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COVID-19 Vaccine intent in appalachian patients with multiple sclerosis

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ABSTRACT

Background: Rural people with Multiple Sclerosis (PwMS) face distinctive challenges in the COVID-19 pandemic. The purpose of this study was to determine the COVID-19 vaccine intent and factors associated with vaccine hesitancy among Appalachian adults with MS.

Method: We conducted a cross sectional phone and in-person survey of PwMS in a large academic center in West Virginia (WV) from February to May 2021. The study sample consists of 306 adult participants.

Results: Among the 306 participants, 104 (33.99%) indicated vaccine hesitancy. Statistically significant factors ($p < 0.05$) associated with vaccine hesitancy compared to those who received or intend to get vaccinated included concerns about vaccine safety, vaccine causing MS relapse, vaccine making MS medication ineffective, vaccine causing other diseases, getting the COVID-19 infection, vaccine fast approval, vaccine ingredients, how well the vaccine works, and its side-effects. Additional factors included prior bad experiences with other vaccines, history of not getting the flu vaccine, and lack of consultation about COVID-19 vaccine with healthcare providers.

Conclusions: Vaccine hesitancy among Appalachian adult PwMS is higher compared to PwMS in the larger United States. Vaccine hesitancy is especially higher among those who are female, younger than 50 years old, and residing in rural areas. Concerns about vaccine safety, perception of infection risks, past vaccine behaviors and consultation with healthcare providers are important factors associated with vaccine intent. Factors influencing vaccine hesitancy in Appalachian PwMS are largely consistent with the general public, however, concerns for interaction between the vaccine and MS are specific to this population and thus could be the focus of further vaccine effort.

Abbreviations

CI	Confidential Interval
COVID-19	Coronavirus disease 2019
DMT	Disease Modifying Therapy
MS	Multiple Sclerosis
OR	Odds Ratio
PwMS	People with multiple sclerosis
SD	Standard Deviation
WV	West Virginia
US	United States

1. Introduction

The unprecedented scale and severity of the current COVID-19 pandemic has catalyzed joint efforts globally to develop vaccines

against the COVID-19 infection (Li et al., 2021). Despite the well-known fact that vaccinations have contributed to the significant reduction in mortality, morbidity and the eradication of several infectious diseases in the past, vaccine hesitancy, defined as “delay in acceptance or refusal of vaccination despite availability of vaccination services” (MacDonald and SWGoV, 2015) continues to post as a main hurdle to overcoming COVID-19. Rural PwMS face distinctive challenges in the pandemic (Murthy et al., 2021). Immunosuppressive mechanisms of action of some MS disease modifying therapies (DMTs) have raised concerns regarding increased risk of severe COVID-19 complications (Reyes et al., 2021; Simpson-Yap et al., 2021). Comorbidities and degree of MS-related disability may also influence risk of severe COVID-19 disease course in PwMS (Reyes et al., 2021; Chaudhry et al., 2020). PwMS living in rural areas may have more underlying chronic health conditions and less access to healthcare as well as lack of health insurances which puts them at additional disadvantage for COVID-19 complications (Murthy

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et al., 2021). Moreover, there are common misconceptions regarding the linkage between vaccination and MS/MS exacerbations (Marrie et al., 2021). Some newer DMTs (excluding interferons and glatiramer acetate) are also thought to be associated with safety concerns due to their long lasting immunosuppressive and immunomodulatory effects and require monitoring for infectious diseases (Jalkh et al., 2020). It is therefore important to know and understand the vaccine intent of this population. In this study, we conducted a cross-sectional survey aimed to determine COVID-19 vaccine intent in Appalachian PwMS and to examine factors associated with vaccine hesitancy.

2. Material and methods

We conducted either a phone or in-person survey (at the end of their regular office visit) among PwMS in a single academic center in Appalachian WV from the beginning of February to the end of May 2021. We contacted 824 patients with a confirmed diagnosis of MS from the directory/ list of patient information listed in their medical record within three years preceding the study. The response rate was 37.13% and 306 participants completed the survey. Inclusion criteria included (1) Diagnosis of any subtype of MS (as confirmed by medical record review), (2) age 18 or older, and (3) seen in this academic center in the past 3 years.

The survey was adapted from a recent survey published on COVID-19 vaccine hesitancy (Puteikis and Mameniskiene, 2021), and divided into three parts: (1) vaccine intent (2) factors associated with vaccine hesitancy (3) demographic information. Questions related to “factors associated with vaccine hesitancy” were further categorized as “perceived vaccine safety,” “perceived disease susceptibility,” “past vaccine behaviors,” “influence from others,” and “concerns related to vaccine access.”

