

<p>List any papers in which cleaned/derived variables have been used</p>	<ul style="list-style-type: none"> • Lu <i>et al.</i> (2019) Cognition at age 70: life course predictors and associations with brain pathologies, <i>Neurology, in press</i> • Characterising cognition in later life and its relationship with biomarkers of Alzheimer's disease: a study of members of the National Survey of Health and Development (the British 1946 birth cohort). PhD thesis (Kirsty Lu) • Blood and cerebrospinal fluid biomarkers in Alzheimer's disease – from clinical to preclinical cohorts. PhD thesis (Ashvini Keshavan). • Plasma amyloid, tau and serum neurofilament light chain in Insight 46 – associations with cognition and brain imaging. AAIC 2019 poster (Keshavan et al.)
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* See list of categories on Swift

± Please delete as appropriate

Background to cognitive tests

Full details of these cognitive tests have been published in the following two papers:

- Lane *et al.* (2017) Study protocol: Insight 46 – a neuroscience sub-study of the MRC National Survey of Health and Development, *BMC Neurology*, 17:75, doi: 10.1186/s12883-017-0846-x
- Lu *et al.* (2019) Cognition at age 70: life course predictors and associations with brain pathologies, *Neurology, in press*

A summary is provided below:

The **Mini Mental State Examination (MMSE)** is a 30-point composite screening tool for cognitive impairment which is widely used within clinical practice (Folstein, M. F., Folstein, S. E. and McHugh, P. R. (1975) "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician., *Journal of Psychiatric Research*, 12(3), pp. 189–198. doi: 10.1016/0022-3956(75)90026-6). The item-by-item scores are provided in this dataset, as well as the total score.

Digit-Symbol Substitution from the Wechsler Adult Intelligence Scale-Revised is an index of executive function and psychomotor speed (Wechsler D. (1981b) *Wechsler Adult Intelligence Scale - Revised*. San Antonio, TX: The Psychological Corporation). The score is the number of items completed correctly within 90 seconds.

Logical Memory IIa from the Wechsler Memory Scale assesses free recall of a short story, which the participant is asked to recall immediately and after a delay of approximately 20 minutes (Wechsler D. (1987) *Wechsler Memory Scale - Revised: Manual*. San Antonio, TX: Psychological Corporation). The maximum score is 25. The exact delay duration is recorded so that it can be accounted for in analyses.

The **Face-Name test (FNAME-12)** assesses associative memory for face-name and face-occupation pairs (Papp, K. V *et al.* (2014) *Development of a psychometrically equivalent short form of the Face-Name Associative Memory Exam for use along the early Alzheimer's disease trajectory*, *Clin Neuropsychol.* 2014/05/13, 28(5), pp. 771–785. doi:10.1080/13854046.2014.911351).

Two versions exist: FNAME-12A and FNAME12-B. This study used FNAME-12A. Participants are shown 12 unfamiliar face-name and face-occupation pairs (e.g. "Sarah, Reporter"),

with 8 seconds to study each one. They are then presented with each face and asked to recall the associated name and occupation. This process is repeated with a second learning phase and a second recall test. After a ~10-minute delay they are again shown each face and asked to recall the names and occupations (the third recall test). After a ~30-minute delay participants are shown 12 sets of three faces and asked to identify each previously learned face from the two distractors (facial recognition) and to recall the name and occupation (the fourth recall test). If they cannot recall the name and/or occupation, they are asked to select the correct answer from three options comprising: the correct answer, a distractor (a name/occupation that belongs with a different face in the set), and a name/occupation that did not feature in the set. The summary outcomes are FN-N (total names recalled, max. 48), FN-O (total occupations recalled, max. 48) and FNAME-total (FN-N + FN-O, max. 96) – these outcomes are based on the four recall tests.

The **Matrix Reasoning** test assesses non-verbal reasoning, an aspect of fluid intelligence (Wechsler D. (1999) *The Wechsler abbreviated scale of intelligence*. San Antonio, TX: The Psychological Corporation). Participants are shown a matrix of geometric shapes and are required to select the missing piece from five options. There are 32 matrices, graded in difficulty, and the test is discontinued when participants make four consecutive errors (or four errors within five consecutive items), as specified in the manual. Note that the full test contains 35 items but the final 3 items are only to be administered to younger adults, as per the instructions in the manual, so were not used in Insight 46.

Data cleaning

One participant did not complete the full FNAME test, and therefore her total scores (Ffnn, Ffno, Ftot) automatically generated in XNAT were not valid. These total scores were changed to missing. A note to explain this was added to the Fwn variable for this participant.

On the MMSE, It was noted that 2 participants who failed to name all 3 items correctly on the first attempt (see question 11 in the MMSE form below) had missing data for their second attempt. This omission does not affect their MMSE score, since the score for the naming items is based solely on the first attempt. This is likely to be an administration error, as other versions of the MMSE do not require multiple attempts on this question.

No other data-cleaning was required.

