ALTITUDE-AD: Recruitment Strategies for a Global Phase 2 Trial of Sabirnetug in Early Alzheimer's Disease

Robyn Moxon[1], Todd Feaster[1], Kathy Marcozzi Pierce[1], Maddelyn Hyland[1], Victoria Baird[1], Siew Tin Gan[1], Dung Trinh[2], Eric Siemers[1]

[1]Acumen Pharmaceuticals, Inc - Newton, Massachusetts (United States), [2] Healthy Brain Research - Long Beach, California (United States)

Introduction

Recruiting eligible participants for Alzheimer's disease (AD) clinical trials remains one of the most significant barriers to efficient study completion. Trials for early-stage AD face unique challenges due to strict eligibility criteria, the need for study partners, and limited community diagnosis of mild cognitive impairment (MCI) or early dementia due to AD.[1,2] There is a growing need to evaluate not only outreach strategies but also how recruitment source performance varies by demographic and regional subgroups.[2,3]

For ALTITUDE-AD, a global phase 2 trial of sabirnetug, the effectiveness of various site-led recruitment strategies was evaluated across diverse geographies and participant demographics.

Methods

Design: Phase 2, randomized, double-blind, placebo-controlled study of sabirnetug in early Alzheimer's disease (mild cognitive impairment [MCI] or mild dementia)

Sites: 76 across the United States (US), Canada, Germany, Spain, and the United Kingdom (UK)

Participant Screening & Randomization:

- February 2024 to March 2025
- 2,353 unique screens/9 re-screens/2,362 total screens
- 542 randomized

Recruitment Sources:

All recruitment activities were site-led. Participants were sorted into one of six recruitment source types (**Figure 1**).

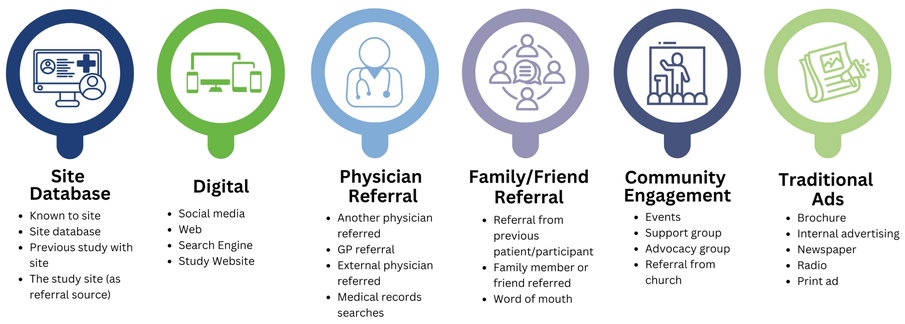

Figure 1. Recruitment Source Categories
Participants were grouped into six referral sources to evaluate which methods were most effective for identification and enrollment in ALTITUDE-AD.

Statistical Analysis:

Recruitment sources were evaluated for screening volume and effectiveness. Source effectiveness was assessed by comparing **enrollment rates** (the percentages of screened participants who enrolled in the study) across categories. All comparisons were conducted using Chi-square tests. No adjustments for multiple comparisons were made in the statistical tests.

Analyses were conducted on sub-groups by:

- Country
- Age group
- Education level
- Sex

Screen fail rates were compared across sources to evaluate effectiveness, consistent with methodologies in prior large-scale recruitment studies.[1,3,4]

Results

Overall Effectiveness of Recruitment Sources

- Site database & physician referral were the most effective recruitment sources with the highest conversion rates (**Figure 2**).
- Site database and physician referral accounted for a greater percentage of randomized participants than they screened (**Figure 3**).
- These findings suggest that established clinical relationships and pre-screened populations may yield higher enrollment rates.
- Digital ads contributed a lower percentage of enrolled participants than they screened, with the highest screen fail rate of all sources at 89%.
- This likely reflects the wide reach but lower precision of digital advertising, which often attracts individuals unfamiliar with research participation or trial eligibility requirements.
- Other sources such as family/friend referrals (4.4% randomized), community engagement (3.7%), and traditional advertising (3.9%) also had higher than average screen fail rates for this study overall.

