CLINICAL INFORMATICS NEWS

Building A Community-Focused Clinical Trial Network For Alzheimer's Disease

Clinical trials for neurological conditions can be some of the hardest to fill and conduct. But there are dedicated groups working with patient and caregiver communities, and with neurological disease researchers to make progress. Clinical Informatics News *spoke with three such initiatives to explore how participant recruitment and other aspects of clinical trials are changing. –The Editor*

By Maxine Bookbinder | February 22, 2018

"The first person to be cured of [Alzheimer's Disease] will be in a clinical trial. The only way to find a solution is to get people in trials to save the next generation and the finances of our country," says John Dwyer, president of the Global Alzheimer's Platform (GAP) Foundation.

Alzheimer's disease is currently the sixth-leading cause of death in the U.S. and is the only disease in the top 10 without a treatment, prevention, cure, or known cause. It costs taxpayers about $153 billion annually in Medicare and Medicaid expenses. Since 2000, deaths from Alzheimer's have increased 89%.

If Dwyer is right, we have no time to lose.

Dementia-related disorder trials, especially Alzheimer's, are harder to recruit for and complete due to dementia's unique characteristics and psychological effects on patients. "It's tough to recruit people who are asymptomatic," says Dwyer. Alzheimer's prevention trials need people who are mildly or non-symptomatic, but the pathogenesis of the disease can start 10 – 15 years before symptoms surface.

The key, Dwyer believes, is adding personal interaction. "We are hitting the conscience of the communities," he says. "We are dedicated to doing something every day to increase awareness about referrals to clinical trials. We're in business to make sure this is for real."

The Global Alzheimer's Platform Foundation is a not-for-profit launched at the end of 2013 as a collaboration between the Global CEO initiative on Alzheimer's disease and the New York Academy of Sciences. Its goal was to analyze and address the difficulty of completing Alzheimer's disease trials timely and cost-efficiently.

Currently, there are 944 AD trials listed on ClinicalTrials.gov. Nearly 100 of those are marked as canceled or terminated; 200 are recruiting. Only 63 are listed as active. Trial success is limited by the inability to find qualified participants; in fact, 85% of trials are delayed because of insufficient enrollment and more than 30% of trial time is consumed with recruitment. Successful clinical trials are critical to finding new therapies, slowing the financial drain, and discovering hope for the victims and their families.

In order to speed start up on Alzheimer's trials, GAP established GAP-Net, a network of 59 leading private and public research centers for Alzheimer's in North America. The combination of well-known

public sites, such as Yale, Cleveland Clinic, and the University of San Francisco and lesser-known private sites allows researchers to share unique best practices throughout GAP-Net. “We learn from each other and improve performance in an old-fashioned information exchange,” says Dwyer.

GAP-Net’s mission is to increase efficiency by decreasing redundancies, non-essential paper work, and general bureaucracy. “Little things choke the process in neurology trials,” says Dwyer. “If we do just 30 things differently, we could increase [trial] capacity by 100%. We have great research centers in North America with insufficient participants [that are] struggling to get people into trials. Our motto is, ‘Just get stuff done.’ Lots of people saw this data; we moved on it. This is our brand: find those 30 things and attack them.”

Kansas City Approach

GAP approached recruitment from a civic perspective, starting with the Memory Strings Kansas City Alliance pilot project anchored by the University of Kansas Alzheimer’s Disease Center. “We looked at the problem as a community and not as a pharma problem,” says Dwyer. “Kansas City has 55,000 residents with AD. For every AD patient—and this is true for almost all neurological patients—there are two caregivers. That represents about 10% of the Kansas City community. There are 5.4 million Americans with disease. Put that in community settings, and it has unbelievable ramifications.”

Eighteen months ago, GAP launched the recruitment campaign in a multi-segmented outreach program with monthly activities, including a front-page story and op-ed in *Kansas City Star*, lunch-and-learns at businesses, physician awareness programs, radio spots, support from the mayor and health insurer Blue Cross Blue Shield of Kansas City. GAP was able to increase referrals in Kansas City by more than 200%.

