

Data-Driven Participant Recruitment: Findings from the Alzheimer's Disease Neuroimaging Initiative 3

C. Barger³, J. Fockler^{1,2}, W. Kwang^{1,2}, S. Moore³, D. Flenniken^{1,2}, A. Ulbricht^{1,2}, P. Aisen³, M.W. Weiner^{1,2} on behalf of the Alzheimer's Disease Neuroimaging Initiative

1. Center for Imaging of Neurodegenerative Diseases, San Francisco Veteran's Administration Medical Center, San Francisco, CA, USA; 2. University of California San Francisco (UCSF) Department of Radiology and Biomedical Imaging, San Francisco, CA, USA; 3. Alzheimer's Therapeutic Research Institute, University of Southern California (USC) San Diego, CA, USA

Corresponding Author: Charissa Barger, Alzheimer's Therapeutic Research Institute, University of Southern California (USC) San Diego, CA, USA, charissa.barger@synoeshealth.com, 213-253-8387

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Abstract

BACKGROUND: Effective and measurable participant recruitment methods are urgently needed for clinical studies in Alzheimer's disease.

OBJECTIVES: To develop methods for measuring recruitment tactics and evaluating effectiveness.

METHODS: Recruitment tactics for the Alzheimer's Disease Neuroimaging Initiative (ADNI3) were measured using web and phone analytics, campaign metrics and survey responses.

RESULTS: A total of 462 new participants were enrolled into ADNI3 through recruitment efforts. We collected metrics on recruitment activities including 82,003 unique visitors to the recruitment website and 3,335 calls to study phone numbers. The recruitment sources that produced the most screening and enrollment included online advertisements, local radio and newspaper coverage and emails and referrals from registries.

CONCLUSIONS: Analysis of recruitment activity obtained through tracking methods provided some insight for effective recruitment. ADNI3 can serve as an example of how a data-driven approach to centralized participant recruitment can be utilized to facilitate clinical research.

Key words: Clinical trials, recruitment, Alzheimer's disease.

Introduction

In the United States, an estimated 5.8 million people are currently living with Alzheimer's disease (AD) (1) and this is projected to increase to 13.8 million by 2050 (2). AD and other dementias are estimated to cost the United States \$290 billion in healthcare, long-term care and hospice and that could reach as much as \$1.1 trillion by 2050 (1). There is an increasing need of effective treatments and preventative measures for AD as the prevalence and overall costs of AD care will continue to dramatically rise within the next 30 years. However, a major obstacle in clinical research progress and developing new AD treatments is the identification and enrollment of participants in clinical research (3). Because clinical trials commonly experience high screen failure rates, it is crucial to reach as many potential participants

as possible and then implement more innovative ways to pre-screen a large volume of interested individuals. Difficulty in participant recruitment commonly results in early termination of clinical trials (4). In contrast, this issue can also lead to extending the duration of clinical trials, which in turn increases costs and delays study progress (3). Although participant recruitment has been primarily conducted at the research site-level, as studies become more competitive for participants, there is a greater need to expand efforts and provide referrals to research sites through more centralized activities, including utilizing online advertising, media coverage and web-based registries (4-8), that can reach a larger number of potential participants across multiple research sites.

Launched in 2004, the Alzheimer's Disease Neuroimaging Initiative (ADNI), funded by the National Institutes of Health, is a longitudinal observational study aimed at discovering, optimizing, standardizing and validating clinical trial measures and biomarkers used in ongoing AD research. Participation in ADNI includes clinical/cognitive, imaging, biomarker and genetic assessments. It is now in its third phase of trials termed ADNI3, which is a continuation of ADNI, ADNI-GO and ADNI2. ADNI3's cohort includes both new participants and participants retained from previous iterations of ADNI. Recruitment began September 2016 and is currently ongoing with aims to enroll up to 1,200 new participants across 59 research sites in the United States and Canada. Participants are ages 55 to 90 and enrolled across three cohorts: cognitively normal, mild cognitive impairment and mild AD dementia.

To address the need to expand recruitment efforts to targeted populations, the ADNI3's Coordinating Center utilized a range of recruitment activities that can be linked to measurable outcomes. The Coordinating Center collected recruitment metrics, which provided some preliminary insights on which methods were more effective at reaching a greater number of potential participants. By using a multi-faceted recruitment plan, ADNI3 can serve as an example of how a data-driven

approach to centralized participant recruitment can be utilized to facilitate clinical research.

Methods

Recruitment Activities

On behalf of ADNI3, the Coordinating Center managed recruitment activities to connect potential participants directly with local research sites. These activities included: national newspaper and radio coverage; local TV and newspaper coverage; and search engine, website, social media and newspaper advertisements.

