

Supplementary Methods

1. Additional description of data collection

The data collection follows the protocol described in (Regan et al., 2010; Wan et al., 2018). Clinical parameters included: FEV1_FVC_pre (average Forced expiratory volume in one second over forced vital capacity pre-Broncho dilation); Resting_SaO2 (Oxygen saturation as measured by blood analysis) ; Distwalked (Distance walked in feet) ; BMI (Body mass index) ; SmokCigNow (Active cigarette smoking) ; cancer. The number of physical comorbidities other than COPD included: Pneumothorax, Angina, Atrial Fibrillation, Congestive Heart Failure, Coronary Artery Disease, Diabetes, High Blood Pressure, High Cholesterol, Heart Attack, Blood Clots, Macular Degeneration, Peripheral Vascular Disease, Stroke, TIA, Cognitive Disorder, Anemia, Gastro Esophageal Reflux, Kidney Disease, Liver Disease, Stomach Ulcers, Compression Fracture Back, Connective Tissue Diseases, Gout, Hip Fracture, Osteoarthritis, Osteoporosis, Rheumatoid Arthritis. The count of the number of medication for COPD included: long-acting beta2-agonists (LABAs), Combination of Corticosteroids and beta-agonists, Combination of LABAs and Long-acting muscarinic antagonists (LAMAs), ipratropium bromide and albuterol (Combivent), Inhalatory Corticosteroids, Oral Corticosteroids, ipratropium bromide, nebulizer, theophylline, tiotropium, Combivent Puffs, Macrolide Antibiotic, Phosphodiesterase 4 inhibitors.

2. Sensitivity analyses

The effect of continuous and ordinal sociodemographic factors (age, education, income) was examined by adding these variables as nodes in the network and by re-estimating its structure. The effect of categorical sociodemographic factors (gender and ethnicity) was examined by comparing networks from subsamples (i.e. males vs. females, white vs. African-Americans). Networks were compared for: a) their global structure, using a predictive check method, with Jensen-Shannon Divergence (JSD) as the discrepancy measure, and b) differences in each edge weight, by examining the posterior probability distribution for each edge difference (Williams et al., 2020). The effect of continuous clinical parameters was examined by adding these variables as nodes in the network and re-estimating its structure, while adjusting for age and gender.

3. Predicting psychopathology based on COPD symptoms: potential utility of network models

This is an illustrative example of how a network model could be used to make predictions about the clinical course of anxiety and depression in COPD. Specifically, we sought to simulate the changes in the severity of anxiety and depression symptoms (HADS-derived scores), given a pre-defined COPD symptom profile (CAT scores). Unlike using questionnaire sum-scores in, say, regression models, a network model could be used to predict the onset of a specific symptom profile. In our case, we used the CAT scores from two randomly-selected participants who had equal CAT scores (30), but a slightly different symptom profile (i.e. different severity of cough, chest tightness, weakness). We used the subjects' CAT scores to activate the network with a spreading activation across simulated timepoints. For this purpose we used the spread

R package 0.2.0 version (Siew, 2021). We arbitrarily set the levels of retention and decay for nodes representing HADS-derived (retention: 0.8, decay: 0.1) and CAT (retention: 0.5, decay: 0.6) symptoms to be compatible with a plausible time-dependent clinical trajectory. We present the results of the HADS-derived scores after an elapsed ten simulated timepoints.