Calculation of the Preclinical Alzheimer Cognitive Composite (PACC)

The four components of our version of the PACC were: MMSE total score, Logical Memory delayed recall score, Digit-Symbol Substitution score and FNAME-total. The four components were converted into z-scores based on the full Insight 46 sample, using the following Stata command:

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egen newvar = std(oldvar)
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The four z-scores were then averaged. A higher PACC score indicates better performance. Two participants did not complete the FNAME test and one did not

complete the Digit-Symbol Substitution test. For these three participants, their PACC score was the average of the z-scores for the three tests they completed.

Note that the original PACC (Donohue, M. C. et al. (2014) 'The preclinical Alzheimer cognitive composite: measuring amyloid-related decline.', *JAMA neurology*, 71(8), pp. 961–70. doi: 10.1001/jamaneurol.2014.803) contained the Free and Cued Selective Reminding Test (FCSRT) instead of FNAME. We replaced the FCSRT with FNAME to avoid potential overlap with a similar word-learning memory test administered to the NSHD cohort at multiple time-points throughout adulthood.

MMSE XNAT form - annotated in red with names of variables contained in this dataset

May I ask you some questions about your memory? Ecomp		<input type="checkbox"/> 0 No	
		<input type="checkbox"/> 1 Yes	
		<input type="checkbox"/> 2 Unable for health reasons	
		<input type="checkbox"/> 3 Unable, other _____	
		If 0, 2 or 3 are ticked, specify reason Ewn	
ORIENTATION			
1	What is the year? _____ Eyear	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
2	What is the season? _____ Eseason	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
3	What is the date? __/__/____ (DD/MM/YYYY) Edate	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
4	What is the day of the week? _____ Eday	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
5	What is the month? _____ Emonth	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
6	Can you tell me where you are now? For instance what country are we in? _____ Ecountry	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
7	What is the name of this city? _____ Ecity	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
8	What area of the city are we in? Earea	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
9	What floor of the building are we on? _____ Efloor	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
10	What is the name of this place? _____ Ename	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
REGISTRATION			
11	I am now going to name three objects. The three objects are: APPLE, TABLE, PENNY. Please repeat the name of these three objects back to me. <i>Record the FIRST responses (order of object recall does NOT matter):</i>		
	First object named? _____ Ereg_firstI	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Second object named? _____ Ereg_secondI	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Third object named? _____ Ereg_thirdI	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	If all three objects are repeated correctly (in any order) go to Q12a If the participant does not repeat all three words exactly then allow them two further attempts but DO NOT change their first responses or scores.		

	<p>Attempt 2: I'm going to repeat once more the three objects, APPLE, TABLE, PENNY. Please say them back to me. Ereg_first2 Ereg_second2 Ereg_third2</p> <p>Attempt 3: Can we try one more time? The names are, APPLE, TABLE, PENNY. Please say them back to me. Ereg_first3 Ereg_second3 Ereg_third3</p>		
ATTENTION AND CALCULATION			
12a	Please take seven away from one hundred (Answer: 93) Answer 1: __ _ Esubtract1	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Now I'm going to ask you to take seven away from what you have left over, and then keep taking seven away until I stop you. (Answers: 86, 79, 72 and 65. If the participant gets an answer wrong but then takes seven away correctly from that answer you should score as correct). Answer 2: __ _ Esubtract2	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Answer 3: __ _ Esubtract3	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Answer 4: __ _ Esubtract4	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Answer 5: __ _ Esubtract5	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	If the participant scores 5/5 then go to Q13. If the participant scores less than 5/5 for 12a then complete question 12b.	Total score: _ /5 Esubtract_tot	
12b	Please spell "WORLD" backwards (Answer: D L R O W) <div style="display: flex; justify-content: space-around; width: 100px;"> <div style="border: 1px solid black; width: 30px; height: 30px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 30px; height: 30px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 30px; height: 30px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 30px; height: 30px; display: flex; align-items: center; justify-content: center;"> </div> <div style="border: 1px solid black; width: 30px; height: 30px; display: flex; align-items: center; justify-content: center;"> </div> </div>	TOTAL number of letters in correct order _ /5 Ebackwards	
	Highest score for subtraction or backwards spelling tests	_ /5 Ehighest (note that this variable is only entered for participants who were administered item 12b)	
RECALL			
13	Please name the three objects that I mentioned to you earlier?		
	First object named _ _ _ _ _ Erecall_first	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Second object named _ _ _ _ _ Erecall_second	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
	Third object named _ _ _ _ _ Erecall_third	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
NAMING			
14	What is this called? (show watch) _ _ _ _ _ Ewatch	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
15	What is this called? (show pen) _ _ _ _ _ Epen	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
REPETITION			
16	I am going to say a sentence to you and I would like you to repeat it after I have said it. The sentence is: "NO IFS, ANDS OR BUTS." Did the participant answer correctly? Do not repeat the sentence. If necessary say: I'm sorry, I'm only allowed to say the sentence once. Erepetition	<input type="checkbox"/> 0 Incorrect	<input type="checkbox"/> 1 Correct
THREE STAGE COMMAND			