The study was approved by the West Virginia University IRB (protocol no. 2102228098). Surveys were collected anonymously. The participants consented to take part in the study and were informed that their participation in the survey was completely voluntary and they were free to stop at any time or refuse to answer any questions. They were also informed that all information they provided was confidential and could not be traced back to them. Additionally, they were made aware that there was no monetary compensation for their participation.

All statistical analysis was conducted in SAS version 9.4. Descriptive statistics included frequencies and percentage for categorical variables and means, standard deviation (SD) for continuous variables. The main outcome variable was a dichotomous variable that included a vaccine hesitancy group and those who had received or intended to get vaccinated. This variable was created using two questions. Participants were asked “Have you already received the COVID-19 vaccine?” (yes and no) and “If not, how likely are you going to get the vaccine?” that consisted of a 5-point Likert scale for how likely they were to get the vaccine (1-most unlikely, 2- unlikely, 3- neither likely nor unlikely (unsure), 4- likely, and 5- most likely), which was dichotomized as ‘not likely’ (1–3 points) and ‘likely’ (4–5 points). The participants who answered 1- 3 on this scale were defined as the participants who had vaccine hesitancy and did not intend to get the COVID-19 vaccine. Participants who answered ‘unsure’ were included in the hesitant group as they had not decided to get vaccinated at the time of their survey completion. This group was compared with participants who were either vaccinated or intended to get vaccinated. Age was analyzed as a continuous variable and was also categorized as ≤ 24 , 25 – 34, 35 – 44, 45 – 54, 55 – 64, 65 – 74, and ≥ 75 years old. Education status included a binary variable of \leq high-school and $>$ high-school education. Rural status was defined as residing in an area not delineated as “urban area” using the U.S. Census Bureau urban definition (Bureau. USC. United States Census Bureau. 2010). Due to the common notion that older MS therapies such as interferons and glatiramer acetate are “safer” due to their well-established long-term safety profiles and monitoring strategies (Jalkh et al., 2020), we also grouped participants by their disease-modifying therapy (DMT)

types. DMT was categorized as older, newer, and none. For this study, “older” DMTs include interferons and glatiramer acetates and the rest of the DMTs were categorized as “newer” DMTs. The survey question regarding “how well are you doing in terms of MS?” used the 5-point Likert scale and 1–3 points were categorized as ‘not doing well’ and 4–5 points were categorized as ‘doing well’. The questions that inquired about the participant’s concern about different aspects of the vaccine included two types of responses. One was a 5-point Likert scale that included levels of concern (1- not at all concerned, 2- slightly concerned, 3- somewhat concerned, 4- moderately concerned, 5- strongly concerned), which was dichotomized as ‘not concerned’ by combining the 1–3 points and ‘concerned’ by combining the 4–5 points.

The second response included a binary response of ‘yes’ and ‘no’. Independent samples *t*-test was used to determine statistically significant difference between the means of the two groups (vaccine hesitancy group and the comparison group of those who had received or intend to get vaccinated) for the continuous variables. The Chi Square statistic and binary logistic regression was used to determine whether there is a statistically significant association between the two groups (vaccine hesitancy group and those who received or intend to get vaccinated) and categorical variables. The significance level of $\alpha = 0.05$ was used to reject the null hypothesis of no difference between the two groups.

3. Results

3.1. Survey participants

Among the 306 participants, 237 (77.45%) were female with a mean age 49.39 (SD=13.5) and 69 (22.54%) were male with a mean age 53.59 (SD=13.31). Majority of the survey participants (52.61%) were older than 50 years old. The median age of all the survey participants was 50 years and the most prevalent age group was 45–54 years (26.14%). More than one third of the participants ($n = 105$, 35.12%) had less or equal to high school education and 151 (50.5%) survey participants lived in a rural area. Nearly one fifth of the participants (21%) were not on any DMTs, 33 (11%) were on older therapies and 204 (68%) were on newer DMTs. In terms of disease susceptibility, a majority of the survey participants considered themselves to be at low risk for COVID-19 infection (73.6%). Nearly half of the participants (51.97%) considered themselves as “not doing well” in terms of MS and 146 (48.03%) considered themselves as “doing well” (Table 1).