Figure S1. Histograms of CAT and HADS sum-scores and their correlation

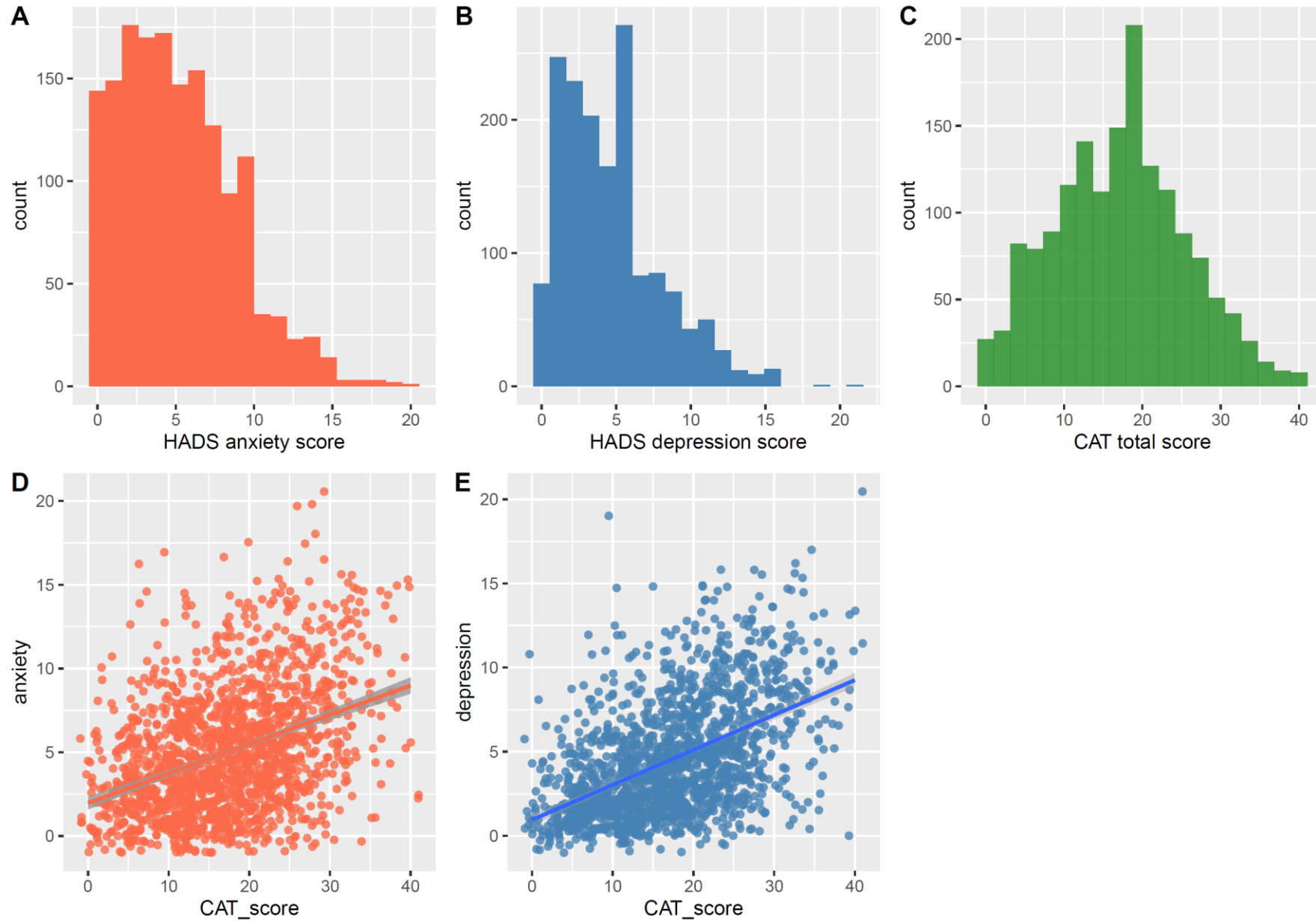
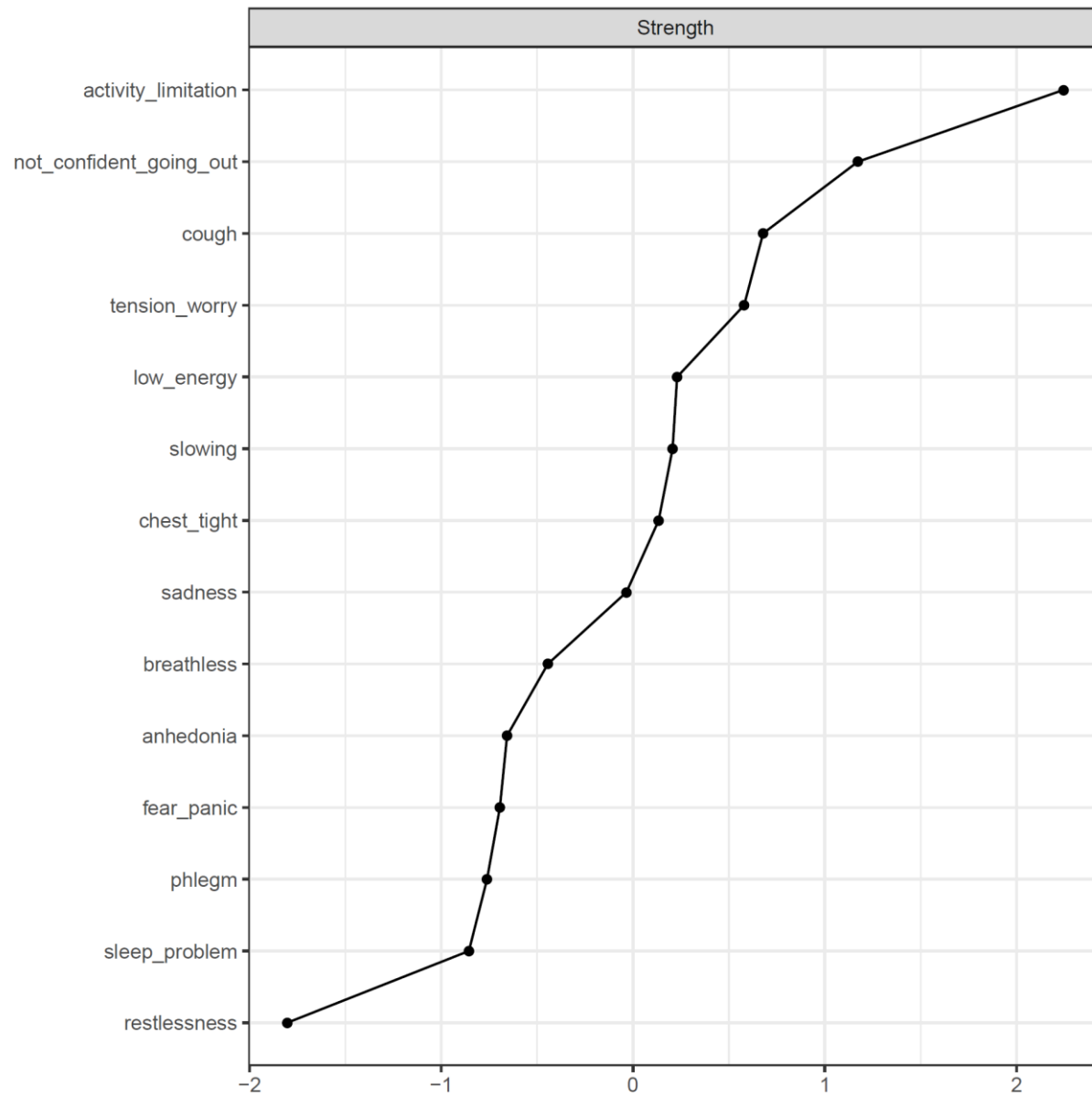