17	Please take this paper with your right hand, fold it in half and put it on your lap. Do not repeat the sentence. If necessary say: I'm sorry, I'm only allowed to read that out once. Did the participant take the paper in their right hand? Erighthand	<input type="checkbox"/> 0 No	<input type="checkbox"/> 1 Yes
	Did the participant fold the paper in half or quarter (both allowed)? Efolded	<input type="checkbox"/> 0 No	<input type="checkbox"/> 1 Yes
	Did the participant put the paper on their lap? Elap	<input type="checkbox"/> 0 No	<input type="checkbox"/> 1 Yes
READING			
18	Now give the sheet called "MMSE CLOSE YOUR EYES" to the participant and say: Please read the sentence at the top of this sheet and do what it says. Did the participant close their eyes? Ereading	<input type="checkbox"/> 0 No	<input type="checkbox"/> 1 Yes
WRITING			
19	Please write a sentence in the space here. Indicate the space under "Write a sentence". Did the participant write a sentence? Esentence	<input type="checkbox"/> 0 No	<input type="checkbox"/> 1 Yes
20	Please copy this drawing. Indicate the space to the right of the design. Did the participant copy the drawing correctly? Edrawing	<input type="checkbox"/> 0 No	<input type="checkbox"/> 1 Yes
Score		__ /30 Es	

Logical Memory Immediate Recall XNAT form - annotated in red with names of variables contained in this dataset

WMS Logical Memory – Immediate Recall completed Licomp	<input type="checkbox"/> 0 No
	<input type="checkbox"/> 1 Yes
	<input type="checkbox"/> 2 Unable for health reasons
	<input type="checkbox"/> 3 Unable, other (Specify)_____
	If 0, 2 or 3 are ticked, specify reason Liwn
Total number of story units recalled:	__ /25 Lis

Logical Memory Delayed Recall XNAT form - annotated in red with names of variables contained in this dataset

WMS Logical Memory – Delayed completed Ldcomp	<input type="checkbox"/> 0 No
	<input type="checkbox"/> 1 Yes
	<input type="checkbox"/> 2 Unable for health reasons
	<input type="checkbox"/> 3 Unable, other (Specify)_____ Ldwn
	If 0, 2 or 3 are ticked, specify reason Ldwn

Total number of story units recalled:	__ __ /25 Lds
Time elapsed since Logical Memory-Immediate:	__ __ (minutes) Lt

Matrix Reasoning XNAT form - annotated in red with names of variables contained in this dataset

WASI Matrix Reasoning completed Mcomp	<input type="checkbox"/> 0 No
	<input type="checkbox"/> 1 Yes
	<input type="checkbox"/> 2 Unable for health reasons
	<input type="checkbox"/> 3 Unable, other (Specify) _ _ _ _ _ _ _ _ Mwn
	If 0, 2 or 3 are ticked, specify reason Mwn
Total correct:	__ __ /32 Ms

Digit-Symbol XNAT form - annotated in red with names of variables contained in this dataset

WAIS Digit Symbol Substitution Test completed Wcomp	<input type="checkbox"/> 0 No
	<input type="checkbox"/> 1 Yes
	<input type="checkbox"/> 2 Unable for health reasons
	<input type="checkbox"/> 3 Unable, other (Specify) _ _ _ _ _ _ _ _ Wwn
	If 0, 2 or 3 are ticked, specify reason Wwn
Total correct:	__ __ /93 Ws

FNAME XNAT form - annotated in red with names of variables contained in this dataset

Face Name Associative Memory Exam completed Fcomp	<input type="checkbox"/> 0 No
	<input type="checkbox"/> 1 Yes
	<input type="checkbox"/> 2 Unable for health reasons
	<input type="checkbox"/> 3 Unable, other (Specify) _ _ _ _ _ _ _ Fwn
	If 0, 2 or 3 are ticked, specify reason Fwn
Learning Trial 1	
INR1: Finr1	__ __ /12
IOR1: Fior1	__ __ /12
Learning Trial 2	
INR2: Finr2	__ __ /12
IOR2: Fior2	__ __ /12

Total INR: Finrt	__ /24
Total IOR: Fiort	__ /24

Cued Name and Occupation Recall	
CRN: Fcrn	__ /12
CRO: Fcro	__ /12

Delayed Cued Recall of Names and Occupations	
Facial Recognition Frecog	__ /12
CRN 30: Fcrn30	__ /12
CRO30: Fcro30	__ /12
MCN: Fmcn	__ /12
MCO: Fmco	__ /12
Totals	
FN-N (Total INR + CRN + CRN30) Ffnn	__ /48
FN-O (Total IOR + CRO + CRO30 Ffno)	__ /48
Total FNAME Score (CN-N + FN-O) Ftot	__ /96