3.2. Outlook on vaccines

At the conclusion of the survey collection out of 306 participants, 148 participants (48.37%) had already received a COVID-19 vaccine and two additional participants were scheduled to receive the vaccine. 156 participants (50.98%) had not received the vaccine. Among those who had not been vaccinated, 66.24% did not intend to get vaccinated. Overall, 104 participants (33.99%) indicated that they were unlikely to be vaccinated and 202 (66.01%) had either received the vaccine or intended to get vaccinated.

Vaccine safety concerns were associated with vaccine hesitancy (OR=7.14, 95% CI: 4.18–12.17). The safety concerns included concerns about vaccine side effects (OR=10.45, 95% CI: 6.02–18.15), fast vaccine approval process (OR=8.91, 95% CI: 4.81–16.51), vaccine ingredients (OR=6.33, 95% CI: 3.74–10.7), and vaccine efficacy (OR=4, 95% CI: 2.41–6.62). Concerns about the vaccine causing other diseases also contributed to vaccine hesitancy (OR=7.12, 95% CI: 4.14–12.24). Additional factors specific to PwMS include concerns about the vaccine causing MS relapse and making DMTs ineffective (OR=4.94, 95% CI: 2.97–8.23 and OR=4.06, 95% CI: 2.42–6.81 respectively). The perceptions of how well survey participants were doing in terms of MS was not associated with vaccine intent ($p = 0.6194$, OR=0.89, 95% CI: 0.55–1.42) but the perception of infection risks was statistically significantly associated with vaccine hesitancy (OR=1.77, 95% CI: 1.05–3). Having not

Table 1
Population characteristics of the study among patients with Multiple Sclerosis (MS) in a single academic center in Appalachian WV (February to May 2021, N=306).

Variables	Categories	N	%
Age	≤ 24	7	2.29
	25 – 34	34	11.11
	35 – 44	65	21.24
	45 – 54	80	26.14
	55 – 64	65	21.24
	65 – 74	47	15.36
	≥ 75	8	2.61
	Mean (SD)		50.34
Education	≤ High School	105	35.12
	> High School	194	64.88
Gender	Female	237	77.45
	Male	69	22.55
Geographic location ¹	Rural	151	50.5
	Urban	148	49.5
Perception of current MS condition ²	Not good	158	51.97
	Good	146	48.03
Use of Disease Modifying Therapy (DMT) ³	No	63	21
	New	204	68
	Old	33	11
Vaccine intent ⁴	Do not intend	104	33.99
	Received/scheduled/intend	202	66.01
Perceived risk of getting the COVID-19 infection	High	80	26.4
	Low	223	73.6
Concerned about vaccine causing MS relapse	Yes	122	40.13
	No	182	59.87
Concerned about vaccine making MS medication ineffective	Yes	97	32.77
	No	199	67.23
Concerned about MS medicine making the vaccine ineffective	Yes	93	31.53
	No	202	68.47
COVID-19 vaccine information source	Doctor(s)	57	18.94
	Friends	4	1.33
	Internet	95	31.56
	TV	47	15.61
	Others	98	32.56
Concerned about where to get the vaccine	Yes	24	7.89
	No	280	92.11
Concerned about vaccine cost	Yes	12	3.99
	No	289	96.01
Have a ride to get the vaccine	Yes	288	96
	No	12	4
Received the flu vaccine in the past year	Yes	169	55.59
	No	135	44.41

¹Geographic location was categorized as Rural and Urban using zip code level data using the U.S. Census Bureau rural definition (United States Census Bureau, 2010).

²Participants were asked “How well you are doing in terms of MS?” and the response was collected using a 5-point Likert scale and 1–3 points were categorized as ‘not doing well’ and 4–5 points were categorized as ‘doing well’.

³DMT New drugs included: Aubagio (teriflunomide), Cellcept (mofetil), Gilenya (fingolimod), Kesimpta (ofatumumab), Lemtrada (alemtuzumab), Mavenclad (cladribine), Mayzent (siponimod), Ocrevus (ocrelizumab), Rituxan (rituximab), Tecfidera (dimethyl fumarate), Tysabri (natalizumab), Vumerity (diroximel fumarate) Old drugs included: Avonex (interferon beta-1a), Copaxone (glatiramer acetate), Plegridy (peginterferon beta-1a).