Table S2. Reduction of HADS items with Unique Variable Analysis

<i>14 original HADS items</i>	<i>Combined items</i>
I feel tense or 'wound up'	Tension/worry
Worrying thoughts go through my mind	
I can sit at ease and feel relaxed	
I get a sort of frightened feeling as if something awful is about to happen	Fear/panic
I get sudden feelings of panic	
I get a sort of frightened feeling like 'butterflies' in the stomach	
I feel restless as I have to be on the move	Restlessness
I still enjoy the things I used to enjoy	Anhedonia
I can enjoy a good book or radio or TV program	
I look forward with enjoyment to things	
I have lost interest in my appearance	
I can laugh and see the funny side of things	Sadness
I feel cheerful	
I feel as if I am slowed down	Slowing

Figure S3. Node strength centrality



Values of strength centrality are standardized (z-scores) sum of the connections of each node

Table S4. Node predictability

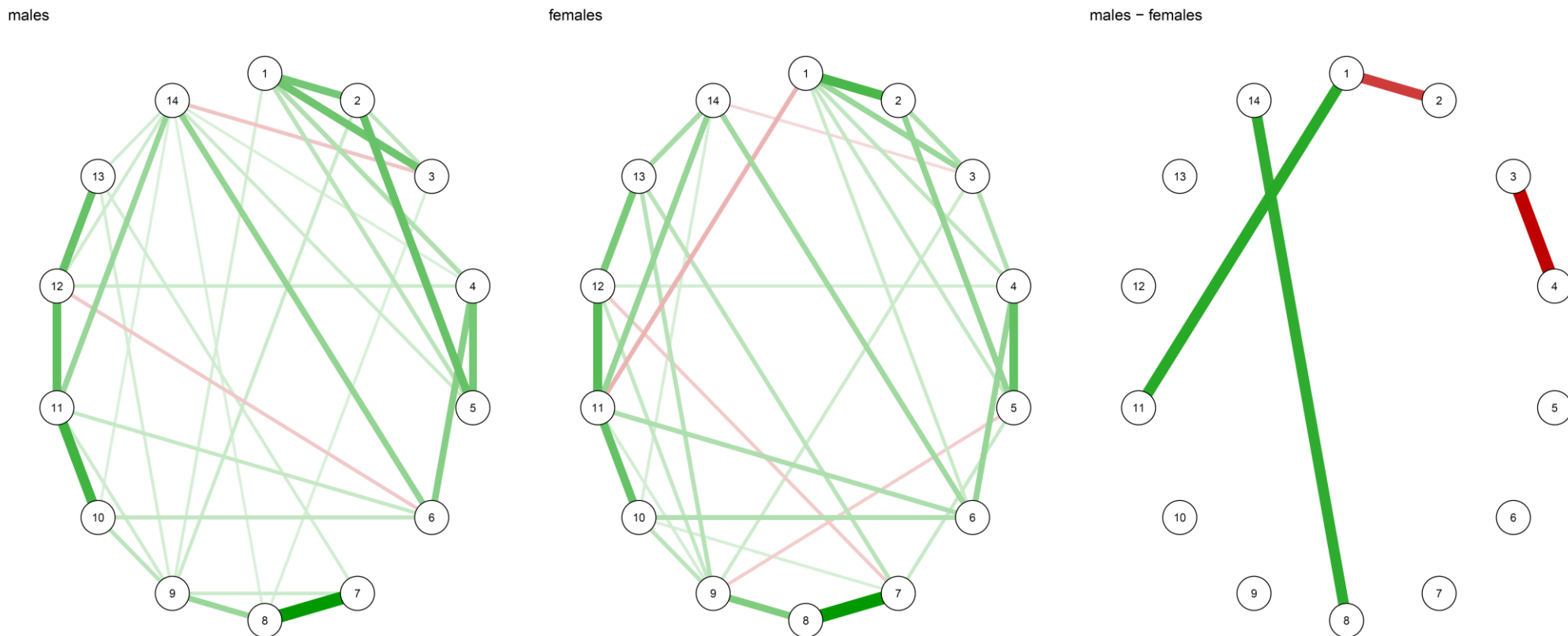
Node	Post.mean	Post.sd	Cred.2.5.	Cred.97.5.
Sadness	0.577	0.018	0.542	0.611
Lack of confidence going out	0.543	0.017	0.509	0.577
Activity limitations	0.535	0.018	0.5	0.572
Chest tightness	0.511	0.018	0.477	0.546
Phlegm	0.506	0.017	0.474	0.541
Fear/panic	0.493	0.017	0.46	0.529
Anhedonia	0.490	0.021	0.448	0.532
Low energy	0.453	0.018	0.416	0.489
Tension/worry	0.427	0.017	0.392	0.461
Cough	0.417	0.017	0.385	0.449
Slowing	0.380	0.019	0.342	0.417
Sleep problems	0.329	0.016	0.299	0.363
Restlessness	0.275	0.017	0.241	0.306
Breathlessness	0.258	0.013	0.234	0.285

In-sample predictability from bayesian posterior probability R^2 values (with 95% Credible Intervals). Values indicate the shared covariance of each node explained by other neighbor nodes in the network (e.g. 0.577 = 57.7%)

Table S5 Network of HADS-derived symptoms with sociodemographic factors

	tension_worry	fear_panic	restlessness	anhedonia	sadness	slowing	cough	phlegm	chest_tight	breathless	activity_limitation	not_confident_going_out	sleep_problem	low_energy	age_visit	School Completed	Income
tension_worry		0.38	0.24	0.18	0.11						-0.11	0.06				-0.09	
fear_panic	0.38		0.17		0.21				0.07						-0.10		-0.06
restlessness	0.24	0.17							0.08				0.10	-0.10			0.09
anhedonia	0.18				0.29	0.24						0.11		0.06	-0.09		-0.13
sadness	0.11	0.21		0.29		0.12	0.10		-0.06					0.14		0.17	0.13
slowing				0.24	0.12					0.17	0.15	-0.08		0.24	0.13	0.10	
cough					0.10			0.59	0.06	0.10		-0.09	0.12		-0.07		
phlegm								0.59	0.27								
chest_tight		0.07	0.08		-0.06		0.06	0.27		0.14	0.11	0.11	0.12		-0.09		
breathless						0.17	0.10		0.14		0.39			0.10			
activity_limitation	-0.11					0.15			0.11	0.39		0.37		0.24		-0.07	
not_confident_going_out	0.06			0.11		-0.08	-0.09		0.11		0.37		0.31			-0.07	-0.09
sleep_problem			0.10				0.12		0.12			0.31		0.16	-0.08		
low_energy			-0.10	0.06	0.14	0.24				0.10	0.24		0.16				
age_visit		-0.10		-0.09		0.13	-0.07		-0.09				-0.08			0.11	0.15
School Completed	-0.09				0.17	0.10					-0.07	-0.07			0.11		0.21
Income		-0.06	0.09	-0.13	0.13							-0.09			0.15	0.21	

