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Long COVID and Cognitive Impairment: 2022 survey results from 29 states with relevance to Alzheimer's Disease

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Abstract

Background: Evidence is accumulating of similarities between COVID and Alzheimer's Disease (AD) and dementia.

Objective: To compare long COVID (symptoms ≥3 months) and cognitive impairment (CI) which can be an early step toward AD.

Methods: Using 2022 Behavioral Risk Factor Surveillance data from 169,894 adults in 29 states, respondents with CI and long COVID were compared using Stata. Unadjusted and adjusted analysis for each outcome included age, gender, race/ethnicity, education, 7 dementia risk factors (obesity, diabetes, smoking, physical inactivity, depression, excessive drinking, and difficulty hearing) or 5 COVID risks (obesity, diabetes, CVD, COPD, and asthma), individually and as composite measures, COVID vaccine doses received, plus the alternate outcome.

Results: Prevalence of long COVID was 7.4% and CI was 13.4% with both rates higher among women, ages 18-64 years, Hispanics, American Indians, those with more risk factors in either group, plus respondents reporting the other outcome. Rates were 35% (CI) or 38% (long COVID) lower among respondents reporting ≥3 vaccine doses vs <3, in both cases reducing rates to those for adults with ≤1 risk factor and suggesting vaccination could be as effective an intervention as risk factor reduction for both outcomes. Logistic regression confirmed most results except the magnitude of reduction of CI rates for ≥3 vaccines was less than expected.

Conclusions: Results confirm similarities between COVID and CI, most notably for risk factors and reaction to vaccines, suggesting the possibility that COVID vaccines might be able to slow development of AD from an early step in the progression.

Keywords: Cognitive impairment; long COVID; Alzheimer's Disease; COVID; Vaccines; BRFSS

Introduction

Cognitive problems such as "brain fog" are a common complaint among adults reporting long COVID (symptoms lasting ≥3 months) [1]. Post-COVID cognitive dysfunction (PCCD) has been described [2] as a condition in which patients who had long COVID exhibit subsequent cognitive impairment that cannot be explained by an alternate diagnosis. Cognitive impairment has also been studied as an early step in progression to Alzheimer's Disease (AD) which is the most common form of dementia [3,4]. More evidence of the similarities between COVID and cognitive

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issues comes from studies showing COVID-19 is a risk factor for AD [5,6] and that patients with AD are at increased risk of severe complications and death from COVID [7]. In addition, the COVID risk factors of obesity, diabetes, asthma, cardiovascular disease (CVD), hypertension, and chronic obstructive pulmonary disease (COPD)[8,9] overlap some of the 12 AD risk factors of obesity, diabetes, hypertension, smoking, physical inactivity, depression, low education, hearing impairment, excessive alcohol consumption, low social contact, traumatic brain injury, and air pollution which were estimated to account for up to 40% of all AD cases worldwide and suggest the potential for prevention[10]. That study updated an earlier one [11] that had estimated up to half of AD cases could be attributed to the first 7 of the 12 RFs. That earlier study [11] was among the evidence the Alzheimer's Association considered in its 2014 report [12] that concluded that there was strong evidence for the first 5 risk factors and less support for cognitive inactivity/low education and depression as increasing the risk of cognitive decline.

The main objective of this current study was to describe similarities and differences between cognitive impairment and long COVID especially as they might relate to prevention strategies. Data were chosen to include the 29 states that asked optional questions on COVID vaccines on their 2022 Behavioral Risk Factor Surveillance Survey. Measures focus on potentially modifiable risk factors, especially those defined as dementia [10] and COVID risks [8,9], and the COVID vaccines.

Methods

The study used publicly available 2022 telephone survey data from 169,894 adults ages 18 and older in the 29 states that asked the COVID vaccine module on the ongoing Behavioral Risk Factor Surveillance System (BRFSS). Data and questionnaires are available on the Centers for Disease Control and Prevention (CDC) website [13] and files from three different survey versions were combined per CDC instructions [14] to create the final data set. Data were already weighted to adjust for the probability of selection and to reflect the adult population of each state by gender, age, race/ethnicity, education level, marital status, home ownership, regions within states, and telephone source. The median response rate for the 29 states for land line and cell phone surveys combined was 44.9% [13], ranging from 33.9% in NY to 58.4% in ND.

Measures

Cognitive impairment (CI) was defined as a "yes" response to this disability question asked on all federal surveys [15,16]: "Because of a physical, mental, or emotional condition, do you have serious difficulty concentrating, remembering, or making decisions?" The question appears to be an acceptable measure for cognitive impairment but not cognitive decline because it lacks a time frame [3,4]. COVID questions addressed ever testing positive for COVID-19 and if so, did any symptoms last 3 months or longer, which was the definition of long COVID [13,17]. Other measures included age, race/ethnicity, gender, education, employment, a depression diagnosis, census region (Northeast, Midwest, South and West), and the 5 COVID risk factors of obesity (body mass index ≥30 based on self-reported height and weight), self-reported asthma, diabetes, cardiovascular disease (CVD; heart attack, angina, coronary heart disease, or a stroke), and Chronic Obstructive Pulmonary Disease (COPD) [8,9]. In addition, 7 of the 12 risk factors shown to be associated with dementia [10] (obesity, diabetes, depression, physical inactivity {no leisure time physical activity}, excessive drinking {binge or heavy drinking as defined separately for male and female respondents}, hearing impairment, and current smoking were included and termed "dementia risks". With overlap between the COVID and dementia measures, there were a total of 10 separate risk factors plus reporting less than a high school education. Both sets of risk factors also included hypertension which was excluded from this study because data on hypertension was not available. Data on traumatic brain injury, low social contact, and air pollution [10] were also not available. Low education was included as < a high school education in the demographic measure of education. The 5 COVID risks and the 7 dementia risks (excluding low education) were included in separate composite measures to check for dose response gradients with increasing numbers of risk factors. Vaccine measures included receipt of any COVID vaccine, number of doses, and ≥3 doses vs <3 which was previously shown to be effective [17].

