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Supplementary Material

Article Title: Depression, Cognitive Functions, and Impaired Functioning in Middle-Aged Adults From the CONSTANCES Cohort

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Appendix 1

Assessment of depressive symptoms

The CES-D consists of 20 items that are designed to measure self-reported depressive symptoms during the week prior to the test ¹ with adequate internal consistency (Cronbach's alpha: 0.88 in the current sample). The total score ranged from 0 (no depressive symptom) to 60. We used a cut-off score of 19 (CES-D score ≥ 19 versus < 19) to define depression status, according to the validation study of the French version of the CES-D (sensitivity/specificity for the diagnosis of major depression: 0.853/0.859) ².

Assessment of cognitive functions

The DSST is a subtest of the Wechsler Adult Intelligence Scale-Revised, a timed paper- and pencil- task that measures psychomotor speed, sustained attention and logical reasoning ³. It consists of matching symbols with their corresponding numerical digit as fast as possible. The DSST score represents the number of correctly matched symbols in 120 seconds. TMT-B requires to draw lines sequentially connecting alternatively encircled numbers and letters (e.g., 1, A, 2, B, 3, C, etc.) distributed on a sheet of paper ⁴. The TMT-B score represents the amount of time required to complete the task. SVF requires participants to say as many words as possible from the "Animal" category in 60 seconds ⁵.

Assessment of functioning

The SF-12v2 is a widely used measure of health-related quality of life, with adequate reliability and validity ⁶⁻⁸. It measures eight health aspects, namely general health, physical functioning, role limitations due to physical health problems, bodily pain, vitality, social functioning, role limitations due to emotional problems, and mental health. Mental health and

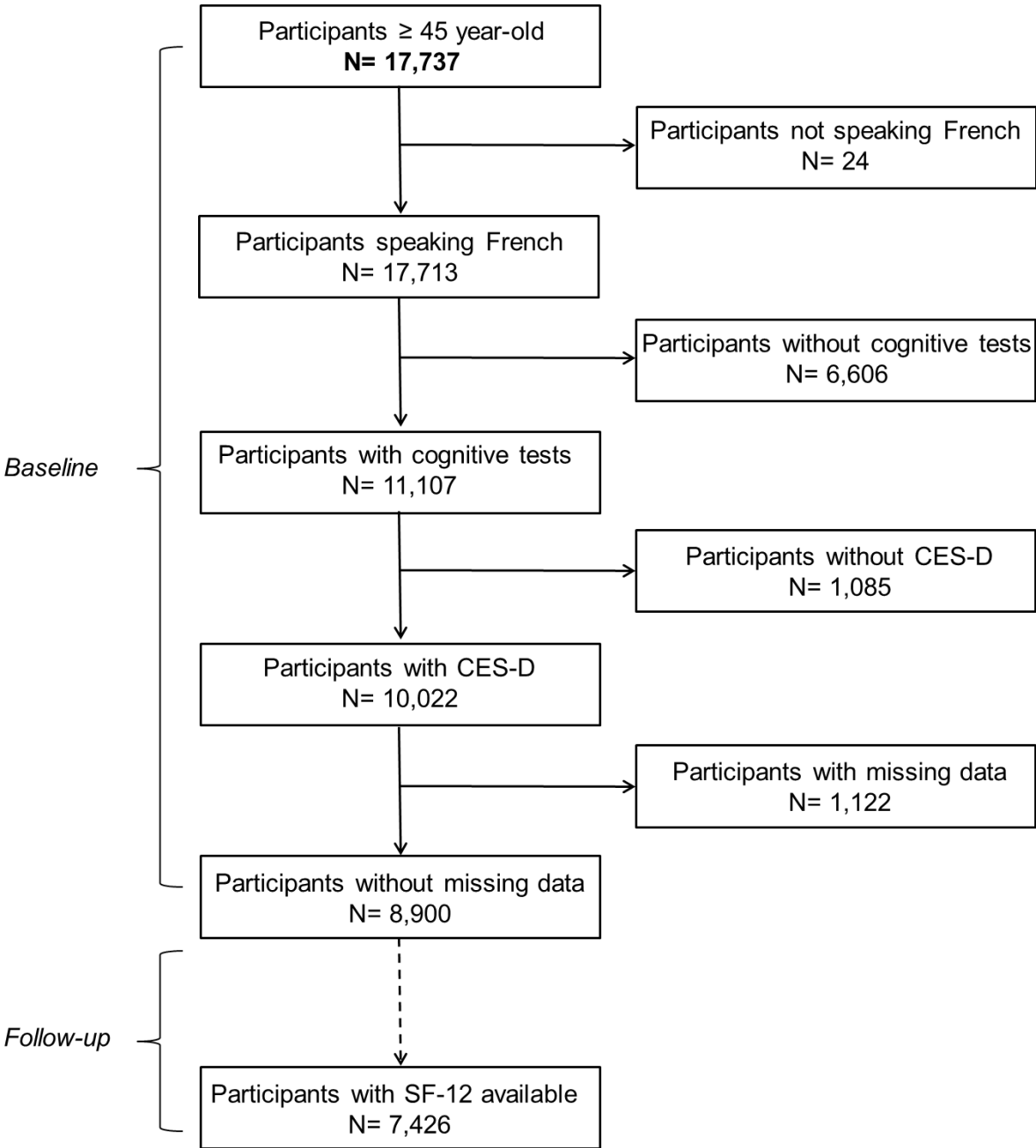
vitality subscales were not taken into account because of their obvious overlap with CES-D items ("Did you have a lot of energy?", "Have you felt downhearted and depressed?"). Because we were interested in functional impairment associated with depression specifically, we a priori decided to use two subscales as primary outcomes⁹: role limitations due to emotional problems and social functioning. These three items were rated from 1 ("All of the time") to 5 ("None of the time"), leading to a score from 2 to 10 for role limitations and from 1 to 5 for social functioning⁹. For both scales, a higher score corresponds with a better functioning. Role limitations due to emotional problems, henceforth referred to as "role limitations", was assessed with two items: "During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? 1) Accomplished less than you would like, 2) Did work or other activities less carefully than usual". Social functioning was assessed with one item: "During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?". These three items were rated from 1 ("All of the time") to 5 ("None of the time"), leading to a score from 2 to 10 for role limitations and from 1 to 5 for social functioning⁹. For both scales, a higher score corresponds with a better functioning.

