The Journal of Nutrition, Health & Aging©
Volume 16, Number 4, 2012

EDITORIAL

RECRUITMENT, RETENTION AND OTHER METHODOLOGICAL ISSUES RELATED TO CLINICAL TRIALS FOR ALZHEIMER'S DISEASE

B. VELLAS

Gerontopole, Inserm U 1027, Alzheimer's Disease Research and Clinical Center, Toulouse, University Hospital, France. Vellas.b@chu-toulouse.fr

1. In the past few years, many drug trials have been conducted in the field of Alzheimer's disease (AD). While there has been much written (1-9) in this journal about methodological aspects of these trials -- cognitive tests, global function and neuropsychiatric measures, biomarkers and imaging - strategies for recruitment and retention have been largely neglected. In fact, there has been virtually no research on these topics by either academia or industry over the past 20 years, despite the development of many trials. As a result, trials have had unreasonably long periods of recruitment, too many centers but too few patients recruited by each center, and unacceptably high drop-out rates. In order to recruit 400 patients for a trial today, more than 200 centers are needed from the United States, Europe and Asia. Yet substantial variability among centers results in difficulty interpreting trial results; and with the inclusion of imaging and biomarker studies in these trials, variability has increased while at the same time it has become more difficult to recruit and retain subjects in trials.

2. While we may not be able to find a cure for Alzheimer's disease in the near future, one or several drugs presently in trials have shown promise; however, we may not be able to demonstrate efficacy due to issues of recruitment, retention, site-to-site variability and other methodological issues. It is thus incumbent on the scientific community to find solutions to these problems, particularly as the field moves toward treating the disease in its prodromal stages, where these methodological issues will become even more critical. We need to better understand why participants agree or refuse to enter drug trials, and why both primary care physicians and Alzheimer's specialists agree or refuse to involve their patients (10-17). We also need to quantify the impact of requiring imaging studies and lumbar punctures on recruitment and retention. With these concerns in mind, an international task force of experts from academia and industry in the United States, European Union and Japan met in San Diego, California on November 2, 2011 to focus on recruitment, retention and other methodological issues related to clinical trials for AD. We present in this JNHA issue the papers presented during this Task Force Meeting. MMRM Versus Slope Models in Alzheimer's Disease Clinical Trials; Alzheimer's Disease Therapeutic Trials: EU/US Task Force Report on Recruitment, Retention, and Methodology; Are Biomarkers Harmful to Recruitment and Retention in Alzheimer's Disease Clinical Trials? An International Perspective; Is There a Rationale for Including Only Patients Already Being Treated with Acetylcholinesterase Inhibitors in a Prodromal AD Trial?; Recruitment Methods for United States Alzheimer Disease Prevention Trials; Task Force on Alzheimer's Disease Trial Methodology: Recruitment and Retention, Data Management and Analysis. The use of imaging in recruitment: maintenance and methodological issues in Alzheimer's trials; Representations and Practices of Prevention in Elderly Populations: Investigating Acceptance to Participate in and Adhesion to an Intervention study for the Prevention of Alzheimer's Disease (ACCEPT study) – The Need for a Multidisciplinary Approach; Recruitment Strategies for Frail Older Adults. The MAPT Study.

