



Innovative Digital Patient Recruitment Strategies in Prodromal Alzheimer's Disease Trials



Lynne Hughes, B.Med.Sci., PhD., PMP, Vice President & Therapeutic Strategy Head, Neurology, Global Project Management, Quintiles

Cathy Vanbelle, Director, Therapeutic Strategy Lead, Neurology, Global Project Management, Quintiles

Roza Hayduk, M.D., M.S., FAASM, Executive Medical Director, Global Medical Head, Neurology, CNS Therapeutic Delivery Unit, Quintiles

Background: Prodromal Alzheimer's disease

Currently, around 35.6 million people worldwide have dementia, forecast by Alzheimer's Disease International to increase to 115.4 million – or one in 85 people – by 2050.^{1,2} AD is the most common form of dementia³, accounting for 50-75% of cases.⁴ Clinically, AD is very well understood.⁵ This devastating, progressive neurological disorder is characterized by cognitive impairment, psychiatric symptoms, behavioral disturbances, and ultimately, the impairment of daily activities.⁶ Around 43% of AD cases need a high level of care equivalent to that provided by nursing homes. If interventions were available to delay both disease onset and progression by just one year, there would be almost 9.2 million fewer cases of AD in 2050, and most of this fall would be due to a decrease in the number of people requiring a high level of care.⁷

Table of Contents

Background: Clinical research on prodromal Alzheimer’s disease	03
New study involves 440 patients across eight possible protocols	04
Study results indicate a large pool of community-based patients	04
Conclusions: Digital outreach holds promise	05
References	06
About the Authors	07

Alzheimer's disease (AD) can have a long 'prodromal' phase, with signs of cognitive decline appearing as long as 12 years before the onset of dementia.⁸ This is termed prodromal Alzheimer's (pAD), Mild Cognitive Impairment (MCI) or mild-to-moderate AD. Many patients with early symptoms of AD can be reliably diagnosed in advance of fully manifest dementia. However, despite the improved resolution in early disease detection, there are many instances where the limits of diagnostic sensitivity and specificity are tested. Many patients in the AD prodrome are likely to present with atypical symptoms confounded by medical comorbidities, making early disease diagnosis ambiguous at best.

Background: Clinical research on prodromal Alzheimer's disease

A goal of clinical research programs is to identify patients at an early stage of AD in the hope of influencing its course using disease-modifying treatments. These treatments are now moving towards the final analysis stage of development in the mild-moderate population, with a switched focus towards utilizing DMD products in the earlier stages of AD. This is driven by the potential effect that DMDs may have in decreasing (or preventing) the amyloid burden and thus slowing down the progression of AD. However, current screen failure rates are around 70 to 80% for clinical trials on pAD, representing a significant burden at the site level.⁹ It is extremely challenging to identify suitable subjects for inclusion in clinical trials for pAD/MCI. While symptoms are prevalent in the community, patients do not self-identify with these conditions.

Online patient communities and the broader digital patient universe hold promise in supporting protocol level feasibility and patient recruitment.

In surveys done to date by Quintiles via the online patient community, MediGuard.org – a free medication monitoring service that provides safety alerts and updates to over 2.5 million members in the US, UK, France, Germany, Spain and Australia – no patients have ever self-reported a diagnosis of pAD and only 5% have reported a diagnosis of MCI. Rather, individuals seem to align with the symptoms they experience. Types of symptoms most commonly mentioned include: less interest in hobbies/activities (16%), daily problems with thinking/memory (12%), problems with judgment (e.g., making decisions, 10%), trouble remembering appointments (9%), repeating the same things (8%), trouble handling financial affairs (7%), trouble learning how to use a tool/gadget/appliance (7%), and forgetting the month/day/year (3%). Of the patients reporting at least one symptom, only 15% were being treated for cognitive functioning issues.

Over the past three years, Quintiles has conducted 15 programs using digital outreach to screen potential subjects online about their self-reported cognitive symptoms, AD, pAD and MCI.

Many patients in the AD prodrome are likely to present with atypical symptoms confounded by medical comorbidities, making early disease diagnosis ambiguous at best.