Analysis

Stata version 18.0 (StataCorp LLC, College Station TX) was used to account for the complex sample design of the BRFSS in unadjusted analysis and controlled for the listed factors in logistic regression. The survey measures used to describe the survey design were _psu and _ststr, weight=_ llcpwt or the survey version weight; linearized variance estimation was selected, with the option to center at the grand mean for strata with a single sampling unit. Missing values were excluded from analysis of that variable. Separate univariate analysis was done for comparison due to the large overlap between long COVID and CI measures and variables to be included in logistic regression models were selected from those results. Results for 3 different logistic regression models are presented, all using the same variables but different composite measures (or none). Apparent vaccine effectiveness was determined by comparing prevalence rates for long COVID and CI respectively for each additional vaccine dose from 1 to ≥4 compared with 0, and for ≥3 vaccine doses vs <3 [17].

Adams ML, et al., Arch Intern Med Res 2024
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Results

Prevalence of CI for all adults ages 18 and older was 13.4% (95% confidence interval 13.0%-13.7%) and of long COVID was 7.5% (7.3%-7.8%) with both measures having wide ranges across the 29 states (Table 1). The CI and long COVID rates were both higher among women, ages 18-64 years, Hispanics, American Indians, and those with <3 vaccine doses (vs ≥3 doses) and were lowest in the Northeast and Midwest regions (Table 1). Measures of health status indicate adults with CI were more likely than those with long COVID to report poor health, 14+ days of activity limitation in past month and being unable to work. Results also show a strong association between long COVID and CI (shown in Table 1 as the alternate measure). Results also show the increase in unadjusted rates for long COVID with each of the separate COVID risk factors except CVD and each of the 7 dementia risk factors for CI. Not shown are results indicating that 72.2% of study adults reported any of the 7 dementia risk factors with ranges across states from 65.7% in HI to 79.2% in WV and AR. Adults with CI were significantly more likely to report any of the 7 dementia risk factors than those without CI (90.2% vs. 69.4% respectively).

While 80.1% of all study adults reported any COVID vaccines, only 47.1% reported ≥3 doses which had been found to be effective [17]. That rate ranged across states from 31.9% in ID to 61.6% in RI. By age, vaccination rates increased from 30.6% for ages 18-34 years, 37.0% for ages 35-44, 45.4% for ages 45-54, 55.0% for ages 55-64, and 67.8% for age 65 years and older (not shown). Most recipients of ≥3 vaccines (97.9%) reported receiving their first vaccine dose in 2021 or earlier which was before they were surveyed.

Table 1: Long COVID (symptoms ≥3 months) and Cognitive impairment (CI), 2022 Behavioral Risk Factor Surveillance System, 29 states, N=202,202. Weighted analysis in Stata.

		Long COVID			Cognitive Impairment		
		%	95%CI	N	%	95%CI	N
Total		7.5	7.3-7.8	177,613	13.4	13.0-13.7	191,049
Gender							
Males		5.6	5.3-5.9	83,342	11.7	11.3-12.1	89,343
Females		9.4	9.0-9.8	94,271	14.9	14.4-15.5	101,706
	P value	<.001			<.001		
Age (years)							
18-24		6.8	6.0-7.7	10,466	22.4	21.0-23.9	11,119
25-34		9.3	8.6-10.1	18,028	15.2	14.3-16.1	19,273
35-44		9.5	8.9-10.2	22,442	12.9	12.1-13.8	24,250
45-54		9.4	8.7-10.1	23,983	11.4	10.7-12.1	26,089
55-64		7.2	6.7-7.8	32,639	11.8	11.1-12.5	35,162
65+		4.4	4.1-4.8	67,181	10.5	9.9-11.1	71,723
	P value	<.001			<.001		
Race/ethnicity							
White (non-Hispanic)		7.6	7.3-7.9	130,486	12.5	12.1-12.8	139,531
Black		6.7	6.0-7.5	13,943	13.4	12.5-14.4	15,471
Hispanic		9.5	7.9-11.4	4,132	19.5	17.2-22.0	4,358
American Indian/AK Native		9.1	7.6-11.0	2,421	24.7	19.4-30.9	2,629
Asian		4.6	3.6-6.0	6,154	7.7	6.4-9.2	6,657
Other		8.5	7.7-9.3	15,740	16.2	15.2-17.3	17,067
	P value	<.001			<.001		
Education							
<High school		6.5	5.7-7.4	10,586	24.9	23.3-26.5	11,521
High school		6.9	6.5-7.4	44,062	16	15.3-16.7	47,822
Some college		9.1	8.6-9.6	48,200	13.6	13.0-14.2	51,650
College grad		7.0	6.6-7.4	74,142	6.7	6.3-7.0	79,297
	P value	<.001			<.001		
Income							

