknowledgments

A special thank you to my advisor, Dr. Matt Henchey, from the MITRE Corporation

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Supplemental Figure

Table 2: Contextual and Clinical trial Characteristics of Clinical Trial. Gov Studies

National Clinical Trial Identifier (NCT)	Title of Study	Study Sponsor	Population	Number of Participants
NCT00803023	Safety and Tolerability Study Comparing Sodium Oxybate Given as an Oral Solution to a Single-blinded Combination of Oral Tablets Plus Oral Solution in Subjects With Fibromyalgia	Jazz Pharmaceuticals	Fibromyalgia	Total: 129, White: 118, Black: 5, Other: 6
NCT01598753	Combined Behavioral and Analgesic Trial for Fibromyalgia	University of Washington	Fibromyalgia	Total: 134, White: 117, Black: 6, Other: 11
NCT03056690	A Study to Assess the Analgesic Efficacy and Safety of ASP0819 in Patients With Fibromyalgia	Astellas Pharma Inc	Fibromyalgia	Total: 186, White: 152, Black: 27, Other: 7
NCT01018264	Solifenacin Succinate (VESIcare) for the Treatment of Overactive Bladder in Parkinson's Disease	University of South Florida	Parkinson's Disease	Total: 23, Hispanic: 2, Non-Hispanic: 21, White: 18, Non-White: 5
NCT01176240	A Two-Part Study (306B) to Assess Droxidopa in Treatment of NOH in Patients With Parkinson's Disease	Chelsea Therapeutics	Parkinson's Disease	Total: 171, White: 167, Non-White: 4
NCT01470027	N-Acetylcysteine for Neuroprotection in Parkinson's Disease	Weill Medical College	Parkinson's Disease	Total: 47, Hispanic: 7, Non-Hispanic: 40, White: 33, Non-White: 14
NCT03000569	A Study to Evaluate SAGE-217 in Participants With Parkinson's Disease	Sage Therapeutics	Parkinson's Disease	Total: 29, Hispanic: 9, Non-Hispanic: 20 White: 26, Non-White: 3
NCT03037203	A 4-Week Study of the Safety, Efficacy, and Pharmacokinetics of JZP-110 [(R)-2-amino-3-phenylpropylcarbamate Hydrochloride] in Subjects With Parkinson's Disease and Excessive Sleepiness	Jazz Pharmaceuticals	Parkinson's Disease	Total: 66, White: 60, Non-White: 6
NCT03194217	BEN-2001 in Parkinson Disease Patients With Excessive Daytime Sleepiness	BenevolentAI Bio	Parkinson's Disease	Total: 244, White: 239, Non-White: 5
NCT03482882	Safety and Efficacy of Pimavanserin in Adults With Parkinson's Disease and Depression	Astellas Pharma Inc	Parkinson's Disease	Total: 47, White: 43, Non-White: 3
NCT01105130	L-Arginine Supplementation With or Without Enzyme Inhibitors Treating Erectile Function of Prostate Cancer Survivors	Wake Forest U	Cancer Survivor	Total: 140, White: 91, Non-White: 49
NCT01340300	Exercise and Metformin in Colorectal and Breast Cancer Survivors	Dana Forber Cancer Institute	Cancer Survivor	Total:139, White: 113, Non-White: 26
NCT01492582	Vaccine Therapy in Preventing Human Papillomavirus Infection in Younger Cancer Survivors	University of Alabama at Birmingham	Cancer Survivor	Total:1499, White: 1134, Non-White: 365
NCT01535040	Memantine Hydrochloride in Helping Cancer Survivors Stop Smoking	Wake Forest University	Cancer Survivor	Total: 130, White: 111, Non-White: 19
NCT01539317	Therapy to Prevent Sexual Pain in Breast Cancer Survivors	OHSU Knight Cancer Institute	Cancer Survivor	Total: 50, White: 44, Non-White: 6
NCT01823991	COGNUTRIN in Breast Cancer Survivors	H. Lee Moffitt Cancer Center and Research Institute	Cancer Survivor	Total:36, White: 31, Non-White: 5
NCT01849250	Study of Docosahexaenoic Acid (DHA) in Triple Negative Breast Cancer Survivors	National Cancer Institute	Cancer Survivor	Total:64, White: 55, Non-White: 9
NCT02509156	Stem Cell Injection in Cancer Survivors	The University of Texas Health Science Center, Houston	Cancer Survivor	Total: 31, White: 21, Non-White: 10