New study involves 440 patients across eight possible protocols

A recent study examined protocol feasibility and patient recruitment, analyzing responses from 440 patients across eight protocol feasibility assessments completed by members of MediGuard.org. The study aimed to target specifically the qualified identification of pAD subjects in order to decrease the screening burden at the site level. This relatively large study contrasts with traditional protocol feasibility assessments, which typically include feedback from approximately 50 members likely to meet study inclusion/exclusion criteria.

Key topics for exploration using this approach included: disease history and care patterns; satisfaction with current therapy and unmet needs; patient interest in a clinical trial; challenges to recruitment; benefits from participation; and expectations for subject compensation. Patients/caregivers also offered suggestions for how to enhance recruitment in pAD trials.

Study results indicate a large pool of community-based patients

An important result from the study included the fact that only 30% of patients experiencing at least one symptom of neurocognitive decline had ever visited their physician, suggesting a large available pool of community-based patients. Also, across the pAD/MCI surveys conducted to date, about 40% of patients would not participate in a study requiring a lumbar puncture. This would have a significant effect on recruitment. Study time commitments, reimbursement for time and travel, and careful screening tools to accurately assess the subjects cognitive functioning are also critical.

Survey response rates averaged 10% for the AD/pAD population, with around 85% of respondents being caregivers. Of the patients likely to have pAD, based on symptoms:

- > None of the patients/caregivers were familiar with the term prodromal Alzheimer's Disease
- > Only 5% have reported a diagnosis of or concern about MCI
- > 30% have visited a physician
- > 15% have been prescribed an anticholinergic medication

One of the greatest barriers to trial participation was the potential for lumbar punctures, and there were also concerns about the route of administration of the investigational drug, the duration of the trial and clinic visits, the chance of receiving placebo or needing to have an annual PET scan (Figure 1). Unexpectedly, only 30% of patients would not participate in a trial if their managing physician expressed concerns about the trial or the product under investigation.

Figure 1: Percentage of Subjects Who Would Not Participate in a pAD trial

Procedure	% of subjects who would not participate
Lumbar puncture	40%
Injectable study medication	20%
Three-year study	20%
Chance of placebo	15%
Monthly clinic visits	15%
Visits are 1 or 2 hours	15%
Annual PET scan	15%
Personal doctor expressed concerns	30%

Once identified, pAD subjects show the highest level of interest in a new oral therapy, while mild AD patients showed the lowest level of interest in a new oral treatment (Figure 2). This could be because the mild AD subjects have already tried a number of oral therapies already, without success and thus are less enthused regarding new therapies or that, in this population, the main drivers for participation in an AD are more the caregivers.

Figure 2: Level of interest in a new oral therapy

Category of patient	Little or no interest	Somewhat interested	Extremely or very interested
pAD/MCI	15%	15%	70%
Mild AD	45%	25%	30%
Moderate AD	25%	40%	35%

Conclusions: Digital outreach holds promise

The study indicates that few subjects experiencing one symptom of neurocognitive decline ever visit their physician, suggesting that there is a large available pool of community-based patients who could potentially participate in pAD clinical trials. Subjects are willing to complete online assessments regarding their symptoms, and thus a digitally-based community outreach pre-screening campaign would help identify and screen potentially appropriate trial subjects, and eliminate inappropriate ones. Thus digital outreach can help make a significant reduction in the burden of work at the site by managing the pre-screening in the community and not within the site and then only a much smaller percentage of subjects would be brought, physically, to the site and the likely screen failure rates would decrease from the current 80% to the “usual” (for AD trials) at around 30 – 40%. Recruitment to pAD trials will depend on communication of positive messaging – via advertisements and within the patient informed consent – about the required trial assessments and their potential benefits to subjects and future AD sufferers.

References

1. Alzheimer's Association. 2010 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2010 Mar;6(2):158-94.
2. Alzheimer's Disease International. World Alzheimer Report 2010: The global economic impact of dementia. London.
3. http://www.who.int/mediacentre/news/releases/2012/dementia_20120411/en/
4. <http://www.alz.co.uk/info/alzheimers-disease>
5. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2881320/>
6. Hughes L, Guthrie S. Chapter: Operationalization of Global Alzheimer's Disease Trials. In *Global Clinical Trials for Alzheimer's Disease: Design, Implementation, and Standardization (Elsevier, October 2013)*.
7. Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting The Global Burden Of Alzheimer's Disease. Johns Hopkins University Johns Hopkins University, Dept. of Biostatistics Working Paper. January 2007. <http://biostats.bepress.com/jhubiostat/paper130/>
8. <http://www.modernmedicine.com/modern-medicine/news/modernmedicine/modern-medicine-news/alzheimers-disease-can-have-long-prodromal->
9. Hughes L, Kalali A, Vanbelle C, Cascade E. Innovative Digital Patient Recruitment Strategies in Prodromal AD trials. Poster at CTAD Annual Meeting, October 29-31, 2012.