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100K+		7.1	6.6-7.5	39,336	5.5	5.0-5.9	41,952
$75+		9.2	8.4-10.1	20,483	8.5	7.6-9.5	21,789
$50-75		8.5	7.8-9.2	25,195	10.9	10.1-11.7	26,739
$25-50		8.2	7.6-8.8	37,849	15.2	14.5-16.0	40,464
$15-25		8.1	7.2-9.1	14,866	23.3	22.0-24.7	15,947
<$15K		6.6	5.6-7.9	8,637	33.2	31.0-35.5	9,250
Unknown		5.8	5.3-6.4	31,245	15.3	14.4-16.1	34,906
	P value	<.001			<.001		
Census Region							
Northeast		6.6	6.1-7.1	41,420	12.2	11.5-12.9	45,049
Midwest		7.5	7.0-8.0	42,438	11.7	11.0-12.3	45,213
South		8	7.6-8.4	66,123	14.6	14.1-15.1	71,746
West		7.9	7.4-8.4	27,632	13.4	12.8-14.1	29,041
	P value	<.001			<.001		
Employment							
Employed/SE		8.5	8.2-8.9	89,566	9.5	9.2-9.9	96,678
Out of work		9.8	8.5-11.3	6,447	24.6	22.8-26.5	6,931
Homemaker		7.4	6.3-8.7	6,914	13.5	11.8-15.3	7,446
Student		6.3	5.2-7.7	4,386	19.2	17.1-21.5	4,663
Retired		4.3	4.0-4.7	57,646	9.5	8.9-10.1	61,519
Unable to work		8.4	7.4-9.4	11,090	44.1	42.1-46.1	11,935
	P value	<.001			<.001		
Alternate measure							
Not alternate measure		6.8	6.5-7.1	155,579	12.6	12.3-13.0	164,134
IS alternate measure		12.2	11.3-13.1	20,929	21.6	20.2-23.1	12,374
	P value	<.001			<.001		
Vaccine doses							
≥ 3 vaccines		5.7	5.4-6.0	90,570	10.3	9.9-10.8	90,855
< 3 vaccines		9.2	8.8-9.6	77,678	15.9	15.4-16.5	77,967
	P value	<.001			<.001		
Risk factors							
Obese							
Yes		9.8	9.3-10.3	56,639	15.2	14.6-15.8	60,211
No		6.4	6.1-6.7	109,038	12.7	12.3-13.1	117,040
	P value	<.001			<.001		
Diabetes							
Yes		8.7	8.0-9.6	25,499	17.9	16.8-19.0	27,298
No		7.4	7.1-7.6	1,51,797	12.7	12.3-13.0	163,399
	P value	<.001			<.001		
Current asthma							
Yes		13.1	12.1-14.1	18,127	24.2	23.0-25.4	19,444
No		6.9	6.6-7.1	158,107	12	11.7-12.4	170,130
	P value	<.001			<.001		
COPD							
Yes		10.7	9.7-11.8	14,505	28.5	27.0-30.1	15,587
No		7.3	7.0-7.6	162,333	12.2	11.9-12.6	174,636

Adams ML, et al., Arch Intern Med Res 2024
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	P value	<.001			<.001		
Cardiovascular disease							
Yes		8.1	7.4-8.9	21,467	23.2	21.9-24.5	23,034
No		7.5	7.2-7.7	154,106	12.2	11.9-12.6	165,845
	P value	0.09			<.001		
Smoking Status							
Non-Smoker		7.6	7.4-7.9	154,784	11.9	11.5-12.2	161,708
Current smoker		7	6.4-7.8	21,610	23.8	22.6-25.0	22,887
	P value	0.13			<.001		
Depression dx							
No		6.5	6.3-6.8	119,044	7.2	6.9-7.5	128,634
Yes		12.4	11.6-13.2	30,126	36.8	35.7-37.9	32,004
P value		<.001			<.001		
Physically inactive							
No		7.4	7.2-7.7	133,312	11.6	11.2-12.0	143,283
Yes		7.8	7.3-8.3	43,921	18.8	18.0-19.5	47,356
	P value	0.26			<.001		
Hearing impaired							
Yes		7.7	6.9-8.7	16,680	28.6	27.1-30.3	17,871
No		7.5	7.3-7.8	160,337	12.2	11.9-12.5	172,553
	P value	0.61			<.001		
Excessive drinking							
Yes		8	7.4-8.6	27,116	14.2	13.4-15.0	27,815
No		7.5	7.2-7.7	146,118	13.1	12.7-13.4	149,225
	P value	0.15			0.012		
Number of 5 COVID risks[a]							
0		5.9	5.6-6.2	77,016	10	9.5-10.4	82,715
Any		9.2	8.8-9.7	84,895	16.4	15.8-16.9	90,536
	P value	<.001			<.001		
0		5.9	5.6-6.2	77,016	10	9.5-10.4	82,715
1		8.4	7.9-8.9	53,935	13.6	13.0-14.3	57,534
2		10.4	9.5-11.4	21,598	18.7	17.6-19.8	23,016
3 or more		12.5	11.1-13.9	9,362	29.9	28.1-31.8	9,986
	P value	<.001			<.001		
Number of 7 dementia risks[b]							
0		5.6	5.2-6.0	45,031	4.7	4.3-5.1	46,074
Any		8.4	8.1-8.8	114,385	16.5	16.1-17.0	116,778
	P value	<.001			<.001		
0		5.6	5.2-6.0	45,031	4.7	4.3-5.1	46,074
1		7.2	6.8-7.7	52,960	10.3	9.7-10.9	54,096
2		8.8	8.2-9.4	36,595	16.9	16.1-17.7	37,362
3		10.9	10.0-11.9	17,626	25.7	24.5-27.0	17,991
4 or more		10.3	9.0-11.8	7,204	42.6	40.4-44.9	7,329
	P value	<.001			<.001		

