

Supplemental Table 1. Component Questions in Cognitive Concerns Latent Class Analysis

Nomenclature	Question	Response Options	Source
Concentrate–1	In the past 2 weeks, how often have you been bothered by trouble concentrating on things such as reading a book or watching TV?	not at all several days more than half the days nearly every day	PHQ-9
Concentrate–2	Over the past 4 weeks, how often have you been bothered by trouble concentrating on things such as reading a book or watching TV?	not at all several days more than half the days nearly every day	n/a
Concentrate–3	In the past month, how much have you been bothered by having difficulty concentrating?	not at all a little bit moderately quite a bit extremely	PCL-17
Attention–1	Over the past 4 weeks, how often have you been bothered by trouble keeping your mind on what you were doing?	not at all several days more than half the days nearly every day	n/a
Attention–2	Over the past 4 weeks, how often have you been bothered by your mind going blank, so you lose track of what you were thinking about?	not at all several days more than half the days nearly every day	n/a
Memory–1	In the past four weeks, how much trouble have you had with your short-term memory (e.g., forgetting where you left your keys, items at the grocery store, etc.)?	not at all a little bit moderately quite a bit extremely	n/a

PHQ-9, Patient Health Questionnaire; PCL-17, PTSD Symptom Checklist

Supplemental Table 2. Cognitive Concerns Latent Class Analysis Summary, World Trade Center Health Program General Responder Cohort, 2002 – 2015, (n=69,605 visits)

	Class 1					Class 2					Class 3					Class 4					Class 5					Class 6				
	Question Response					Question Response					Question Response					Question Response					Question Response					Question Response				
Question Nomenclature	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
LCA-3	52.9%					31.7%					15.5%																			
Concentrate–1	98	2	0	0		24	67	8	1		2	14	41	43																
Concentrate–2	84	15	1	0		11	71	16	2		1	8	40	50																
Concentrate–3	82	17	2	0	0	8	43	34	14	1	2	3	14	44	38															
Attention–1	71	28	0	0		5	78	16	1		1	6	45	49																
Attention–2	72	27	1	0		15	72	12	1		2	13	42	43																
Memory–1	36	46	13	4	1	3	29	37	27	3	1	5	16	48	30															
LCA-4	51.5%					28.6%					12.9%					7.1%														
Concentrate–1	98	2	0	0		31	65	3	0		5	36	50	9		2	5	17	75											
Concentrate–2	87	12	1	0		14	77	8	1		3	22	60	15		1	3	13	82											
Concentrate–3	84	15	1	0	0	10	50	30	9	1	2	8	30	49	11	1	2	5	29	62										
Attention–1	75	24	1	0		7	87	6	0		0	19	71	9		1	2	10	87											
Attention–2	74	24	1	0		19	75	5	0		3	31	58	8		2	5	16	77											
Memory–1	37	46	12	4	1	4	34	37	23	2	1	8	28	50	13	1	3	9	41	46										
LCA-5	39.7%					21.9%					18.6%					12.8%					7.1%									
Concentrate–1	99	1	0	0		90	9	0	0		8	87	4	1		6	34	50	10		2	5	17	76						
Concentrate–2	91	8	1	0		67	30	2	1		3	86	10	1		3	21	60	16		1	3	13	83						
Concentrate–3	93	7	0	0	0	41	46	10	2	0	8	44	35	12	1	2	7	29	50	11	1	2	5	29	63					
Attention–1	91	9	0	0		36	60	3	1		4	90	6	0		1	18	72	10		1	2	10	87						
Attention–2	90	10	0	0		41	53	5	1		16	79	5	0		3	30	59	8		2	5	16	77						
Memory–1	47	45	7	1	0	6	45	31	16	2	5	33	37	24	2	1	8	27	51	13	1	3	9	41	46					
LCA-6	43.8%					13.6%					13.1%					11.6%					11.0%					6.9%				
Concentrate–1	99	1	0	0		95	4	0	0		26	72	2	0		9	82	8	1		4	28	57	11		2	6	15	77	
Concentrate–2	90	9	1	0		83	15	1	1		5	88	7	1		5	77	16	2		2	14	65	18		1	4	12	83	
Concentrate–3	92	7	0	0	0	42	44	11	3	0	18	64	16	1	0	3	22	48	25	2	3	8	26	51	13	1	2	5	29	63
Attention–1	89	11	0	0		38	57	4	1		12	86	2	0		1	82	15	1		1	11	76	12		1	2	9	88	
Attention–2	90	10	0	0		36	57	6	1		34	66	0	0		6	79	13	1		3	24	63	9		2	5	15	78	
Memory–1	46	45	7	1	0	3	40	34	20	3	9	56	29	6	0	1	12	41	41	6	1	9	26	50	13	1	3	9	40	47

Cell values represent the percent distribution of responses for each question within each class. Color gradients correspond to percentage. Concentrate–3 and Memory–1 both have five response options; remaining questions have four response options. Higher response options indicate greater self-reported concern. For example, in the LCA-5 model, 39.7% of visits were assigned to Class 1. Of these visits, for Memory–1, 47% had response=1 (lowest concern), 45% response=2, 7% response=3, 1% response=4 and 0% response=5 (highest concern). The selected model was LCA-5 with classes 2 and 3 combined into a single category.