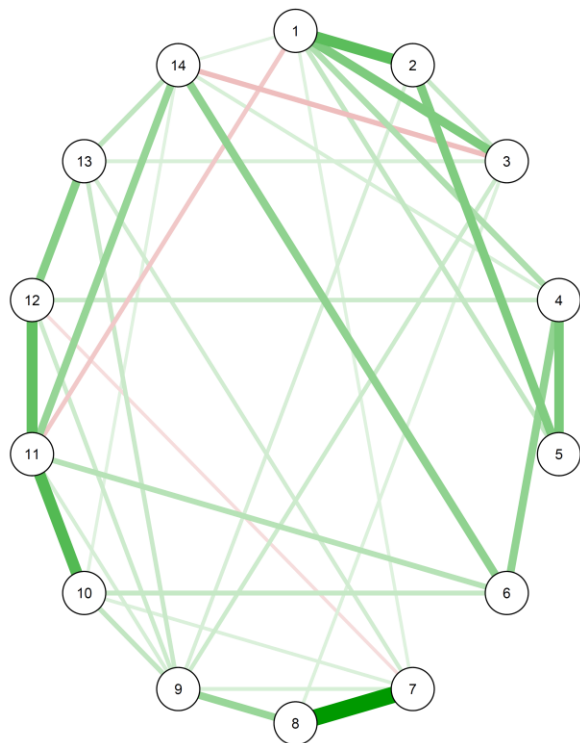
Figure S6. Comparison of the network by gender



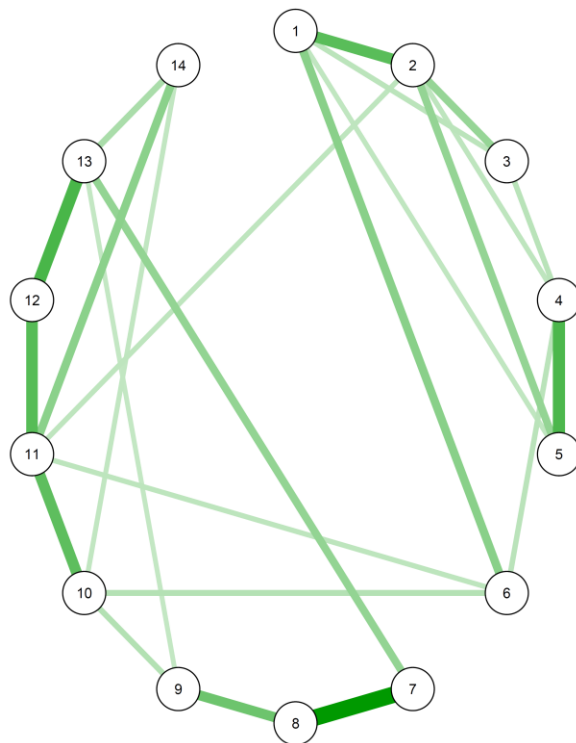
Left panel: network in male participants. Center panel: network in female participants. Right panel: network of edges that are significantly different at 95% level between males and females. A green edge correspond to a positive difference, i.e. the edge is stronger in males than females. 1: tension/worries; 2: fear/panic; 3: restlessness; 4: anhedonia; 5: sadness; 6: slowing. CAT. 7: cough; 8: phlegm; 9: chest tightness; 10: breathlessness; 11: activity limitation; 12: lack of confidence going out; 13: sleep problems; 14: low energy

