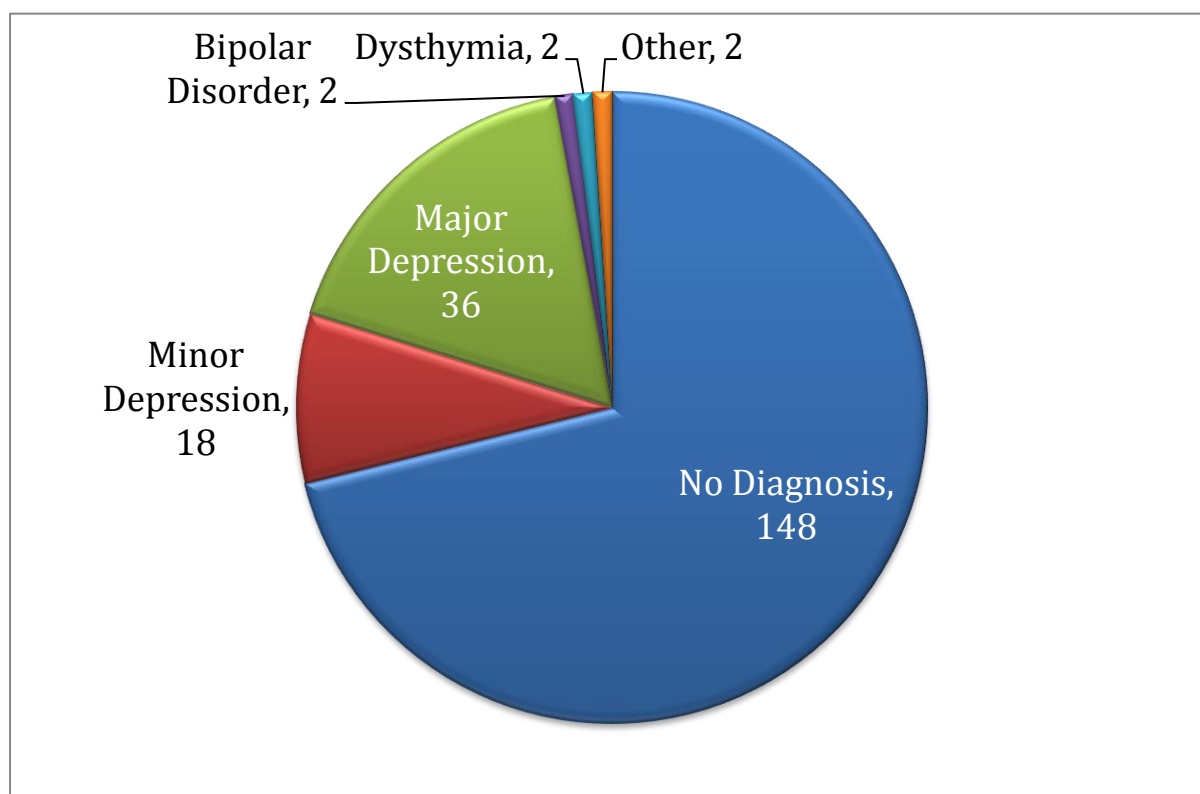


### SCID-Diagnoses in 208 participants:



### Psychometric tests used:

- SCID<sup>1</sup>
- Montreal Cognitive Assessment (MoCA)<sup>2</sup>
- Trail Making Test (TMT A and B)<sup>3,4</sup>
- Ray-Osterrieth Complex Figure (RCF) copy, immediate, delay, recognition<sup>5</sup>
- Category fluency<sup>6</sup>
- Hopkins Verbal Learning Test (HVLT-R) immediate, delay, recognition<sup>7</sup>
- Boston Naming Test (BNT)<sup>8</sup>
- Digit span<sup>9</sup>
- Digit coding<sup>10</sup>
- Test of Premorbid Function (TOPF)<sup>11</sup>