⁴This variable was created using two questions. Participants were asked “Have you already received the COVID-19 vaccine?” (yes and no) and “If not, how likely are you going to get the vaccine?” that consisted of a 5-point Likert scale which was dichotomized as ‘unlikely’ (1–3 points) and ‘likely’ (4–5 points).

received the flu vaccine in the past year and having had bad experiences with vaccines in the past were also shown to influence vaccine intent (OR=4, 95% CI: 2.42–6.61 and OR=2.33, 95% CI: 1.23–4.42 respectively). Lack of consultation with healthcare providers was associated with vaccine hesitancy (OR=3.53, 95% CI: 2.13–5.84) (Table 2).

Female gender (OR=1.96, 95% CI: 1.05–3.63), age younger than 50 years old (OR=2.54, 95% CI: 1.56–4.14) and residing in a rural area (OR=1.83, 95% CI: 1.12–2.98) were significantly associated with vaccine hesitancy. Educational status (p 0.0537, OR=1.63, 95% CI: 0.99–2.67) and DMTs (new vs old) (OR=0.74, 95% CI: 0.35–1.57) were not significantly associated with vaccine intent (Table 2). Most survey participants did not have concerns about vaccine cost (289, 96.01%), transportation (288, 96%), or where to get the vaccine (280, 92.11%). 95 (31.56%) participants listed the internet as their primary source of information about the vaccine, followed by doctors (57, 18.94%), and television (47, 15.61%). About one third of patients chose “other” as their source of information about the vaccine.

4. Discussion

4.1. Appalachian PWMS

Age distribution of participants in this study were consistent with the general MS population (Marrie et al., 2021; Wallin et al., 2019; Dilokthornsakul et al., 2016). Female to male ratio was 3.43, which is also consistent with typical MS demographics (Marrie et al., 2021; Wallin et al., 2019). Several demographic findings in this study are distinctive. The percentage of our survey participants who had less than or equal to high school level of education (35.12%) is higher than the national average (28.1%) (Bureau. USC. U.S 2021) but lower than the average of the Appalachian regions (63.8%) (Pollard and Jacobsen 2021). A high percentage of our study participants (50.5%) lived in rural areas; in the general Appalachian population only 10% of residents live in rural counties (Appalachian Regional Commission 2020) Thus, our study may have important implications specifically regarding vaccine concerns in more rural patients.

4.2. Vaccine hesitancy among appalachian pwms

According to a survey of 7420 participants in the US by Appalachian Regional Commission (2020), estimates of COVID-19 vaccine hesitancy declined from 46% in October 2020 to 35.2% in March 2021. A nationally representative household panel survey during March-May 2021 showed that 23.2% of young adults aged 18–39 years were probably or definitely not going to get vaccinated (Daly et al., 2021). Another national online survey of PwMS (N = 359) in early January 2021, showed that 20.3% were vaccine hesitant (Baack et al., 2021). In comparison, the vaccine hesitancy rate in the survey population in this study was higher (33.76%).

The study findings of higher vaccine hesitancy in younger, female and rural residents are consistent with past literature findings (Ehde et al., 2021; Fisher et al., 2020; Ruiz and Bell, 2021; Kreps et al., 2020). Prior studies of the general public indicated that individuals with lower education were less likely to pursue vaccination (Ehde et al., 2021; Fisher et al., 2020; Kreps et al., 2020), However, educational status was not associated with vaccine hesitancy in our study population. This discrepancy can be potentially explained by lower vaccine hesitancy in people with pre-existing conditions (Pollard and Jacobsen 2021), and factors indicated by Kreps et al. (2020) that included higher awareness and health literacy, higher trust and interaction with healthcare professionals, and lower pre-existing vaccine hesitancy. Factors found in this study to be significantly associated with vaccine hesitancy in Appalachian PwMS are mostly consistent with those found in past studies in the general population: vaccine safety concerns (Ehde et al., 2021; Ruiz and Bell, 2021; Khubchandani et al., 2021), perception of infection risks (Ehde et al., 2021; Fisher et al., 2020; Ruiz and Bell, 2021; Kreps

Table 2

Factors associated with vaccine intent among patients with Multiple Sclerosis (MS) in a single academic center in Appalachian WV (February to May 2021, N= 306).

