Table 1S Precision for Estimates of Rare Events of Interest with Sample Size of 630

Event Rate (Proportion)	Probability of Observing at least One Event	Precision (Half the Width of the 95% CI)
0.001	0.468	0.0025
0.0015	0.612	0.0030
0.002	0.717	0.0035
0.0025	0.793	0.0039
0.003	0.849	0.0043
0.0035	0.890	0.0046
0.004	0.920	0.0049
0.0045	0.942	0.0052
0.005	0.957	0.0055
0.05	1	0.017
0.10	1	0.023
0.12	1	0.025
0.15	1	0.028

Note: Precision is defined as half the expected width of the 95% confidence interval (CI) for the event rate, or the distance from the point estimate to the confidence boundary

Table 2S Participant Main Study (X) evaluations schedule during the follow-up period

Visit Window, Months (+/- 10 days)	Baseline	6	12	18	24	30	36	42	48/ ET[a]
Main Study visit Number (V)	**V0/V1 (w/in 30days of V1)**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**
Cognition									
RBANS	X	X	X	X	X	X	X	X	X
National Adult Reading Test (NART)[b]	X								
Neuropsychological Assessment Battery (NAB) Memory Module	X		X		X		X		X
Neuropsychological Assessment Battery (NAB) Executive Function Module			X		X		X		X
Mini-Mental State Examination (MMSE)	X		X		X		X		X
Cogstate Brief Battery[c]	X	X	X	X	X	X	X	X	X
Clinical Drug Research Assessment System[c]	X	X	X	X	X	X	X	X	X
Delis-Kaplan Executive Function System (DKEFS)[c]	X	X	X	X	X	X	X	X	X
Clinical Scales and Functional Outcome Measures									
Clinical Dementia Rating (CDR)	X	X	X	X	X	X	X	X	X
Mood									
Geriatric Depression Scale (GDS)[b]	X	X	X	X	X	X	X	X	
State-Trait Anxiety Inventory (STAI)[b]	X	X	X	X	X	X	X	X	
Patient Reported Outcome Measures & Physical Activity Revised Perceived Deficits Questionnaire (PDQ)	X	X	X	X	X	X	X	X	X
Work Productivity and Activity Impairment (WPAI)	X	X	X	X	X	X	X	X	X
Health Utilities Index Mark 3 (HUI3)	X	X	X	X	X	X	X	X	X
Imperial Lifestyle Questionnaire (baseline version)[d]	X								
Imperial Lifestyle Questionnaire (follow-up version)[d]		X	X	X	X	X	X	X	X
International Physical Activity Questionnaire (IPAQ)	X	X	X	X	X	X	X	X	X
Scottish Collaborative Group Food Frequency Questionnaire	X	X	X	X	X	X	X	X	X
Sleep									
Berlin Sleep Questionnaire[b, o]	X								

Visit Window, Months (+/- 10 days)	**Baseline**	**6**	**12**	**18**	**24**	**30**	**36**	**42**	**48/ ET[a]**
Main Study visit Number (V)	**V0/V1 (w/in 30days of V1)**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**
Pittsburgh Sleep Quality Index (PSQI)	X	X	X	X	X	X	X	X	X

Participants in the Main Study complete all MS visits conducted at ICL site only.
a. early termination (ET) Visits should be completed for participants with <42 months of follow-up data,
b. completed for all enrolled participants,
c Cogstate Brief Battery, Clinical Drug Research Assessment System, and DKEFS (ICL) are collected in ~33% of enrolled participants each according to the randomization schedule,
d Imperial Lifestyle Questionnaire (baseline and follow-up versions), IPAQ, and Scottish Collaborative Group Food Frequency Questionnaire are at ICL site

Figure 1S CHARIOT-PRO Main Study Participation and Disposition by *APOE* ε4 status