References

1. *Shadyab AH, et al. Alzheimers Dement. 2021;17:1808–1817. doi:10.1002/alz.122483 (EXERT Trial)*
2. *Shadyab AH, et al. Alz Dement Diagn Assess Dis Monit. 2022;8:e12265. doi:10.1002/trc2.12265 (T2 Protect AD)*
3. *Hall T, et al. Alzheimers Dement. 2023;19(Suppl. 22):e077391. doi:10.1002/alz.077391 (rrAD)*
4. *Levin R, et al. Alzheimers Dement. 2022;18(Suppl. 11):e068198. doi:10.1002/alz.068198 (HABS)*

Results

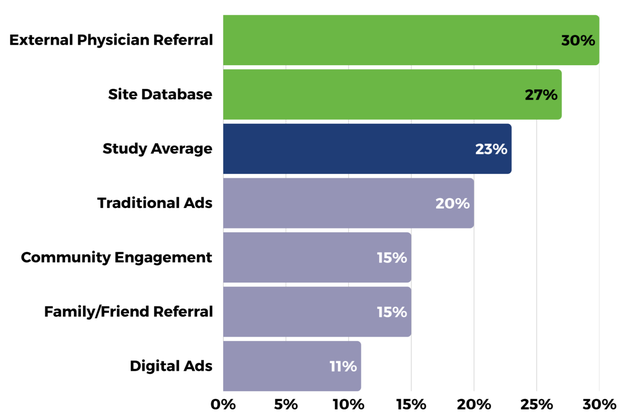

Figure 2. Enrollment Rates by Recruitment Source
Enrollment rates are shown for recruitment sources, calculated as the percentage of screened participants who were enrolled in the study for each source. The 30% enrollment rate (70% screen fail rate) for physician referrals differed significantly from all other sources (X^2=8.9685, p=0.0027). Overall, screen failure rates differed significantly across recruitment sources (X^2= 63.2478, p<0.0001).

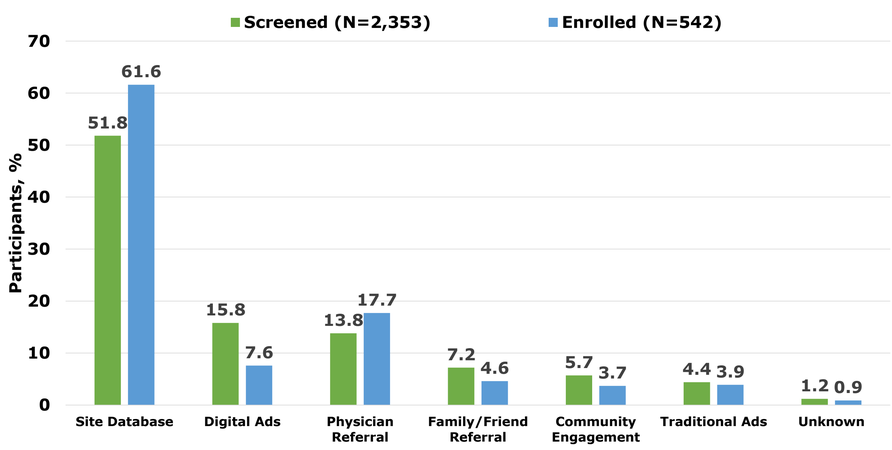

Figure 3. Percentages of Participants Screened and Enrolled by Recruitment Source
Recruitment using site databases and physician referrals were more effective than other recruitment methods.

Recruitment by Country

- Recruitment strategies varied by country. Sites outside the US relied more heavily on the use of site databases (**Figure 4**).
- The UK had the highest use of digital ads, and the US showed the most balanced recruitment source mix.
- Time available for screening and recruitment may have skewed these results due to the rapid enrollment overall.
- The US had two to four times longer for screening than other countries.
- Site database was the predominant recruitment source in countries with shorter windows of recruitment, suggesting that this strategy may require less time than others.

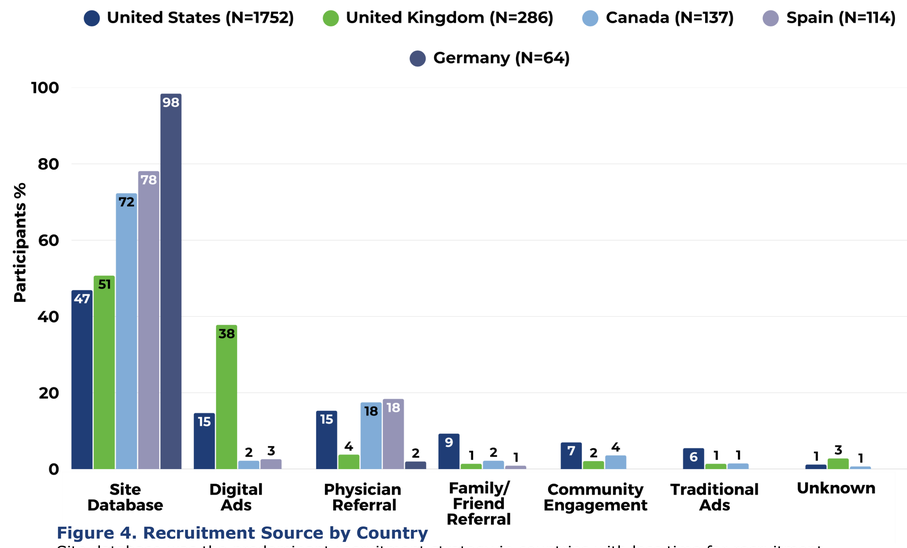

Figure 4. Recruitment Source by Country
Site database was the predominant recruitment strategy in countries with less time for recruitment.