Factors	Variables	Categories	Do Not Intend	Received/ Intend	OR (95% CI)	p-value
	N	306	104 (33.99)	202 (66.01)		
Socio-demographic	Age	< 50	65 (62.5)	80 (39.6)	2.54 (1.56, 4.14)	<0.0001
		≥ 50	39 (37.5)	122 (60.4)	-	
	Education	Mean (SD)	45.90 (13.58)	52.62 (12.99)		<0.0001
		≤ High School	43 (42.57)	62 (31.31)	1.63 (0.99, 2.67)	0.0537
	Sex	> High School	58 (57.43)	136 (68.69)	-	
		Female	88 (84.62)	149 (73.76)	1.96 (1.05, 3.63)	0.0314
Geographic location ¹	Male	16 (15.38)	53 (26.24)	-		
	Rural	61 (60.4)	90 (45.45)	1.83 (1.12, 2.98)	0.0145	
MS related	Use of DMT ²	Urban	40 (39.6)	108 (54.55)	-	
		No	24 (23.3)	39 (19.8)	0.95 (0.4, 2.25)	0.9012
	Perception of current MS condition ³	New	66 (64.08)	138 (70.05)	0.74 (0.35, 1.57)	0.4272
		Old	13 (12.62)	20 (10.15)	-	
	Concerned about vaccine causing MS relapse	Not good	52 (50)	106 (53)	0.89 (0.55, 1.42)	0.6194
		Good	52 (50)	94 (47)	-	
	Concerned about vaccine making MS medication ineffective	Yes	67 (65.05)	55 (27.36)	4.94 (2.97, 8.23)	<0.0001
		No	36 (34.95)	146 (72.46)	-	
	Concerned about MS medicine making the vaccine ineffective	Yes	54 (53.47)	43 (22.05)	4.06 (2.42, 6.81)	<0.0001
		No	47 (46.53)	152 (77.95)	-	
	Perceived risk of getting COVID-19 infection	Yes	38 (38.38)	55 (28.06)	1.6 (0.96, 2.66)	0.0716
		No	61 (61.62)	141 (71.94)	-	
Anticipated reasons/ concerns	Concerned about how well COVID-19 vaccine works	High	35 (33.98)	45 (22.5)	1.77 (1.05, 3)	0.0318
		Low	68 (66.02)	155 (77.5)	-	
	Concerned about vaccine causing other diseases	Yes	63 (52.5)	39 (21.67)	4 (2.41, 6.62)	<0.0001
		No	57 (47.5)	141 (78.33)	-	
	Concerned about vaccine approved fast	Yes	77 (75.49)	61 (30.2)	7.12 (4.14, 12.24)	<0.0001
		No	25 (24.51)	141 (69.8)	-	
	Concerned about vaccine ingredients	Yes	88 (85.44)	79 (39.7)	8.91 (4.81, 16.51)	<0.0001
		No	15 (14.56)	120 (60.3)	-	
	Concerned about vaccine safety	Yes	67 (65.69)	46 (23.23)	6.33 (3.74, 10.7)	<0.0001
		No	35 (34.31)	152 (76.77)	-	
	Concerned about side-effects of the vaccine	Yes	66 (64.08)	39 (20)	7.14 (4.18, 12.17)	<0.0001
		No	37 (35.92)	156 (80)	-	
Others	Received the flu vaccine in the past year	Yes	74 (71.15)	38 (19.1)	10.45 (6.02, 18.15)	<0.0001
		No	30 (28.85)	161 (80.9)	-	
	Had adverse experience with vaccine in the past	Yes	69 (66.35)	66 (33)	4 (2.42, 6.61)	<0.0001
		No	35 (33.65)	134 (67)	-	
	Talked to doctor about COVID 19 vaccine	Yes	23 (22.33)	22 (11)	2.33 (1.23, 4.42)	0.0086
		No	80 (77.67)	178 (89)	-	
		Yes	55 (53.4)	49 (24.5)	3.53 (2.13, 5.84)	<0.0001
		No	48 (46.6)	151 (75.5)	-	

¹Geographic location was categorized as Rural and Urban using zip code level data using the U.S. Census Bureau rural definition (United States Census Bureau, 2010).

²Disease Modifying Therapy (DMT) New drugs included: Aubagio (teriflunomide), Cellcept (mofetil), Gilenya (fingolimod), Kesimpta (ofatumumab), Lemtrada (alemtuzumab), Mavenclad (cladribine), Mayzent (siponimod), Ocrevus (ocrelizumab), Rituxan (rituximab), Tecfidera (dimethyl fumarate), Tysabri (natalizumab), Vumerity (diroximel fumarate) Old drugs included: Avonex (interferon beta-1a), Copaxone (glatiramer acetate), Plegridy (peginterferon beta-1a).