Adams ML, et al., Arch Intern Med Res 2024
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Health Status							
Fair or poor		10.4	9.7-11.2	32,108	31.3	30.2-32.4	34,464
Good or better		6.9	6.6-7.2	145,081	9.5	9.1-9.8	156,123
	P value	<.001			<.001		
14+ days/30 poor mental health							
Yes		12.4	11.6-13.3	23,610	41.2	39.9-42.4	25,314
No		6.6	6.4-6.9	150,754	7.8	7.5-8.1	162,262
	P value	<.001			<.001		
14+ days/30 activity limitation							
Yes		12.8	11.7-14.0	16,741	45	43.4-46.6	17,987
No		7	6.7-7.2	158,678	9.6	9.3-9.9	170,708
	P value	<.001			<.001		
State							
AR		8.2	7.2-9.3	4,450	19.2	17.6-20.8	4,894
CT		6.3	5.6-7.1	8,098	11.3	10.3-12.4	8,912
DE		6.7	5.5-8.2	3,419	12.1	10.7-13.7	3,800
GA		7.7	6.8-8.6	7,790	13.2	12.1-14.4	8,517
HI		4.1	3.5-4.8	7,068	9.1	8.2-10.0	7,471
ID		8.8	7.9-9.7	5,958	15	13.9-16.2	6,143
IL		7.2	6.3-8.3	3,619	10.8	9.6-12.1	3,885
IA		7.7	7.0-8.5	8,213	11.8	11.0-12.8	8,624
KS		8.2	7.4-8.9	10,159	13.4	12.5-14.4	10,759
LA		9.1	8.1-10.3	4,913	18.9	17.5-20.5	5,330
ME		5.1	4.3-6.0	4,894	15.2	13.7-16.9	5,059
MD		5.4	4.6-6.2	9,115	10.9	9.9-11.9	9,952
MA		5.7	5.0-6.5	6,387	13.7	12.6-15.0	6,730
MT		10.2	9.2-11.2	6,597	13.7	12.6-14.8	6,836
NE		8.1	7.2-9.1	6,855	10.5	9.5-11.6	7,239
NH		5.7	4.9-6.7	5,806	13.5	12.2-15.0	6,336
NJ		7.1	6.3-8.0	6,547	10.1	9.1-11.2	7,344
NM		8	6.8-9.3	4,356	15.2	13.8-16.8	4,612
NY		7	6.1-8.1	4,760	12.3	11.0-13.7	5,200
NC		7	6.1-8.0	4,183	14.9	13.4-16.7	4,375
ND		10	8.8-11.3	3,881	11	9.8-12.4	4,021
OK		10.4	9.1-11.9	2,480	17.7	16.0-19.6	2,640
RI		5.8	4.9-6.8	4,928	14	12.6-15.5	5,468
SC		7.4	6.7-8.2	8,423	13.9	12.8-15.0	9,302
TN		10.2	9.1-11.5	4,608	16.5	15.1-18.0	4,950
TX		7.9	7.1-8.8	12,135	13.5	12.5-14.7	13,148
WV		11.1	10.0-12.3	4,607	18.8	17.4-20.3	4,838
WI		7	6.4-7.7	9,711	13	12.1-14.0	10,685
WY		10	8.8-11.4	3,653	12.3	10.9-13.8	3,979
Total		7.5	7.3-7.8	177,613	13.4	13.0-13.7	191,049
	P value	<.001			<.001		

[a]obesity, diabetes, cardiovascular disease (CVD), asthma, or COPD
[b]obesity, diabetes. hearing impaired, smoking, depression, inactivity, excessive drinking

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Apparent vaccine effectiveness of ≥3 doses vs <3 was 38.0% for long COVID, reducing rates from 9.2% for <3 doses to 5.7% for ≥3, and 35.2% for CI, reducing rates from 15.9% to 10.3% (Table 2). Results for CI limited to respondents without long COVID or who never tested positive for COVID were similar to results for all respondents with CI as shown in Table 2. When limited to adults who also had long COVID, prevalence rates were higher for both vaccine doses and the apparent effectiveness was lower. Dose response gradients are shown for 1 to 4+ vaccine doses vs 0 for both outcomes but most results are reported for ≥3 doses vs <3 to include all respondents with non-missing vaccine data. Vaccines were apparently not very effective for either outcome for ages 18-24 years, where P values were >0.05. For comparison, apparent vaccine effectiveness for the 34.8% of all adults with a positive COVID test was 21.4%, and 16.2% for the majority with a positive test that did not develop long COVID.

Table 2: Rates of long COVID and cognitive impairment (CI) at various doses of COVID vaccine with % reduction representing apparent effectiveness. 2022 Behavioral Risk Factor Surveillance System, 29 states[a], N=168,822.