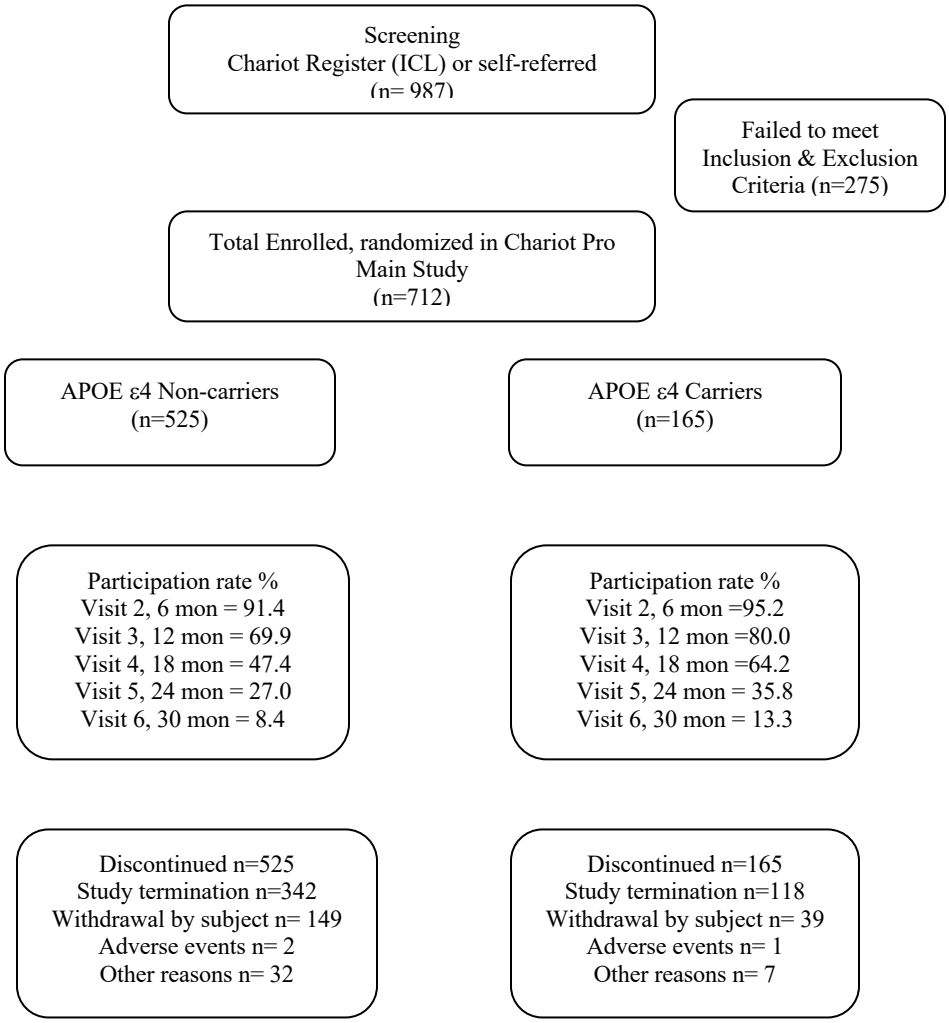

Table 3S STROBE statement checklist for the CHARIOT PRO Main study

Item No	Checklist Item	Requirement/s	Explanation	Page Reference
1	Title and abstract	(a) Indicate the study's design with commonly used term in title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and found	Prospective evaluation of cognitive health in a community-based register of elderly without dementia in United Kingdom.	
	Introduction			
2	Background/rationale	Explain the scientific background and rationale	There is limited information on people with minimal cognitive changes who are likely to progress to both the earliest stage of cognitive impairment due to Alzheimer's disease (AD) and then to clinically evident dementia. The goal of main study is to better understand the natural history of cognitive and functional changes in participants asymptomatic at risk for developing AD. Further determine what baseline measures are sensitive at predicting longitudinal AD related cognitive and functional decline.	
3	Objectives	State specific objectives, including any prespecified hypotheses	1) To describe the baseline characteristics, including demographics, cognitive status, and other measures of persons at risk for developing AD. 2) To describe cognitive and functional changes among persons at risk for developing AD	
	Methods			
4	Study design	Present key elements of study design early on	A prospective single center study of participants 60 to 85 years with varying levels of risk (high, medium and low for developing mild cognitive impairment-AD were recruited from CHARIOT register at Imperial College London (ICL) and referral centers in ICL catchment area. Approximately 700 were enrolled and randomly assigned (1:1:1) to complete one of three supplemental tests. A series of neuropsychological evaluations were performed every 6 months until termination. The study was	

Item No	Checklist Item	Requirement/s	Explanation	Page Reference
			terminated early by the sponsor with a median follow-up time of 18.1 months.	
5	Setting	Describe the setting, locations and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Participants in the CHARIOT prospective cohort study were either self-referred or recruited from the CHARIOT register with approximately 24 months for recruitment managed by Imperial College of London. The study was conducted at ICL from February 2014 to December 2016. Participants underwent a series of neuropsychological evaluations at baseline visit and at 6 month intervals during the median follow-up period of18 months. Schedule of assessments for scales and participant outcomes are given in Table 2.	
6	Participants	Cohort study- Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Eligibility of participants aged 60-85 years without dementia was based on prospective cohort risk group classification and other criteria assessed in two separate baseline visits, V0 and V1 (within 30 days). Excluded participants diagnosed with MCI or met clinical criteria for AD dementia or any degenerative brain disorder associated with dementia, chromosome 21 trisomy, whose age-and education adjusted baseline cognitive performance was >1.5 standard deviation below normal on any RBANS index score, and or meeting exclusion criteria. Data collection occurred at baseline and every 6 months thereafter at the clinic during the follow-up period of median 18 months.	
7	Variables	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria if applicable	Eligible participants classified high, medium or low risk for developing MCI-AD based on the initial RBANS performance ,were randomized in a balanced manner to 1 of 3 supplemental tests (CogState, Clinical Drug Research Assessment System, or Delis Kaplan Executive Function System).	