In addition, GAP funded specific local activities to reach the African-American and Latino populations, which are at higher risk of AD (2x and 1.5x respectively.) Recruiting under-represented demographics for clinical trials in which there are disparities in access to care or in proportion to those affected by the disease is imperative.

GAP has built relationships within African-American and Latino communities through organizations including the Kansas City Black Healthcare Coalition, local congregations, and the US Against Alzheimer’s African-American and Latino Networks to increase participant diversification. “We find leaders to complement us and amplify our message,” says Dwyer. “We generate partnerships at the grassroots level. We work with people who know the community, can allay fears and encourage participation. We need to grapple with problems at the local level.”

Based on the Kansas City area success, GAP plans to expand Memory Strings Alliance communities to at least eight this year, concentrated in areas with older populations, such as Southern California, Southern and Central Florida, and Boston. GAP has sponsored an award-winning play, *Forget Me Not,* that tells the story of an African-American patriarch with AD, the caregiver burdens of his family and friends, and the importance of clinical trials. The play was performed in several cities, including Kansas City, Boston, and Phoenix. Afterward, contact information for potential patient volunteers was obtained for those interested in volunteering for clinical trials at their local GAP-Net research centers.

Therapeutic trials sponsored by Pharma companies can help to increase recruitment and speed start up, says Dwyer. Pharma sponsors “need to rethink how they structure the cash flow in their studies. They

pay a lot of money, but more money is not the answer. It's where they spend the money that is the answer." Dwyer says that academic sites can't hire people prior to launch without sufficient funding; therefore, he suggests pharma reallocate money and provide a lump sum at the beginning to allow all sites to hire necessary personnel, such as additional recruiting coordinators.

Speedy Start

Of the 59 GAP-Net sites, 47 share one Institutional Review Board (IRB), the largest collection of sites subscribed to a single IRB in North America for AD trials. A central IRB increases participants' safety and decreases start-up time, possibly by about 3-6 months, Dwyer says. GAP also standardizes clinical trial agreements, providing GAP-Net sites with a master contract that requires no negotiation, slashing about another six months off trial completion time.

Budgeting with clinical research organizations, or CROs, should also be revamped, says Dwyer, by bundling activity together rather than invoicing for multiple, specific items. "Minimize invoicing to minimize time for negotiating. Bundling reduces non-productive accounting time and makes life easier."

Finally, Dwyer believes Cognitive Rater certification should be standardized. Because many raters have already taken these tests many times, repeated training is a waste of time and money. Standardization of a rater certification may also reduce or eliminate rater variability and bias, and improve consistent test interpretation.

Each new process proposed by GAP can reduce start-up time by weeks and months; compiled with additional adjustments, GAP hopes trials can be reduced by several years and millions of dollars. While some of the models being implemented by GAP are already in place in cancer and heart disease trials, they could all, except for the rater certification, be adopted industry-wide.

One of GAP's biggest contributions is the requirement that all GAP-Net members share their data. "Our job is to make everybody better," says Dwyer. "Reporting data on what works and what doesn't and then sharing among sites makes trials more efficient and effective. We first report, then measure, change behavior, report, and measure again. The biggest contributions will be reporting the data off those developments."

These data are analyzed to help identify best practices, says Dwyer: to determine the best recruiting practices; to organize screening processes more accurately and efficiently; to modernize and improve trials; and "to be more effective once more research sites adopt new processes with increasingly good results."

This year, pharma will use the GAP network to conduct trials to test the efficacy of new therapies developed to defer or possibly even cure AD symptoms. GAP is also launching Acti-v8 Your Brain, a community brain-health initiative.

Dwyer is hopeful, and committed to success. "We define success by making trials faster and higher quality than the average in the field."

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