Additional recruitment activities were provided by internet-based registries including: the National Institute on Aging's Alzheimer's and related Dementias Education and Referral Center (ADEAR); Banner Alzheimer's Institute's Alzheimer's Prevention Registry (APR); and University of California, San Francisco's (UCSF) Brain Health Registry (BHR). These registries aim to provide a pool of screened potential participants who have provided information including contact information and demographics and have already expressed a willingness to participate in research (6, 9). The recruitment activities included: online study listings (provided by APR, ADEAR, ClinicalTrials.gov), emails to their existing list of registrants (provided by APR and BHR) and direct referrals to research sites (provided by BHR). Direct BHR referrals applied exclusion/inclusion criteria to their pool of over 65,000 participants nationally to pre-screen and refer them to local research sites (9). The selected BHR participants were provided research site contact information and a referral code to be brought with them to their screening visit.

Website and Data Collection

Most digital activities funneled visitors to the ADNI3 recruitment website, ADNI3.org, which was developed as a collaboration between the Alzheimer's Therapeutic Research Institute (ATRI) at the University of Southern California and the Brain Health Registry (BHR) at UCSF.

The website, powered by BHR, provided education about ADNI3 with multiple links to a pre-screener questionnaire to guide visitors to complete it as the preferred call to action. The questionnaire asked study-specific questions to determine eligibility. Those who were potentially eligible were prompted to enter their contact information in a sign up form, which connected referrals to a local research site to enroll. The website also included a "research site finder" map with the ability to cater to the needs of individual research sites by pausing or stopping referrals from the website.

The website captured data using the methods listed below to track visitors during the recruitment process:

1. **Trackable Links:** Custom URLs were used to identify how web visitors arrived at the recruitment website. These were placed in all digital communication, advertisements, emails, articles and social media posts.

2. **Sign Up Form:** This web-based form collected contact information, birth year and zip codes from visitors to determine if there was a research site enrolling in their area. They were then provided with a referral code and the research sites' contact information immediately or once their local site began enrolling.

3. **Phone Numbers:** Unique phone numbers were used to track phone calls to research sites from recruitment campaigns and the recruitment website. Masked local phone numbers, that rang through to the research site's phone number, enabled tracking of how many calls were placed from the recruitment website. Also, an interactive voice response (IVR) system automatically forwarded calls for interested participants to their local site after providing their zip code. The system then logged any activity and provided data on what calls were placed and where they were forwarded. Additionally, the phone number a participant called was used as a referral code for measuring conversion into the study.

4. **Contact Us Form:** This web-based form allowed visitors to provide their contact information for a specific research site. This was provided to the site along with a referral code to track them into enrollment.

Additional information was collected and recorded in an electronic case report form at the in-person screening visit to determine where the participant heard about the study. Once the participant was in clinic, they were asked questions about how they heard about the study and whether they had a referral code in the screening questionnaire. Questions include: "How did you hear about the study?" and "From whom did you hear about the study?". If the participant had a referral code, the site staff was responsible for entering the specific referral code into the online form. Any additional comments or specifics were collected in qualitative responses.

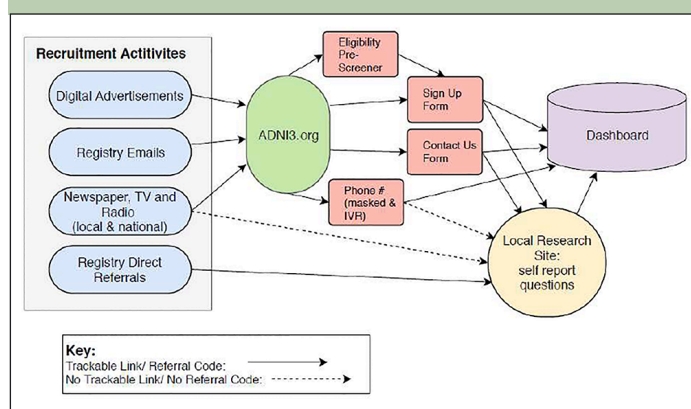
Data Analysis

All data was reported visually through an active dashboard, allowing all recruitment metrics described above to be seen in real-time, in one place. The dashboard, managed by the BHR, included, but was not limited to: the number of sign up forms completed and what site the interested participant was referred to, how many calls were placed from the recruitment website and how many consented study participants provided referral codes. Additionally, recruitment campaigns that could not have specific data attached, like radio interviews, could be filtered by date to show website activity within a specified timeframe. Google Analytics Dashboards were also used to view website traffic data and duration of web sessions. Figure 1 shows the flow of recruitment activities through the website to study enrollment with

data displayed by the dashboard.