The MoCA is a 30-point cognitive screening test with subtests for verbal recall, clock-drawing, cube copying, phonemic fluency, attention task, naming and orientation, amongst others. The TMT requires subjects to ‘connect the dots’ of twenty-five consecutive targets on a sheet of paper as fast as possible. In TMT A the targets are numbers, and in TMT B alternating numbers and letters. The RCF involves initially copying and then recalling a complex geometric diagram at increasing time intervals. In the HVLT-R task the subject must recall a list of twelve words over the course of three trials immediately and after a delay. The BNT examines semantic memory and requires naming of a series of images shown to the participant. Digit Span includes recall of a lengthening list of digits forwards, backwards, and rearranged in ascending order (DSF, DSB, DSS). In Digit Coding, participants have to write the appropriate novel symbol for each number under time pressure. The TOPF consists of a

list of written words, which must be read aloud and is marked according to pronunciation. Premorbid IQ can be calculated from the raw score, adjusted for sex and years of education.

## MRI acquisition

Multi-modal MRI scans were acquired at the FMRIB centre, University of Oxford using a 3 Tesla, Siemens scanner with a 32-channel head coil. Structural images were acquired using a high-resolution three-dimensional T1-weighted sequence: repetition time 2530 ms, echo time 7.37 ms, flip angle 7°, field of view 256mm and voxel dimensions 1.0x1.0x1.0 mm. T2-weighted FLAIR (Fluid Attenuated Inversion Recovery) images, used to characterise white-matter changes were acquired with: repetition time 9000 ms, echo time 73.0 ms, flip angle 150°, field of view 220 mm and voxel dimensions 0.9x0.9x3.0 mm. For further information see Filippini et al.<sup>12</sup>

**Table DS1 Comparison of MRI sample of 208 with Phase 11 sample**

Variable	MRI Sample			Phase 11 Participants		
	N	Mean	S.D.	N	Mean	S.D.
<b>Age [years]</b>	208	69.2	5.3	6306	69.8	5.9
<b>Sex</b>	207	100%		6306		
<i>Female</i>	39	<b>18.8%</b>		1947	29.3%	
<i>Male</i>	169	<b>81.3%</b>		4459	70.7%	
<b>Socio-economic Stratum</b>	206	100%		5771		
<i>Executive</i>	121	<b>58.7%</b>		2743	47.5%	
<i>Professional</i>	77	37.4%		2470	42.8%	
<i>Clerical</i>	8	<b>3.9%</b>		558	9.7%	
<b>Full time education [years]</b>	208	<b>14.6</b>	3.4	5101	15.1	4.2
<b>CES-D</b>	208	<b>6.0</b>	7.0	5855	7.3	7.6
<b>Alcohol [U/week]</b>	200	<b>16.5</b>	15.6	6227	9.5	11.2
<b>BMI [kg/m<sup>2</sup>]</b>	208	26.5	4.4	5615	26.7	4.5
<b>Heart Rate [BPM]</b>	204	67.7	13.0	5634	68.1	12.2
<b>Systolic BP [mmHg]</b>	207	<b>143</b>	17.7	5652	127.8	16.5
<b>Diastolic BP [mmHg]</b>	206	<b>78</b>	10.0	5652	70.8	9.9

95% confidence intervals for difference between means are: Age: -1.34 to 0.14 years; Education: -0.98 to -0.02 years; CES-D: -2.35 to -0.25; Alcohol: 4.8 to 9.2 units/week; BMI: -0.82 to 0.42 kg/m<sup>2</sup>; HR: -2.11 to 1.31 BPM; Systolic BP: 12.9 to 17.5 mmHg; Diastolic BP: 5.8 to 8.6 mmHg. Sex: Chi<sup>2</sup> = 13.78; p = 0.0002. Social Class: Total Chi<sup>2</sup> = 14.51; |Chi| = 3.81 (2 DF); p = 0.0007.

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