	Long COVID			Cognitive impairment		
	Prevalence rates			Prevalence rates		
Ages	**<3 vax**	**≥3 vax**	**% Reduction**	**<3 vax**	**≥3 vax**	**% Reduction**
All ages	9.2	5.7	38.0%	15.9	10.3	35.2%
65+	5.8	3.9	32.8%	13.2	8.8	33.3%
45+	9	5.2	42.2%	13.8	8.9	35.5%
<45	9.8	7.2	26.5%	17.8	13.8	22.5%
All ages	N=115,011 never tested positive			16	10.1	36.9%
All ages	N=155,505 without long COVID			15.1	9.9	34.4%
All ages	Limited to 4,037 w/ long COVID			23.9	16.7	30.1%
Dose-response results for all ages, # vaccine doses vs 0, N varies.						
	Long COVID			Cognitive impairment		
# doses	**0 doses**	**Max dose**	**% Reduction**	**0 doses**	**Max dose**	**% Reduction**
1	9.5	9.9	----	16.7	18.2	----
2	9.5	8.9	6.3%	16.7	14.9	10.8%
3	9.5	5.9	37.9%	16.7	10.8	35.3%
4 +	9.5	5	47.4%	16.7	8.7	47.9%
Long COVID: symptoms lasting ≥3 months.						
Cognitive impairment: disability question asked on all federal surveys “serious difficulty concentrating, remembering, or making decisions”.						

[a]AR, CT, DE, GA, HI, ID, IL, IA, KS, LA, ME, MD, MA, MT, NE, NH, NJ, NM, NY, NC, ND, OK, RI, SC, TN, TX, WV, WI, WY

Table 3: Weighted results of logistic regression with vaccine data, controlled for the measures listed, 2022 Behavioral Risk Factor Surveillance System, 29 states, N=143,201 COVID risks: obesity, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, asthma. Dementia risks: obesity, diabetes, depression, physical inactivity, excessive drinking, hearing impairment, and current smoking. Adjusted odds ratios (AOR) and 95% confidence intervals for the outcomes of Cognitive impairment (CI) and Long COVID.

A. 5 COVID risks in composite + 5 other risks so all 10 risk factors are in model						
Outcome>>>>	**Long COVID**			**Cognitive impairment**		
Measure in model	**AOR**	**95% CI**	**P value**	**AOR**	**95% CI**	**P value**
Female v male	1.74	1.60-1.90	<.001	1.08	1.00-1.17	0.049
Age 55-64 v age 65+	1.70	1.49-1.94	<.001	1.09	0.97-1.23	0.138
Age 45-54 v age 65+	2.25	1.97-2.58	<.001	1.15	1.02-1.29	0.022
Age 35-44 v age 65+	2.29	2.00-2.63	<.001	1.41	1.24-1.61	<.001
Age 25-34 v age 65+	2.23	1.92-2.60	<.001	1.87	1.65-2.12	<.001
Age 18-24 v age 65+	1.63	1.36-1.97	<.001	3.04	2.64-3.50	<.001
Black v non-Hispanic white	0.81	0.70-0.93	0.003	1.17	1.04-1.31	0.008
Hispanic v non-Hisp white	1.03	0.83-1.28	0.797	1.13	0.93-1.36	0.217
Am Ind/AK native	1.12	0.87-1.43	0.385	1.42	1.02-1.09	0.039