The dashboards were reviewed regularly to assess current recruitment activities and make informed decisions on recruitment tactics. We assessed increases in website traffic, use of trackable links, website activities completed and phone call volume to gauge effectiveness of recruitment activities compared to daily averages.

Figure 1. ADNI3 referral flow by recruitment Activities



Results

Enrollment Summary

As of August 2019, 892 individuals enrolled into ADNI3, including 430 participants that continued from ADNI2 and 462 newly enrolled participants. The average age of new participants was 71; 13% were minority participants, defined as either Latino/Hispanic or non-White; 54% were female; and the average education was 16.6 years.

Data collected at the screening visits showed that approximately 52% of new participants were enrolled through site-driven activities, such as physician referrals, community outreach events and patient database outreach. The remaining 48% of new participants were enrolled through recruitment activities managed by the Coordinating Center, which will be focused on for this paper.

Recruitment Efforts

Figure 2 summarizes the recruitment activities utilized by the Coordinating Center and subsequent data collected. As a result of central recruitment efforts, there have been 82,003 unique visitors to ADNI3.org, 2,189 phone calls to the IVR phone number and 1,146 phone calls through local masked phone numbers. Of the visitors to the website, 15.5% engaged in some form of website activity by completing the pre-screener, contact us form, sign up form, or calling a site directly using the masked phone number. In total 12,728 referrals

were provided to research sites through the recruitment website.

Of the 82,003 website visitors, 56,170 (68.5%) can be linked directly to the source of recruitment through trackable links. The majority of the website visitors tracked by links came from Facebook advertisements with 40,833 tracked users (72.7%). The trackable links identified only two individuals who had referral codes which were reported to site staff at the screening visit. In contrast, APR had only 2,319 tracked users (4.13%) but ultimately led to 13 referral codes reported at the screening visit.

764 in-person questionnaires were completed at the screening visit to collect information on where participants heard about the study. These included 132 referral codes but no local phone number referral codes. Of the questionnaires completed, several included conflicting information about the source of recruitment. For example, of the 206 individuals that selected a registry as the source from which they heard about the study, 13% indicated a conflicting source in how they heard about the study (5 from advertising, 2 from media coverage and 20 from site outreach).