Figure S8. Comparison of the network by ethnicity

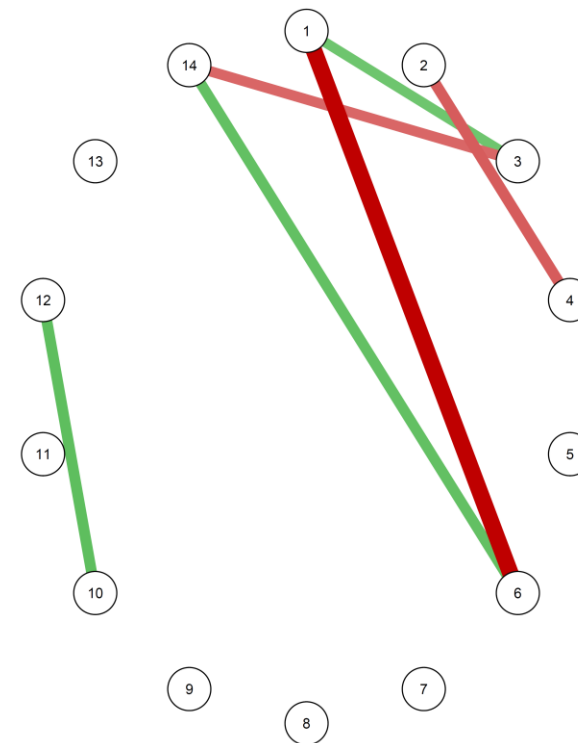
white



african american

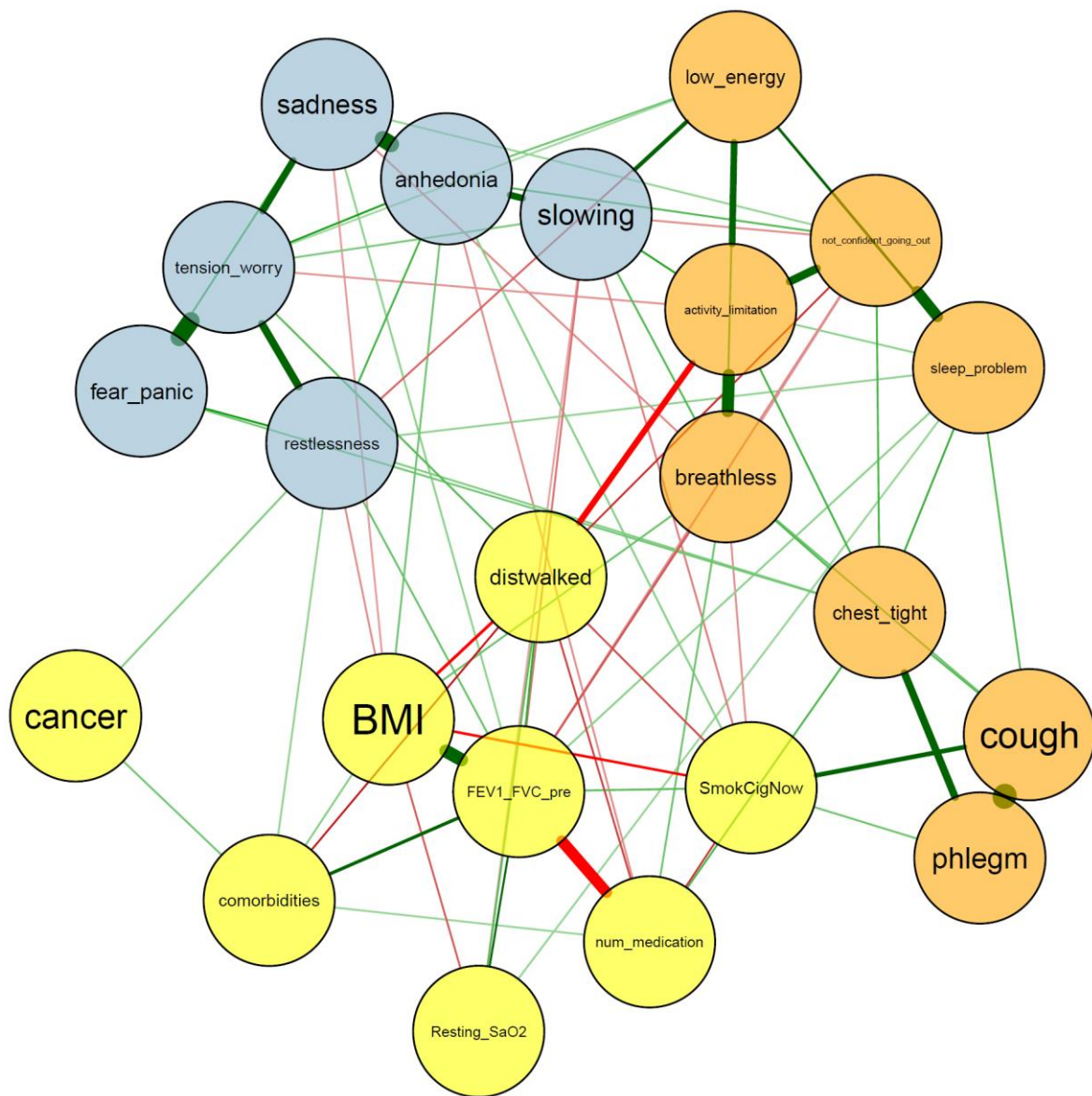


white - african american



Left panel: network in white participants. Center panel: network in African American participants. Right panel: network of edges that are significantly different at 95% level between white and African American participants. A green edge correspond to a positive difference, i.e. the edge is stronger in white than African Americans. 1: tension/worries; 2: fear/panic; 3: restlessness; 4: anhedonia; 5: sadness; 6: slowing. CAT. 7: cough; 8: phlegm; 9: chest tightness; 10: breathlessness; 11: activity limitation; 12: lack of confidence going out; 13: sleep problems; 14: low energy

Figure S10. Network of anxiety, depressive and COPD symptoms plus clinical parameters



Colors indicate items derived from the HADS (blue), from the CAT (orange) or clinical parameters (yellow)

Table S11. Weighted adjacency matrix of the network of anxiety, depressive and COPD symptoms plus clinical parameters

	Tension/ worry	Fear/panic	Restlessness	Anhedonia	Sadness	Slowing	Cough	Phlegm	Chest tightness	Breathlessness	Activity limitations	Lack of confidence going out	Sleep problems	Low energy	FEV1/FVC	Resting SaO2	Distance walked	BMI	Smoked Cigarettes	Cancer	N. of comorbidities	N. of medications	
Tension/worry		0.41	0.24	0.13	0.23	0.08					-0.06			0.05			0.10						