Adams ML, et al., Arch Intern Med Res 2024
DOI:10.26502/aimr.0175

Asian v non-Hisp white	0.6	0.42-0.87	0.007	1.06	0.83-1.36	0.636
Other v non-Hisp white	1.12	0.98-1.28	0.09	1.1	0.98-1.23	0.118
Some college v coll grad	1.13	1.02-1.25	0.016	1.61	1.47-1.76	<.001
High school v coll grad	0.91	0.81-1.02	0.113	1.99	1.81-2.20	<.001
< High school v coll grad	0.67	0.56-0.81	<.001	3.32	2.88-3.84	<.001
1 COVID risk v 0	1.43	1.30-1.57	<.001	1.22	1.12-1.33	<.001
2 COVID risks v 0	1.91	1.67-2.18	<.001	1.57	1.40-1.77	<.001
3+ COVID risks v 0	2.44	2.07-2.88	<.001	2.28	1.99-2.62	<.001
Hearing impaired v not	1.13	0.98-1.30	0.091	2.75	2.45-3.08	<.001
Physical inactivity v no	1.02	0.93-1.13	0.645	1.38	1.27-1.50	<.001
Depression dx v no	1.35	1.22-1.49	<.001	6.55	6.06-7.07	<.001
Current smoker v not	0.72	0.62-0.83	<.001	1.42	1.30-1.56	<.001
Excessive drinking v no	1.01	0.91-1.13	0.811	1.03	0.94-1.13	0.517
Long Covid OR CI	1.44	1.28-1.62	<.001	1.47	1.31-1.64	<.001
≥3 vaccines v <3	0.63	0.58-0.69	<.001	0.86	0.79-0.93	<.001
B. 7 dementia risks in composite + 3 other measures						
Outcome>>>>	**Long COVID**			**Cognitive impairment**		
Measure in model	**AOR**	**95% CI**	**P value**	**AOR**	**95% CI**	**P value**
Female v male	1.77	1.63-1.93	<.001	1.35	1.25-1.45	<.001
Age 55-64 v age 65+	1.65	1.44-1.88	<.001	1.19	1.07-1.34	0.002
Age 45-54 v age 65+	2.15	1.88-2.46	<.001	1.33	1.18-1.49	<.001
Age 35-44 v age 65+	2.12	1.85-2.44	<.001	1.75	1.54-1.98	<.001
Age 25-34 v age 65+	2.05	1.76-2.38	<.001	2.45	2.16-2.78	<.001
Age 18-24 v age 65+	1.54	1.27-1.87	<.001	4.56	3.98-5.23	<.001
Black v non-Hispanic white	0.83	0.72-0.95	0.008	0.93	0.83-1.04	0.182
Hispanic v non-Hisp white	1.03	0.83-1.27	0.812	1.13	0.95-1.35	0.165
Am Ind/AK native	1.11	0.86-1.41	0.425	1.32	0.98-1.76	0.067
Asian v non-Hisp white	0.61	0.42-0.88	0.008	0.93	0.74-1.17	0.54
Other v non-Hisp white	1.17	1.03-1.32	0.018	0.95	0.85-1.06	0.346
Some college v coll grad	1.12	1.01-1.23	0.026	1.57	1.44-1.72	<.001
High school v coll grad	0.88	0.78-0.99	0.032	1.77	1.62-1.95	<.001
< High school v coll grad	0.63	0.53-0.76	<.001	2.79	2.43-3.19	<.001
1 Dementia risk v 0	1.24	1.10-1.39	<.001	2.2	1.94-2.50	<.001
2 Dementia risks v 0	1.47	1.30-1.65	<.001	3.75	3.31-4.25	<.001
3 Dementia risks v 0	1.68	1.45-1.94	<.001	6.16	5.38-7.06	<.001
4+ Dementia risks v 0	1.39	1.15-1.69	0.001	11.6	9.92-13.58	<.001
CVD v no	1.21	1.06-1.38	0.005	1.96	1.74-2.20	<.001
COPD v no	1.23	1.07-1.42	0.004	1.63	1.45-1.83	<.001
Asthma v no	1.60	1.41-1.81	<.001	1.49	1.35-1.64	<.001
Long COVID OR CI	1.50	1.35-1.68	<.001	1.53	1.38-1.71	<.001
≥3 vaccines v <3	0.65	0.60-0.71	<.001	0.92	0.85-1.00	0.043
C. All 10 risk factors separate						
Outcome>>>>	**Long COVID**			**Cognitive impairment**		
Measure in model	**AOR**	**95% CI**	**P value**	**AOR**	**95% CI**	**P value**
Female v male	1.72	1.58-1.87	<.001	1.1	1.02-1.19	0.013
Age 55-64 v age 65+	1.66	1.45-1.90	<.001	1.18	1.04-1.33	0.008

Adams ML, et al., Arch Intern Med Res 2024
DOI:10.26502/aimr.0175

Age 45-54 v age 65+	2.18	1.90-2.50	<.001	1.3	1.15-1.47	<.001
Age 35-44 v age 65+	2.2	1.90-2.53	<.001	1.65	1.43-1.90	<.001
Age 25-34 v age 65+	2.13	1.82-2.49	<.001	2.17	1.89-2.48	<.001
Age 18-24 v age 65+	1.54	1.27-1.87	<.001	3.4	2.93-3.94	<.001
Black v non-Hispanic white	0.81	0.70-0.93	0.004	1.19	1.06-1.33	0.003
Hispanic v non-Hisp white	1.02	0.82-1.27	0.844	1.14	0.94-1.37	0.178
Am Ind/AK native	1.12	0.87-1.43	0.373	1.42	1.01-1.98	0.041
Asian v non-Hisp white	0.61	0.42-0.87	0.007	1.02	0.80-1.31	0.868
Other v non-Hisp white	1.13	0.99-1.29	0.063	1.11	0.99-1.24	0.085
Some college v coll grad	1.14	1.03-1.26	0.011	1.62	1.48-1.78	<.001
High school v coll grad	0.92	0.82-1.03	0.162	2.01	1.82-2.22	<.001
< High school v coll grad	0.68	0.56-0.82	<.001	3.27	2.83- 3.77	<.001
Obesity v no	1.35	1.24-1.47	<.001	0.93	0.86-1.00	0.053
Diabetes v no	1.25	1.10-1.42	0.001	1.36	1.22-1.52	<.001
CVD v no	1.18	1.03-1.34	0.018	1.83	1.61-2.08	<.001
COPD v no	1.3	1.12-1.50	<.001	1.42	1.25-1.60	<.001
Asthma v no	1.53	1.35-1.74	<.001	1.33	1.20-1.47	<.001
Inactive v not	1.02	0.93-1.13	0.629	1.38	1.27-1.51	<.001
Depression v no	1.34	1.21-1.48	<.001	6.48	6.01-7.00	<.001
Smoker v not	0.72	0.62-0.83	<.001	1.35	1.23-1.49	<.001
Hearing impaired v not	1.12	0.97-1.29	0.123	2.66	2.37-2.98	<.001
Excessive drink v no	1.01	0.91-1.13	0.836	1.04	0.95-1.14	0.438
Long COVID OR CI	1.44	1.28-1.62	<.001	1.47	1.31-1.65	<.001
≥3 vaccines v <3	0.63	0.57-0.69	<.001	0.85	0.79-0.93	<.001

Abbreviations: CI: Cognitive impairment (unless indicating 95% confidence interval); CVD: cardiovascular disease; COPD: chronic obstructive pulmonary disease; Am Ind: American Indian

Combining results for vaccines and risk factors finds that prevalence rates for CI ranged from 3.8% for adults with ≥3 vaccine doses and 0 dementia risk factors up to 47.4% for those with 4 or more of the 7 dementia risk factors and <3 vaccines. For long COVID, rates ranged from 4.3% for adults with ≥3 vaccine doses and 0 COVID risk factors to 15.1% for those with <3 COVID vaccines and 3 or more of the 5 COVID risk factors.