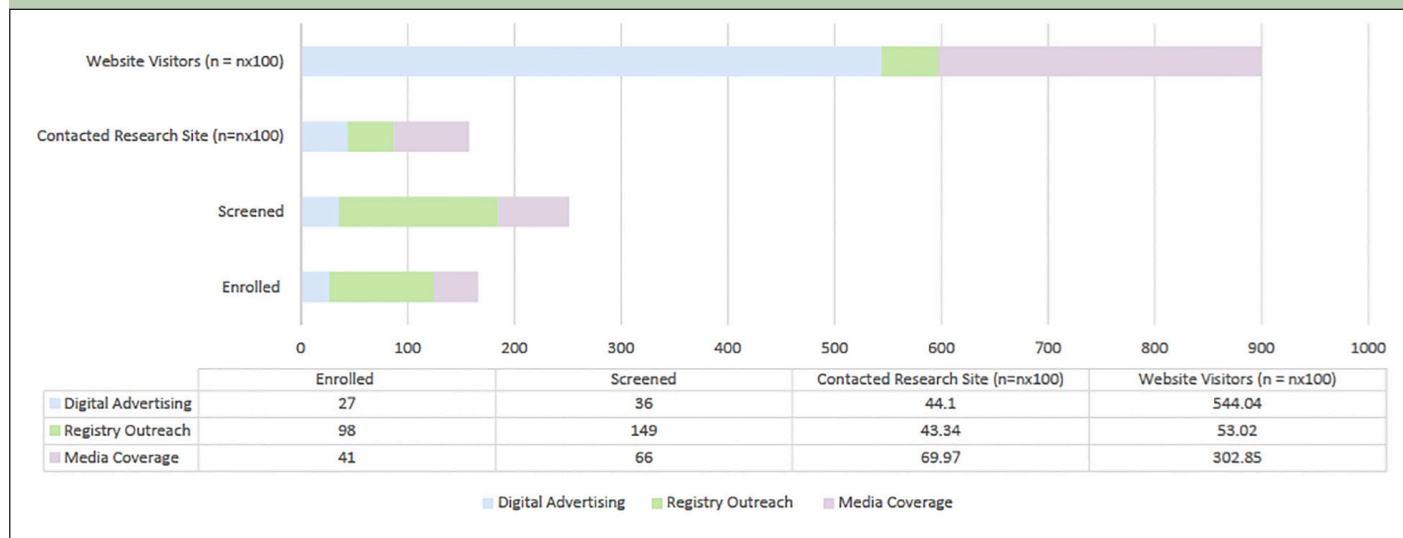
Most Effective Recruitment Sources

The recruitment sources that produced the most referrals through ADNI3.org include: Facebook and Google advertisements targeted by age and location; radio interviews in local markets with the Principal Investigator; articles and press releases in local newspapers; and emails from Caring.com and APR. These activities resulted in 65% of the total website traffic, 46% of the total completed website pre-screeners and 26% of the total calls. 27% of new participant enrollment can be linked to a registry using the self-reported data collected at the screening visit. The most effective registry activity for recruitment was direct referrals provided by BHR resulting in at least 73 individuals screened and 48 enrolled, as shown in the referral codes collected.

Using Data to Improve Recruitment Activities

Analyzing data throughout the study provided insight on how recruitment activities were performing and helped to determine recruitment plans. Following the April 2018 email from APR, a total of 1,159 trackable links were collected on the website and 496 of these visitors (42.7%) were referred to a research site. As a result of this information, additional emails were conducted with APR to provide referrals to sites, which resulted in 1,265 more trackable links collected and 448 of these visitors (35.4%) were referred to a research site.

Figure 2. Recruitment activities conducted by the coordinating center



NOTE: Figure 2 includes 35% of screening and enrollment data that can accurately be linked to recruitment activities conducted by the Coordinating Center. Numbers included in Website Visitors and Contacted Research Site are 100 times the actual number. Condensed numbers were provided for visibility.

Use of Website Pre-screener

The most popular action on ADNI3.org was to complete the pre-screener form (12%). Of those that completed the pre-screener, 56% were deemed eligible and referred to a site. This minimized site burden by eliminating approximately 4,294 participants deemed ineligible, or 72 individuals per site.

Discussion

The major conclusion from this study was that quantitative data concerning all steps of the recruitment process provided useful information concerning the efficiency of each step. The data provided some insight into which recruitment activities were producing the most referrals, which was helpful for recruitment planning. We were able to connect a large number of recruitment activities to website traffic but data on the source of enrollment was only available for a small percentage due to several limitations.

Use of trackable links provided some insight on which recruitment activities led a potential participant to the website and subsequent enrollment. However, some trackable link data is not captured due to private browsing, firewalls and website blocking cookies. Furthermore, some responses to the screening questionnaire collected at the clinic visit conflicted with the referral code provided. These discrepancies might be due to human error from participants and study staff or might suggest that multiple touchpoints of recruitment are needed for successful enrollment. Our efforts to track campaigns by using local phone numbers that could serve as referral codes during the screening visit was ineffective, and no phone numbers were provided as

referral codes. In addition, the more manual methods of tracking recruitment activities, such as the metrics that rely on site data entry, were completed partially or inconsistently.

We would recommend collecting self-report screening questionnaires and referral codes at the initial contact with the participant (i.e., during the pre-screening telephone call) to improve accuracy. Questions asked should be simplified for clarity with limited choices to avoid confusion and provide cleaner data. More robust methods for collecting referral codes should also be employed, such as limiting data entry fields to ensure consistency in referral codes or automating referral codes through the use of a QR codes.

Analyzing recruitment metrics, we were able to obtain a preliminary assessment of central recruitment efforts in real-time to inform recruitment planning. We increased the most successful recruitment activities based on these assessments. Additionally, we realized that the quality of the source was sometimes more important than the quantity of users reached. For instance, Facebook reached a far larger number of users than APR yet APR had a larger number of users who were screened in clinic. We believe this was because APR’s registry members already had a greater interest in participating in research studies whereas Facebook reached a broader audience. With more accurate and complete data, we would be able to more effectively measure tactics to gauge the most successful recruitment activities and connect these to actual enrollment.

Although the use of an online pre-screener is not a recruitment tactic, we found that it was an effective entry method for referrals to reduce site burden by eliminating referrals that do not meet the basic study criteria. This conclusion was possible due to tracking website activity including the number of online pre-screeners completed

and the user's subsequent eligibility status.

We found that central recruitment efforts using a multi-faceted approach of media coverage, online advertising and registry outreach can be effective at providing sites with eligible referrals, and subsequently leading to increased screening and enrollment. Driving recruitment activities to a central website with tracking capabilities allows efforts to be measured and evaluated for efficacy. This data can then be used to inform recruitment planning. Using this data-driven approach to centralized recruitment, investigators can effectively and efficiently pursue enrollment goals.

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