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Supplementary Figure 1. Flow chart of the study population selection



Supplementary Table 1: Characteristics of participants according to depression status

(N=7426)

	Depression status					
	(CES-D score <19)		(CES-D score ≥19)		t	p
	N=6443		N=983			
Continuous variables	mean	sd	mean	sd		
Age	57.91	7.24	57.03	6.88	-3.70	<0.001
N of days between inclusion and FU	497.47	158.52	497.47	148.74	0.03	>0.99
CES-D score	7.34	4.91	26.56	6.95	83.53	<0.001
DSST score	67.55	14.99	65.48	15.62	-3.89	<0.001
TMT-B score	66.79	31.39	70.78	32.69	3.59	<0.001
SVF score	23.92	5.78	23.18	5.75	-3.78	<0.001
Role limitations	8.73	1.59	6.70	1.93	-31.56	<0.001
Social functioning	4.26	0.83	3.29	0.95	-30.37	<0.001
Discrete variables	N	%	N	%	χ ²	p
Sex					115.17	<0.001
Men	3238	50.26	313	31.84		
Women	3205	49.74	670	68.16		
Date of inclusion					1.11	0.29
2012	1046	16.23	146	14.85		
2013	5397	83.77	837	85.15		
Education level					30.77	<0.001
No diploma	103	1.60	27	2.75		

Lower secondary education	513	7.96	99	10.07		
Professional education	1207	18.73	203	20.65		
Upper secondary education	1104	17.13	197	20.04		
Bachelor	1477	22.92	211	21.46		
Fourth year university level	658	10.21	88	8.95		
Master degree or higher	1174	18.22	134	13.63		
Other	207	3.21	24	2.44		
Alcohol intake					53.38	<0.001
Never	189	2.93	45	4.58		
≤1glass/month	714	11.08	179	18.21		
2-3glasses/month	1224	19.00	187	19.02		
≥1glass/week	4316	66.99	572	58.19		
Life cannabis use					2.10	0.35
Yes	1140	17.69	192	19.53		
No	5263	81.69	786	79.96		
No intent to answer	40	0.62	5	0.51		

CES-D: Center for Epidemiologic Studies Depression Scale; DSST: Total score for Digit

Symbol Substitution Test; TMT-B: Total time for Trail Making Test B, SVF: Semantic Verbal

Fluency; FU: follow-up; sd: standard deviation; χ^2 : chi-square value; t: t value.

Supplementary Table 2: Characteristics of lost to follow-up participants and comparisons with the study population

	Participant status					
	Included in the study		Lost to follow-up			
	N=7426		N=1474			
Continuous variables	mean	sd	mean	sd	t	p
Age	57.80	7.20	57.19	7.23	-2.93	0.003
CES-D score	9.88	8.35	12.28	10.05	8.60	<0.001
DSST score	67.27	15.09	62.88	15.31	-10.08	<0.001
TMT-B score	67.32	31.60	75.38	38.20	7.60	<0.001
SVF score	23.82	5.78	22.51	5.76	-7.99	<0.001
Discrete variables	N	%	N	%	χ^2	p
Sex						
Men	3551	47.82	743	50.41	3.20	0.07
Women	3875	52.18	731	49.59		
Date of inclusion						
2012	1192	16.05	251	17.03	0.79	0.37
2013	6234	83.95	1223	82.97		
Education level						
No diploma	130	1.75	81	5.50	143.23	<0.001
Lower secondary education	612	8.24	195	13.23		
Professional education	1410	18.99	317	21.51		
Upper secondary education	1301	17.52	229	15.54		

Bachelor	1688	22.73	290	19.67		
Fourth year university level	746	10.05	102	6.92		
Master degree or higher	1308	17.61	204	13.84		
Other	231	3.11	56	3.80		
Alcohol intake					0.90	0.82
Never	234	3.15	44	2.99		
≤1glass/month	893	12.03	179	12.14		
2-3glasses/month	1411	19.00	266	18.05		
≥1glass/week	4888	65.82	985	66.82		
Life cannabis use					4.61	0.10
Yes	1332	17.94	274	18.59		
No	6049	81.46	1184	80.33		
No intent to answer	45	0.61	16	1.09		

CES-D: Center for Epidemiologic Studies Depression Scale; DSST: Total score for Digit

Symbol Substitution Test; TMT-B: Total time for Trail Making Test B, SVF: Semantic Verbal

Fluency; FU: follow-up; sd: standard deviation; χ^2 : chi-square value; t: t value.