Results of logistic regression for long COVID and CI (Table 3 A-C), include all the measures shown and confirmed most unadjusted results in Table 1 except CVD was a significant predictor of long COVID only when results were adjusted, and obesity and excessive drinking were no longer significantly higher for adults with CI once adjusted. The highest adjusted odds ratio (AOR) for long COVID was 2.4 for 3 or more of the 5 COVID risk factors (Table 3A) and for CI was 11.6 for ≥ 4 of the 7 dementia risk factors (Table 3B). Apparent vaccine effectiveness had P values <0.05 for all models shown in Table 3 although the vaccines apparently reduced long COVID rates to a greater extent than CI rates (35-37% vs. 8-15% respectively) with all measures in the models.

Discussion

This study confirms similarities between long COVID and CI in the groups disproportionately affected that include women, ages 18-64 years, Hispanics, and American Indians. Rates of both long COVID and CI increased with more risk factors, whether defined as COVID or dementia risks which may help explain the similarity in groups with higher rates. Also, there was considerable overlap between the two measures, with AOR in each case over 1.4 indicating the odds of reporting the other measure were > 1.4. There were differences in prevalence rates between the 2 measures, with the CI rate about 1.8 times the long COVID rate. Cognitive impairment appears to have a more adverse impact on health status than long COVID as measured by general health, ability to work, and days of activity limitations. As noted in results, once adjusted, all separate risk factors except obesity and excessive drinking had significantly higher AORs for CI and all except < high school education, inactivity, smoking, hearing impairment, and excessive drinking had higher AORs for long COVID.

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Adams ML, et al., Arch Intern Med Res 2024
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Relevance to dementia and Alzheimer's Disease

There were two apparently new findings with potential relevance to dementia and AD: 1) over 2/3 of adults surveyed (72.2%) reported at least one of the 7 dementia risk factors available for the study (obesity, diabetes, depression, physical inactivity, excessive drinking, hearing impairment, and current smoking) and 2) the COVID vaccines were apparently effective against both long COVID and CI. Each of the 7 dementia risk factors separately increased unadjusted rates of CI and in combination had AORs as high as 11.6 for ≥4. An earlier study in 21 states [18] defining 6 dementia risk factors as obesity, diabetes, depression, inactivity, current smoking and hypertension found 77.3% of adults ages 45 and older reported any of the 6 factors. That study included 232 adults with dementia and 9,769 with cognitive decline and found dose response gradients for more risk factors for both outcomes in unadjusted and adjusted results. For those few with all 6 risk factors the highest AOR was 11.2 for cognitive decline and over 100 for those with dementia (with a wide confidence interval). Thus, this current study is consistent with those results which included dementia along with cognitive decline.

In this current study, where 72.2% of all adults reported any of the 7 dementia factors, about 15% reported 3 or more. In the older study [18], limited to adults ≥45 years, about 25% of all adults reported 3 or more dementia risk factors, which included hypertension, the most common of the six. These results add key information because the study which estimated 40% of AD cases could be attributed to 12 dementia risk factors [10] had very limited data that included all or most of the risk factors together. These new results suggest that addressing multiple risk factors (i.e. 3 or more together) could be a key issue in planning prevention programs and illustrate the challenge of decreasing future AD cases if the magnitude of an early step in the progression to AD can be increased based on the presence of these common risk factors individually or in combination.

The second new and totally unexpected finding was the reaction of CI to the COVID vaccines. An earlier study [19] found that COVID vaccines not only reduced risk of long COVID compared with those not vaccinated but also showed that vaccination reduced the risk of cognitive impairment (as a symptom) in those with long COVID. That finding is not directly comparable to our findings because we were able to show vaccine effectiveness for CI among adults without long COVID or a positive COVID test to assure we were not measuring any vaccine effect due to the presence of the COVID-19 virus. We were also able to show that the apparent effectiveness of the COVID vaccine on CI was very similar to the results for adults with long COVID including showing dose-response gradients for more doses and when controlled for demographic measures and risk factors. The apparent effectiveness of COVID vaccines on CI is consistent with our findings of higher vaccination rates for adults aged 65+ along with lower prevalence rates for CI and long COVID for that age group.

The results shown in Table 2 indicate that long COVID rates drop from 9.2% to 5.7% and CI rates drop from 15.9% to 10.3% for respondents with ≥3 vaccine doses vs <3. Results in Table 1 indicate that the number of risk factors representing approximately those rates - 5.7% for long COVID and 10.3% for CI - are close to zero COVID risk factors and <1 dementia risks. That suggests that reducing COVID or CI rates via risk factor reduction would require almost total elimination of the COVID and/or dementia risk factors used in this study to match the potential achievement of a successful vaccination campaign (see Table 1).This does not seem to be an easy task when our results show that half of study adults have at least one COVID risk factor and 72% have at least one dementia risk factor and many have two or more. Recognizing study differences in state vaccination rates, and knowing how hard reducing the obesity rate is [20], neither prevention option would be easy but perhaps combining them would offer a better chance of success. For example, combine an education campaign to increase awareness of the potentially modifiable risk factors for dementia and the possibility that COVID vaccines might help reduce CI. Any successful intervention offers the potential for reducing future AD cases if it can reduce rates of CI long term and stop or slow progression to AD. Study results also suggest that even if the intervention on CI by risk factor modification or vaccine is short term and does not slow progression to AD, there should be health benefits in terms of days of activity limitation and ability to work.