³Participants were asked “How well you are doing in terms of MS?” and the response was collected using a 5-point Likert scale and 1–3 points were categorized as ‘not doing well’ and 4–5 points were categorized as ‘doing well’.

et al., 2020; Khubchandani et al., 2021; Reiter et al., 2020), flu vaccine status (Ehde et al., 2021; Fisher et al., 2020; Ruiz and Bell, 2021), past experience with other vaccines (Reiter et al., 2020), and consultations with healthcare providers (Ehde et al., 2021; Khubchandani et al., 2021; Reiter et al., 2020). Among the safety concerns, participants indicated that they were concerned about vaccine side effects, fast vaccine approval, vaccine ingredients, and vaccine efficacy. PwMS were specifically concerned about the vaccine causing MS relapses and reducing the efficacy of the DMTs. This is consistent with past findings in MS patients (Marrie et al., 2021).

Common barriers affecting health disparities in the Appalachian region such as access, transportation, cost and health insurance issues were not concerns in our survey population. Partnering with local independent pharmacies and distribution by the national guards aided initial success of the vaccine rollout in West Virginia (Dube et al., 2013). Other health indicators influencing Appalachian health disparities (How West Virginia became a U.S 2021), such as lack of access to healthcare providers, chronic health conditions, health behaviors,

mental health conditions, and health cultures were not measured in this study.

4.3. Study limitations

The study was a cross-sectional study based on phone and in-person surveys, therefore, limited due to respondent bias, especially when participants were interviewed directly by their healthcare providers. Moreover, since the study sample was not random, the results may not be generalizable due to the nature of its sample selection. The study needs to be replicated in multiple academic centers in different geographic areas to ensure generalizability of this study. Last, the survey process spanned over several months, during which vaccine availability steadily increased and specific vaccine recommendations for MS became more widely available and thus those who indicated vaccine hesitancy in the beginning of the survey may have changed their mind later on (Appalachian Regional Commission 2017).

5. Conclusions

Vaccine hesitancy is a complex issue which is largely influenced by cultural, economic, political, and demographic context (Puteikis and Mameniskiėne, 2021). The results from our study showed that compared to the national survey result of PwMS (Baack et al., 2021), Appalachian adult PwMS in a large academic center in WV demonstrated higher vaccine hesitancy, especially among those who are female, younger than 50 years old, and residing in rural areas. Concerns about vaccine safety, perception of infection risks, past vaccine behaviors and consultation with healthcare providers are important factors associated with vaccine intent. Factors influencing vaccine hesitancy in PwMS are largely consistent with the general public, however, concerns for interaction between the vaccine and MS are specific to this population thus could be the focus of further vaccine effort. Vaccine cost and transportation to vaccine sites were not barriers to vaccination in this Appalachian population. Health disparity concerns in general Appalachian population such as lack of health insurance/cost or access to a vaccination site were not barriers to vaccination in our survey population.

Thus far, there have been no significant concerns about either increased risk of MS relapses or lowered MS DMT efficacy from the COVID-19 vaccines that were available to patients in this study (KFF 2021). In contrast, some data does suggest worse outcomes in some MS patients who contracted COVID-19, depending on specific DMT, degree of disability and other comorbid conditions (Reyes et al., 2021). In our study, the majority of patients felt their risk of COVID-19 infection was low, and concerns about vaccine-related MS risks were associated with vaccine hesitancy. A recently published survey of the MS population by Marrie et al. (2021) found that 43% of participants reported that their neurologist had ever asked about their immunization history (Marrie et al., 2021). In our study a lower percentage of patients received most of their information about vaccines from their healthcare providers, instead receiving information from the internet, television, or other combined sources. This has particular implications regarding potential opportunities for interventions to improve vaccine uptake in Appalachian PwMS, especially rural patients. On a public health level, information distributed through media channels (internet, television, etc.) may be more likely to effectively reach patients. On an individual level, referring patients to reliable internet resources for vaccine information (such as those available from the National Multiple Sclerosis Society) (Kelly et al., 2021) as well as direct discussion between providers and patients regarding vaccine safety and MS-specific risks of COVID-19 infection may also be opportunities for improvement in vaccine acceptance in this population.

Contributor's statement page

Ms. Hongyan Wu conceptualized and designed the study, conducted phone and in office surveys, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Melanie Ward conceptualized and designed the study, conducted phone and in office surveys, and critically reviewed the manuscript for important intellectual content.

Ms. Ashlyn Brown and Ms. Erica Blackwell conducted phone and in office surveys and critically reviewed the manuscript for important intellectual content.

Dr. Amna Umer conceptualized and designed the study, carried out the statistical analyses, interpreted the data findings, and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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