Supplemental Table 3. Indirect Effects – Exposure to Mediator: Adjusted^a Associations between World Trade Center Exposure and Longitudinal Markers of Mental and Physical Health Status, World Trade Center Health Program General Responder Cohort, 2002 – 2015

	Adjusted ^a Odds Ratio (95% Confidence Interval)					
	Model 1	Model 2	Model 3	Model 4		Model 5
	Depression	Anxiety	PTSD	Psychotropic Use		Physical Comorbidity ^b
	N = 15,056	N = 15,008	N = 16,300	N = 16,380		N = 16,311
				Monotherapy	Polytherapy	
WTC Exposure Index						
Low	1.0	1.0	1.0	1.0	1.0	1.0
Medium	1.62 (1.27, 2.06)	1.61 (1.27, 2.05)	2.36 (1.81, 3.07)	1.08 (0.81, 1.45)	1.17 (0.71, 1.94)	0.82 (0.64, 1.05)
High	2.48 (1.86, 3.30)	2.70 (2.04, 3.58)	5.56 (4.09, 7.57)	1.38 (0.99, 1.93)	2.06 (1.15, 3.69)	0.88 (0.66, 1.16)
p-value	<0.001	<0.001	<0.001	0.004		0.21

Reference group for psychotropic use is none and for all other models is absence of condition

^a Adjusted for sex, race/ethnicity, primary language, educational attainment, pre-9/11 occupation, clinic (time-varying), age (time-varying), employment status (time-varying), smoking status (time-varying), time since 9/11/2001

^b Physical comorbidity: diagnosis with sleep apnea, asthma, chronic obstructive pulmonary disease, lung scarring, rhinitis or sinusitis paired with self-reported use of antihistamines, inhaled glucocorticoids or oral steroids

Supplemental Table 4. Indirect Effects – Mediator to Outcome: Adjusted ^a Associations between Longitudinal Markers of Mental and Physical Health Status and Longitudinal Cognitive Concerns, World Trade Center Health Program General Responder Cohort, 2002 – 2015

	Cognitive Concerns Class				
	None	Low	Medium	High	
	Adjusted ^a Odds Ratio (95% Confidence Interval)				p-value
Model 1 (n=16,311)					
Probable Depression					<0.001
No	1.0	1.0	1.0	1.0	
Yes	1.0	12.71 (9.66, 16.7)	578 (436, 767)	6522 (4400, 9670)	
Model 2 (n=16,311)					
Probable Anxiety					<0.001
No	1.0	1.0	1.0	1.0	
Yes	1.0	7.42 (5.75, 9.57)	283 (217, 369)	1914 (1390, 2640)	
Model 3 (n=16,311)					
Probable PTSD					<0.001
No	1.0	1.0	1.0	1.0	
Yes	1.0	21.54 (16.9, 27.5)	368 (285, 475)	1492 (1110, 2010)	
Model 4 (n=16,380)					
Psychotropic Use					<0.001
None	1.0	1.0	1.0	1.0	
Monotherapy	1.0	2.97 (2.48, 3.55)	7.71 (6.18, 9.62)	13.68 (10.5, 17.8)	
Polytherapy	1.0	7.46 (5.13, 10.9)	30.91 (20.7, 46.0)	64.11 (41.4, 99.3)	
Model 5 (N=14,869)					
Physical Comorbidity ^b					<0.001
No	1.0	1.0	1.0	1.0	
Yes	1.0	1.33 (1.19, 1.48)	1.67 (1.42, 1.95)	2.05 (1.69, 2.50)	

^a Adjusted for sex, race/ethnicity, primary language, educational attainment, pre-9/11 occupation, clinic (time-varying), age (time-varying), employment status (time-varying), smoking status (time-varying), time since 9/11/2001

^b Physical comorbidity: diagnosis with sleep apnea, asthma, chronic obstructive pulmonary disease, lung scarring, rhinitis, or sinusitis paired with self-reported use of antihistamines, inhaled glucocorticoids, or oral steroids

Supplemental Table 5. Mediation by Mental Health – Separate Models. Adjusted^a Association between World Trade Center Exposure and Longitudinal Cognitive Concerns, World Trade Center Health Program General Responder Cohort, 2002 – 2015