Results for long COVID were somewhat different in addition to requiring exposure to the COVID virus. For long COVID, adjusted results showed obesity, diabetes, CVD, COPD, asthma and depression were still significantly associated with higher rates but inactivity, hearing impairment, excess drinking, smoking and < high school education, were not. The highest AOR for long COVID was 2.4 for respondents reporting 3 or more of the 5 COVID risk factors. In the model with the composite dementia risk variable, ages 25-54 years had highest AORs of 2.12-2.15, suggesting the COVID risk factors had a greater effect than the dementia ones on long COVID. However, we found higher rates for long COVID among adults with CI and vice versa (Table 1), with each having adjusted odds ratios >1.4 (Table 3) which is consistent with results showing COVID is a risk factor for AD [5,6] and AD is a risk factor for COVID complications [7].

A brief reminder of how mRNA vaccines work might help to understand the results. The COVID mRNA vaccine uses the SARS-CoV-2 spike protein as antigen to create an

Adams ML, et al., Arch Intern Med Res 2024
DOI:10.26502/aimr.0175

immune response without exposing the vaccine recipient to the virus itself – just the synthetic mRNA that makes the spike protein [21]. Thus, the immune response created is against a protein – the spike protein on the virus. When the vaccine recipient it exposed to the COVID virus, their immune system will recognize it and attack the virus. Because COVID (and the SARs virus) and CI share so many characteristics and risk factors, it seems plausible that the immune system of a COVID vaccine recipient might also recognize and attack a protein similar to the spike protein. One of the key features of Alzheimer's Disease (AD) is amyloid plaques in the brain composed of amyloid-β (Aβ) proteins, which can form as early as 20 years prior to clinical symptoms [5]. In a key study [22] an amyloid precursor protein (APP), precursor of the Aβ proteins of AD, was found to interact with the spike protein of SARS-CoV-2, the protein the COVID vaccine was designed to attack. That finding may be key to understanding the similarities between AD and COVID-19 and add to the plausibility for our vaccine results on CI.

Unanswered questions remain; the exact mechanism of vaccine action on adults with CI without the presence of the COVID virus is still a mystery. Is it possible that the lower rates of both CI and long COVID among US adults age 65+ vs those 18-64 years are due at least partly to them having had more COVID vaccines? Of course, a huge question is whether any reduction in CI rates that results from COVID vaccines – or any other method - will translate to reduction in AD rates or postponing the worsening of AD symptoms.

Limitations

There are at least six limitations to this study. First, results may underestimate true rates of COVID and cognitive impairment because the BRFSS excludes nursing homes. Second, results are self-reported and except as noted for COVID are not based on an actual test or diagnosis. Third, because BRFSS is a telephone survey, only respondents able to complete a survey over the telephone are included. Another BRFSS study that included non-respondents in households with respondents found that some measures of cognitive decline were under-reported by as much as 70% when only respondent data was included [23], suggesting this could be a serious limitation. Fourth, the lack of a measure of hypertension on the survey for 2022 meant that both composite risk factor measures (COVID and dementia) lacked a key component [9,10]. The dementia measure also lacked data on traumatic brain injury, air pollution, and low social contact [10]. Fifth, survey results can't distinguish cause and effect; but we do note that about 98% of vaccine recipients received their first vaccine before the survey started. Sixth, only 29 states had survey data on COVID vaccines.

The study's strengths are that it used a measure of cognitive impairment that is required for use on all federal surveys in the US thus providing a consistent measure of cognition. The data that are available for the 29 states are population based and demonstrate the variation among the states included. As noted above, having multiple risk factors measures available from the same data set allows study of associations between risk factors that might be important when planning interventions.

Conclusion

Two factors seem about equally key to determining who gets long COVID and CI: vaccines and 10 potentially modifiable risk factors. The risk factors appear to be similar enough that the subpopulations with highest rates of long COVID and CI are similar. It also seems that the effectiveness of ≥3 vaccine doses is about equivalent to the effect of the risk factors when considering prevention strategies. And while the dementia risk factors appear to increase rates of both outcomes, they seem to be especially effective at increasing rates of cognitive impairment. These results should help put AD prevention strategies into better perspective.

Although our study leaves many questions unanswered, nothing in the cited studies appears to question the plausibility of our results. The similarity of vaccine effectiveness for CI in adults with and without long COVID, similarity in vaccine results for long COVID and CI for adults of different ages, and the dose response results for 2, 3, and 4 or more vaccines shown in Table 2. are hard to ignore. The potential opportunities these results suggest for reducing cognitive impairment, whether it might progress to AD or not, are exciting.

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Conflict of interest

Ms. Adams works for the Wyoming Department of Health under a contract dba On Target Health Data LLC.

Data availability: All data used in the study are available on the CDC website at: https://www.cdc.gov/brfss/data_documentation/index.htm.

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