private partnerships. The Coalition Against Major Diseases (CAMD) was formed by Critical Path Institute in September of 2008 in response to FDA's Critical Path Initiative (CPI). CPI identified quantitative disease models as an innovative way to accelerate drug development, also recognized by EMA. CAMD developed the first regulatory submission of a drug-disease-trial model for AD. **Methods:** CAMD is based on the value of sharing non-competitive data, to generate generalizable and applicable knowledge for Alzheimer's and Parkinson's diseases. A coalition of sponsors, regulatory agencies, academic experts and patient groups developed an analysis plan for a drug-disease-trial model in mild and moderate AD patients with the ADAS-Cog cognition measure as the outcome. Data standardization and database development resulted in the creation of C-Path Online Data Repository (CODR) comprised of patient-level data from control arms of AD trials. Existing standards from the Clinical Data Interchange Standards Consortium (CDISC) were used, and new ones developed as needed. CAMD analyzed data from published literature, ADNI, and the CAMD-CODR database to develop the model. FDA and EMA input was critical to prepare the regulatory submission. **Results:** The drug-disease-trial model comprises functions for disease progression, placebo and drug effects, which can be combined to simulate clinical trials in mild and moderate AD. The final regulatory submission included a detailed analysis plan, with input from FDA, EMA, CAMD members, and external experts. It also included a detailed context of use for drug development, a description of the data used, analyses results, model development, covariate testing, predictive checks, external validation, and example applications for use in comparing trial designs. Key opinion leaders representing clinicians, statisticians, and pharmacometricians provided advisory input as to the context of use and suitability of the tool. **Conclusions:** The successful development of the current AD drug-disease-trial model was made possible by the consortium approach, and accelerated by continuous regulatory engagement. The model will be made publically available and represents a milestone to the pharmacometrics community as a way to encourage the advancement of drug-disease-trial models for a variety of diseases.

## P3-377 APATHY IN DEMENTIA METHYLPHENIDATE TRIAL (ADMET): RECRUITING FOR APATHY IN ALZHEIMER'S DISEASE

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**Background:** While apathy is now understood as a distinct syndrome in Alzheimer's disease (AD), definition and measurement of apathy have continued to evolve. As depression and apathy overlap in symptoms, applying a standardized definition of apathy is crucial in the context of treatment trials of AD. Clinically, identifying apathy is important as pharmacotherapy may differ. **Methods:** Patients with apathy were recruited for apathy in dementia methylphenidate trial (ADMET), a multi-site, 6-week, randomized placebo-controlled trial of the efficacy and safety of methylphenidate in mild-to-moderate AD. Included participants had a diagnosis of AD (NINCDS-ADRDA criteria) with mini-mental state exam (MMSE) scores $>10$, and were apathetic (Neuropsychiatric Inventory [NPI] Apathy subscale $\geq 4$). Patients with a major depressive episode (DSM-IV TR criteria) or psychotic symptoms were excluded. Cognition was assessed using the MMSE. Apathy and other behaviors were assessed using the Apathy Evaluation Scale (AES) and the NPI. **Results:** Results of the ADMET trial are expected in April 2012. In total, 60 patients were recruited (62% female, 92% Caucasian, mean (SD) age 76 $\pm$ 8 years, mean MMSE 20 $\pm$ 5). Recruited participants showed apathy on both the AES (51 $\pm$ 12), and NPI Apathy subscale (7.5 $\pm$ 2.3). The mean total NPI score was 16 $\pm$ 8, with low scores on the other subscales (1.6 $\pm$ 2.5 Depression/Dysphoria; 1.6 $\pm$ 2.8 Sleep; 1.2 $\pm$ 2.4 Aberrant Motor Behavior; 1.1 $\pm$ 2.1 Irritability; 1.0 $\pm$ 2.3 Appetite; 0.8 $\pm$ 1.3 Agitation; 0.7 $\pm$ 1.6 Anxiety, 0.4 $\pm$ 0.9 Disinhibition, 0.2 $\pm$ 0.6 Delusions, 0.1 $\pm$ 0.5 Hallucinations; 0.1 $\pm$ 0.6 Elation). Concomitant medications included cholinesterase inhibitors (72%), memantine (62%) and SSRIs (19%) and 13% of participants had a history of mood disorders. **Conclusions:** Trial participants had clinically significant apathy and very few other neuropsychiatric symptoms. The results of this trial, which is the first large-scale RCT to recruit specifically for apathy in AD, will provide information of relevance to treatment decisions in those with apathy.

## P3-378 THE DEVELOPMENT OF A DATA DICTIONARY AND SYNTAX FOR OPTIMIZING THE UTILIZATION OF THE COALITION AGAINST MAJOR DISEASES (CAMD) ALZHEIMER'S DISEASE CLINICAL TRIAL DATABASE

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**Background:** The CAMD AD clinical trial dataset represents a unique resource for the AD research community. Data on 5,952 patients from the placebo arms of 20 trials are available for retrospective analyses using a variety of statistical analysis programs. However, a data dictionary and data analytic syntax has yet to be publically provided for SPSS. Given the importance and complexity of this data it is essential to optimize the ease of database setup and analysis. The goal of this project was to develop a publically available set of syntax files to help facilitate review and analysis of the CAMD AD for SPSS users. **Methods:** Twelve data files containing data on demographics, lab values, medical history and test data were obtained. For this initial project, demographic data and neuropsychological test data (i.e., ADAS-Cog and MMSE) were reviewed using SPSS 20. The "DM" file containing demographic and site information has unique subject identifiers, 20 study IDs, and subjects from the US (52%) and 44 other countries. The "QS" file contained all MMSE and ADAS-Cog data (1,048,575 rows), the former includes 39 variables and the latter 109 possible variables. **Results:** When querying the database several important differences across studies emerged in terms of item coding and subtest content that require reconciliation before analyses. For example, MMSE includes WORLD in 1 dataset but serial 7s in the others. Also, ADAS-Cog data are coded at the item-level for 1 study but not others. ADAS-Cog total scores therefore must be derived, and the available options for this calculation are reviewed. These and other observations regarding the datasets have implications for future analyses and are discussed. **Conclusions:** Developing and sharing a common data dictionary and set of syntax files should help facilitate consistent and proficient retrospective analyses of the CAMD AD datasets among SPSS users eventually resulting in more efficient clinical trials of new AD treatments.

## P3-379 BENEFITS OF MEMANTINE IN THE TREATMENT OF ALZHEIMER'S DISEASE IN A NATURALISTIC SETTING

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**Background:** Adequate treatment of patients with Alzheimer's disease (AD) should also be valuable for caregivers. Efficient treatment regimes may lead to improvement of patient's every day competence and/or slower clinical progression of AD. Efficacy and tolerability of once-daily memantine treatment were investigated with regard to the patient's abilities and caregiver's quality of life. **Methods:** Prospective, multicentre, open, non-interventional study over 32 weeks including patients with diagnosed AD. Patients' cognitive abilities were assessed using Mini-Mental-Status