References

1. Andrieu S, Aboderin I, Baeyens JP, Beard J, Benetos A, Berrut G, Brainin M, Cha HB, Chen LK, Du P, Forette B, Forette F, Franco A, Fratiglioni L, Gillette-Guyonnet S, Gold G, Gomez F, Guimaraes R, Gustafson D, Khachaturian A, Luchsinger J, Mangialasche F, Mathiex-Fortunet H, Michel JP, Richard E, Schneider LS, Solomon A, Vellas B. IAGG Workshop: Health Promotion Program on Prevention of Late Onset Dementia. J Nutr Health Aging. 2011 Aug;15(7):562-75.
2. Chao SZ, Lai NB, Tse MM, Ho RJ, Kong JP, Matthews BR, Miller BL, Rosen HJ.Recruitment of Chinese American elders into dementia research: the UCSF ADRC experience Gerontologist. 2011 Jun;51 Suppl 1:S125-33.
3. Schindler RJ. Study Design Considerations: Conducting Global Clinical Trials in Early Alzheimer's Disease. J Nutr Health Aging. 2010 Apr;14(4):312-4.
4. Galvin JE, Meuser TM, Morris JC. Improving physician awareness of Alzheimer disease and enhancing recruitment: the clinician partners program. Alzheimer Dis Assoc Disord. 2012 Jan;26(1):61-7.
5. Cedarbaum JM, Crans G, Grundman M. Seeing with New Eyes: Finding a Path to Early Intervention Trials in Alzheimer's Disease. J Nutr Health Aging. 2010 Apr;14(4):306-9.
6. Petersen RC. Clinical Trials for Early (Pre-Dementia) Alzheimer's Disease: A Case for Mild Cognitive Impairment. J Nutr Health Aging. 2010 Apr;14(4):304-5.
7. Doody RS. Evolving Early (Pre-Dementia) Alzheimer's Disease Trials: Suit the Outcomes to the Population and Study Design. J Nutr Health Aging. 2010 Apr;14(4):299-302.
8. Schneider LS. The Potential and Limits for Clinical Trials for Early Alzheimer's Disease and Some Recommendations. J Nutr Health Aging. 2010 Apr;14(4):295-8.
9. Aisen PS. Pre-Dementia Alzheimer's Trials: Overview. J Nutr Health Aging. 2010 Apr;14(4):294. Review.
10. Schoenmakers B, Buntinx F, De Lepeleire J. The Primary Care Physician and Alzheimer's Disease: An International Position Paper. J Nutr Health Aging. 2011 Aug;15(7):595-6.
11. Salvà A, Andrieu S, Fernandez E, Schiffrin EJ, Moulin J, Decarli B, Rojano-i-Luque X, Guigoz Y, Vellas B, NutriAlz Group. Health and Nutrition Promotion Program for Patients with Dementia (NutriAlz): Cluster Randomized Trial. J Nutr Health Aging. 2011;15(10):822-30.
12. Al-Aloucy MJ, Cotteret R, Thomas P, Volteau M, Benmaou I, Dalla Barba G. Unawareness of Memory Impairment and Behavioral Abnormalities in Patients with Alzheimer's Disease: Relation to Professional Health Care Burden. J Nutr Health Aging. 2011 May;15(5):356-60.
13. Jones RW, Andrieu S, Knox S, Mackell J. Physicians and Caregivers: Ready and Waiting for Increased Participation in Clinical Research. J Nutr Health Aging. 2010 Aug;14(7):563-8.
14. Robinson L, Vellas B, Knox S, Lins K. Clinical Practice Patterns of Generalists and Specialists in Alzheimer's Disease: What Are the Differences, and What Difference Do They Make? J Nutr Health Aging. 2010 Aug;14(7):545-52.
15. Martinez-Lage P, Frolich L, Knox S, Berthet K. Assessing Physician Attitudes and Perceptions of Alzheimer's Disease Across Europe. J Nutr Health Aging. 2010 Aug;14(7):537-44.
16. Wortmann M, Andrieu S, Mackell J, Knox S. Evolving Attitudes to Alzheimer's Disease among the General Public and Caregivers in Europe: Findings from the IMPACT survey. J Nutr Health Aging. 2010 Aug;14(7):531-6.
17. Jones RW, Mackell J, Berthet K, Knox S. Assessing Attitudes and Behaviours Surrounding Alzheimer's Disease in Europe: Key Findings of the Important Perspectives on Alzheimer's Care and Treatment (IMPACT) survey. J Nutr Health Aging. 2010 Aug;14(7):525-30.

Received February 13, 2012
Accepted for publication February 24, 2012