Fear/panic	0.41		0.14		0.11				0.08														
Restlessness	0.24	0.14		0.11					0.07				0.06	-0.09	0.09			-0.06		0.07	0.06		
Anhedonia	0.13		0.11		0.38	0.23						0.10		0.08				0.08	0.07				-0.06
Sadness	0.23	0.11		0.38						-0.07		0.06			0.07			-0.06					
Slowing	0.08			0.23						0.10	0.13	-0.07		0.18	-0.08	-0.05			-0.07				
Cough								0.51	0.09	0.08			0.10						0.19				
Phlegm							0.51		0.24										0.08				
Chest tightness		0.08	0.07				0.09	0.24		0.10	0.11	0.11	0.11										0.10
Breathlessness					-0.07	0.10	0.08		0.10		0.32	-0.06		0.11	-0.10			0.08	-0.06				0.08
Activity limitations	-0.06					0.13			0.11	0.32		0.25	0.06	0.22			-0.21						
Lack of confidence				0.10	0.06	-0.07			0.11	-0.06	0.25		0.30		-0.07		-0.12						
Sleep problems			0.06				0.10		0.11		0.06	0.30		0.16	0.07	0.06							
Low energy	0.05		-0.09	0.08		0.18				0.11	0.22		0.16										
FEV1/FVC			0.09		0.07	-0.08				-0.10		-0.07	0.07			0.15	0.12	0.33	0.10		0.17	-0.30	
Resting SaO2						-0.05							0.06		0.15		0.10	-0.10					
Distance walked	0.10										-0.21	-0.12			0.12	0.10		-0.16	-0.10		-0.14	-0.11	
BMI			-0.06	0.08	-0.06					0.08					0.33	-0.10	-0.16		-0.16		0.07		
Smoked Cigarettes				0.07		-0.07	0.19	0.08		-0.06					0.10		-0.10	-0.16					-0.12
Cancer			0.07																		0.08		
N. of comorbidities			0.06												0.17		-0.14	0.07		0.08		0.06	
N. of medications				-0.06					0.10	0.08					-0.30		-0.11		-0.12		0.06		