Recruitment by Participant Characteristics

- Site database was the most used recruitment strategy for all ages. For this analysis we defined age groups by generations (Generation X participants were born in 1965-1974, Baby Boomers in 1946-1964, and the Silent Generation in 1935-1945). Significant differences were found across age groups for physician referral (5% Generation X vs. 14% Boomers vs. 18% Silent Generation, X^2=18.5692, p<0.0001) and digital ads (31.4% Generation X vs. 15.2% Boomers vs. 10.9% Silent Generation, X^2=48.2472, p<0.0001; **Figure 5A**). This aligns with site-level observations that digital ads were less effective among older adults unfamiliar with research participation, reinforcing the importance of tailoring recruitment approaches to target generation.
- Level of education did not have a notable impact on rate of screen fail (data not shown). Participants with more education were slightly more likely to be recruited via digital ads, while those with less education were most likely to be recruited through site databases (**Figure 5B**).
- Recruitment sources differed significantly by sex (X^2=16.5202, p=0.0112). Significant associations were observed between recruitment by digital ads and females (X^2=6.7775, p=0.0092) and between recruitment by physician referral and males (X^2=8.3343, p=0.0039; **Figure 5C**).

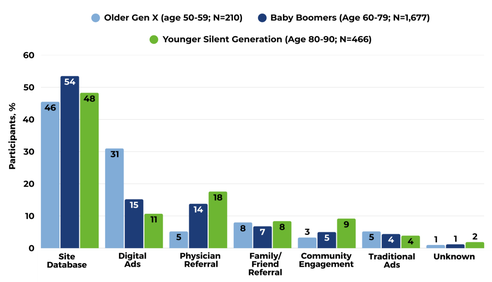

Figure 5A. Recruitment Source Screens by Generation
Recruitment sources differed significantly across generations (X^2=78.5356 , p<0.0001); A greater percentage of younger participants were recruited digitally. A greater percentage of older participants were recruited by physician referral.

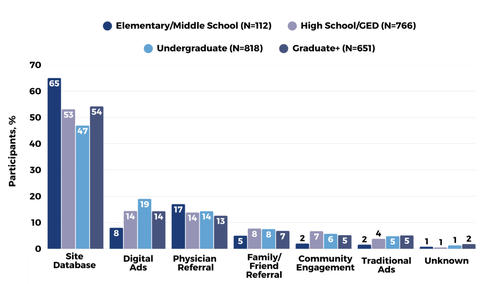

Figure 5B. Recruitment Source Screens by Education
Recruitment sources differed by education with higher-educated participants were more often recruited digitally.

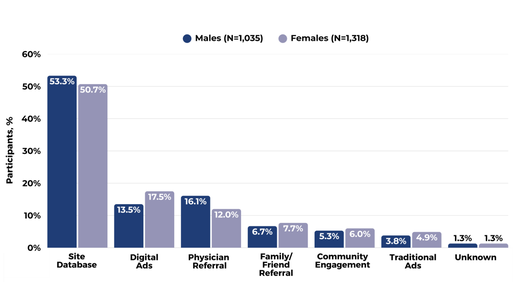

Figure 5C. Recruitment Source Screens by Sex
Conversion rates did not differ by sex (X^2=2.6465, p=0.1038). Recruitment sources did differ significantly by sex (X^2=16.5202, p=0.0112).

RESEARCH HIGHLIGHTS

1. **Site databases and physician referrals were the most effective recruitment sources**, yielding the highest enrollment rates. These strategies reflect established patient relationships, trust in providers, and possible pre-qualification, leading to better eligibility and potentially lower attrition.
2. **Digital ads had the lowest enrollment rate**, especially among the oldest age group for the study, highlighting a potential need for improved pre-screening strategies if using digital sources.
3. **Recruitment sources varied significantly by country, age, and sex,** emphasizing the importance of tailored, demographically aware outreach in global trials.
4. **US sites utilized a more balanced mix of recruitment sources,** likely due to longer active enrollment time and more flexibility in site-level outreach strategies.