Item No	Checklist Item	Requirement/s	Explanation	Page Reference
			Outcome measures given in Table 2 consisted of assessments of: (a) Cognition (ADCS-PACC, RBANS, MMSE, NAB function and memory modules, NART, CogState, CDR, DKEFS); (b) Clinical scales (clinical dementia rating scale, CFI self and study partner, ADCS_ADL-PI); (c) Mood (GDS, State Trait Anxiety Inventory); (d) Patient reported outcome and physical activity (PDQ, WPAI, HUI3, Imperial Lifestyle Questionnaire baseline and follow-up versions, IPAQ, Actigraphy, Scottish Collaborative Group Food Frequency Questionnaire); (e) Sleep (Berlin Sleep Questionnaire-baseline, Pittsburgh Sleep Quality Index).	
8	Data sources/measurement	For each variable of interest, give sources of data and details of methods of assessment.	All study data collected and transcribed by study-site personnel from source documents are captured onto case report forms using electronic data capture tool, and completed as soon as possible after a subject visit to be available for review at the next scheduled monitoring visit.	
9	Bias	Describe any efforts to address potential sources of bias	Data collection included participant retention, and data completeness to minimize potential bias introduced by differential dropouts and missing information.	
10	Study size	Explain how the study size was arrived at	Planned sample size was selected to provide sufficient likelihood of detecting a rare event for the assumed 630 participants followed for at least 1 year with 10% annual dropout rate. Table provided to show event rate in terms of proportions, probability of observing at least one event and the calculated precision (half the width of the 95% CI) for an estimated sample size of 630 participants in the main study. The planned sample size for the main study was 700 enrolled participants (estimated 840 screened).	
11	Quantitative variables	Explain how quantitative variables were analyzed, and	All outcome measures are described in the manuscript. In the	

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		if applicable, which groupings were chosen and why	main study measured outcomes are given with descriptive statistics. Changes from baseline to all available time-points for cognitive measures including disease progression, mood, functional impairments, and quality of life were reported using descriptive statistics with point estimates and 95% confidence interval; and when applicable, nominal p values with a 2-sided alpha level 0.05. For study endpoints with normative data results were normalized based on age-and/or education corrected data. Time to progression and rate of progression analyzed overall and also in demographic and clinical subgroups reported with point estimates and 95% CI and when applicable nominal p-values with a 2-sided alpha level of 0.05. Participant factors related to initiation of therapy, switching therapy, regimen change or discontinuation were assessed.	
12	Statistical methods	(a) Describe statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) Cohort study- if applicable, explain how loss to follow-up was addressed	Standard descriptive analyses performed on qualitative and quantitative data (disease progression, mood, functional impairments and quality of life) and for participant demographics and baseline characteristics. Numerical variables reported as mean, standard deviation, median, 25^{th} and 75^{th} quartiles and range. Change from baseline measures as point estimate with 95% CI. Proportions of participants with observed data reported with 95% CI. Exploratory subgroup analyses performed when applicable. Baseline characteristics were described by demographics, by measures of cognition and by clinical subgroups according to subjects' *APOE* ε4 status The duration of follow-up at the study termination was not adequate to permit robust longitudinal modeling of the neuropsychological outcomes	

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			Multiple approaches to deal with missing data considered. Outreach to participants that are not seen at their regularly scheduled bi-annual visit followed a 2-step approach. First, 3 attempts were made to contact the participant (via email or telephone within 1 week) to determine their health status and then if needed a second step involved contact by a regular mail letter with delivery confirmation sent to participant's home. If the participant fails to respond to all outreach attempts they will be considered lost to follow-up.	
	Results			
13	Participants	Report numbers of individuals at each stage of study- e.g. potentially eligible, examined for eligibility, confirmed eligible, completing follow-up and analyzed Give reasons for non-participation at each stage Consider use of a flow diagram		
14	Descriptive data	(a) Give characteristics of study participants (e.g. demographics, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Cohort study- summarise follow-up time (e.g. average and total amount)		
15	Outcome data	Cohort study- Report numbers of outcome events or summary measures over time		
16	Main Results	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval).		

Item No	Checklist Item	Requirement/s	Explanation	Page Reference
		(b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		
17	Other analyses	Report other analyses done		
	Discussion			
18	Key results			
19	Limitations			
20	Interpretation			
21	General disability			
	Other information			
22	Funding			

Note: STROBE= Strengthening the reporting of observational studies in epidemiology. STROBE checklist available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.co/. CHARIOT = Cognitive health in aging register: investigational, observational, and trial studies in dementia research, PRO= Prospective readiness cohort study