About the Authors



Lynne Hughes, B.Med.Sci., PhD., PMP

Vice President & Therapeutic Strategy Head, Neurology, Global Project Management, Quintiles

Lynne Hughes has worked in clinical research for more than 25 years and has lived and worked during this time period in both the US and in Europe. She has been with Quintiles for 16 years and is currently Vice President and Global Head of Therapeutic Strategy, Neurology. Lynne has worked exclusively in neurology while at Quintiles and has managed global development programs both from the operational perspective as a program director and also from the design perspective – working with many clients on their clinical development plan for their product. She has provided consultancy advice in Alzheimer’s disease, multiple sclerosis, acute care, epilepsy and pain, and has been involved in a number of investment opportunities within Quintiles. In particular, she sits on a number of advisory boards, with particular interest in neurocognitive assessment and design of appropriate studies to assess neurocognitive dysfunction. She is a member of a number of steering and / or executive committees for clients and has responsibility for several consultancy programs for investment opportunities within all areas of neurology.



Cathy Vanbelle

Director, Therapeutic Strategy Lead, Neurology, Global Project Management, Quintiles

Cathy Vanbelle has 23 years experience in conducting and supporting clinical trials. She joined Quintiles in 1998 as a clinical research manager and spent some years in the feasibility group before moving to the CNS therapeutic team in 2008. She is especially qualified in the fields of neurology, psychiatry and haematology oncology. Cathy has solid experience in global strategic study implementation over all therapeutic areas. Outside of Quintiles she has worked 10 years on a paediatric bone marrow transplantation ward and having her father and grandfather suffering from Alzheimer’s Disease she knows the patient/familial challenges living with dementia.



Roza Hayduk, M.D., M.S., FAASM

Executive Medical Director, Global Medical Head, Neurology, CNS Therapeutic Delivery Unit, Quintiles

Dr. Hayduk is a neurologist with subspecialties/fellowships in Sleep Disorder Medicine (Scripps Clinic and Research Foundation, La Jolla, California) and Epilepsy (University of Californian San Diego-UCSD, Department of Neurosciences). She has more than 25 years of clinical experience in neurology and experience as Investigator/Co-Investigator on NIH and Pharmaceutical Industry sponsored research projects while at Scripps Clinical and Research Foundation where she also served as Adj. Assistant Professor in Neurology for several years and as teaching staff at UCSD. Dr. Hayduk also served as a member of the American Board for Sleep Medicine and as a Co-Chair of the Accreditation Committee for Sleep Disorder Centers in US.

In the role of Global Medical and Scientific Advisor, at Quintiles, Dr. Hayduk oversees global international drug studies for Alzheimer’s disease, Parkinson’s disease, epilepsy, MS, insomnia, narcolepsy, migraine, and other neurological diseases. Her responsibilities include consulting and providing general medical expertise to sponsors, investigators, and study coordinators over a wide range of issues including inclusion/exclusion decision making, assessment of potential interaction of concomitant medications with study drug, interpretation of laboratory and ECG data, initial assessment and subsequent analysis of serious adverse events (SAEs), review of AEs for potential trends, etc. She provides medical and clinical assistance to clinical research associates and PMs on ongoing protocols as well as initial protocol set-up and protocol design.

Dr. Hayduk is a member of numerous medical professional organizations. She is a prolific scientific writer/presenter with more than 100 published scientific articles and scientific presentations. She is the recipient of the renowned Fulbright Scholarship, and a life member of the Fulbright Association.

Contact Us:

US Toll Free: 1 866 267 4479

Direct: +1 973 850 7571

On the web: quintiles.com

Email: consulting@quintiles.com