	Cognitive Concerns Class				p-value
	None	Low	Medium	High	
	Adjusted ^a Odds Ratio (95% Confidence Interval)				
Model 1 (n=15,056)					
WTC Exposure Index					
Low	1.0	1.0	1.0	1.0	< 0.001
Medium	1.0	1.18 (0.98, 1.43)	1.10 (0.85, 1.42)	1.56 (1.15, 2.10)	
High	1.0	1.34 (1.08, 1.67)	1.56 (1.15, 2.10)	2.33 (1.47, 3.69)	
Probable Depression					
No	1.0	1.0	1.0	1.0	
Yes	1.0	12.7 (9.63, 16.7)	575 (433, 763)	6460 (4360, 9570)	< 0.001
Model 2 (n=15,008)					
WTC Exposure Index					
Low	1.0	1.0	1.0	1.0	< 0.001
Medium	1.0	1.16 (0.96, 1.39)	1.15 (0.88, 1.50)	1.36 (0.91, 2.01)	
High	1.0	1.31 (1.05, 1.62)	1.55 (1.14, 2.12)	2.12 (1.34, 3.37)	
Probable Anxiety					
No	1.0	1.0	1.0	1.0	< 0.001
Yes	1.0	8.99 (6.78, 11.9)	347 (258, 466)	2780 (1910, 4040)	
Model 3 (n= 16,300)					
WTC Exposure Index					
Low	1.0	1.0	1.0	1.0	0.05
Medium	1.0	1.13 (0.96, 1.33)	0.99 (0.79, 1.25)	1.09 (0.78, 1.52)	
High	1.0	1.20 (0.99, 1.46)	1.17 (0.89, 1.53)	1.36 (0.93, 2.00)	
Probable PTSD					
No	1.0	1.0	1.0	1.0	< 0.0001
Yes	1.0	21.3 (16.7, 27.2)	364 (282, 470)	1470 (1090, 1970)	
Model 4 (n=16,380)					
WTC Exposure Index					
Low	1.0	1.0	1.0	1.0	< 0.0001
Medium	1.0	1.17 (0.99, 1.38)	1.38 (1.07, 1.79)	1.84 (1.30, 2.61)	
High	1.0	1.29 (1.06, 1.56)	2.11 (1.56, 2.86)	3.28 (2.19, 4.92)	
Psychotropic Use					
None	1.0	1.0	1.0	1.0	< 0.001
Monotherapy	1.0	3.01 (2.51, 3.60)	7.65 (6.12, 9.55)	13.6 (10.5, 17.7)	
Polytherapy	1.0	7.42 (5.10, 10.8)	30.1 (20.2, 44.8)	61.6 (39.7, 95.5)	

^a Adjusted for sex, race/ethnicity, primary language, educational attainment, pre-9/11 occupation, clinic (time-varying), age (time-varying), employment status (time-varying), smoking status (time-varying), time since 9/11/2001

Supplemental Table 6. Mediation by Mental and Physical Health. Adjusted^a Association between World Trade Center Exposure and Longitudinal Cognitive Concerns, World Trade Center Health Program General Responder Cohort, Aged ≤ 55 Years on September 11, 2001, 2002 – 2015 (n = 14,164)

	Cognitive Concerns Class				p-value
	None	Low	Medium	High	
	Adjusted ^a Odds Ratio (95% Confidence Interval)				
WTC Exposure Index					
Low	1.0	1.0	1.0	1.0	0.09
Medium	1.0	1.16 (0.96, 1.41)	1.04 (0.78, 1.37)	1.23 (0.79, 1.93)	
High	1.0	1.25 (1.00, 1.56)	1.18 (0.85, 1.64)	1.59 (0.94, 2.72)	
Probable Depression					
No	1.0	1.0	1.0	1.0	<0.001
Yes	1.0	9.06 (6.55, 12.5)	111 (79.8, 155)	573 (371, 885)	
Probable Anxiety					
No	1.0	1.0	1.0	1.0	<0.001
Yes	1.0	4.40 (3.10, 6.25)	25.7 (17.7, 37.2)	91.8 (60.4, 139)	
Probable PTSD					
No	1.0	1.0	1.0	1.0	<0.001
Yes	1.0	13.8 (10.1, 18.9)	55.3 (39.7, 76.9)	95.9 (64.5, 142)	
Psychotropic Use					
None	1.0	1.0	1.0	1.0	<0.001
Monotherapy	1.0	2.49 (1.99, 3.12)	3.10 (2.30, 4.17)	4.28 (2.96, 6.17)	
Polytherapy	1.0	4.97 (2.98, 8.28)	6.24 (3.50, 11.1)	9.82 (5.18, 18.6)	
Physical Comorbidity ^b					
No	1.0	1.0	1.0	1.0	<0.001
Yes	1.0	1.32 (1.17, 1.50)	1.33 (1.09, 1.63)	1.60 (1.20, 2.12)	

^a Adjusted for sex, race/ethnicity, primary language, educational attainment, pre-9/11 occupation, clinic (time-varying), age (time-varying), employment status (time-varying), smoking status (time-varying), time since 9/11/2001

^b Physical comorbidity: diagnosis with sleep apnea, asthma, chronic obstructive pulmonary disease, lung scarring, rhinitis, or sinusitis paired with self-reported use of antihistamines, inhaled glucocorticoids, or oral steroids