Changes in the Rates of Medication Non-Adherence Between 2019 and 2021 Among Patients with Migraine in the United States

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Introduction

- Migraine is the fifth leading cause of years lived with disability (YLD) in the United States (US) and impacts 37 million US adults.[1,2]
- The prevalence of self-reported migraine and severe headache in the US adult population is 15.3% (1 out of every 6 adults) and has been stable over a period of 19 years.[3]
  - Highest prevalence is in American Indian or Alaska Natives (18.4%).
  - Higher burden of migraine in those aged 18-44 (17.9%), who are unemployed (21.4%), those with family income less than $35,000 per year (19.9%), and the elderly and disabled (16.4%).
- Migraine is the fourth or fifth most common reason for visits to the emergency department and the third leading cause of emergency department visits among reproductive-aged women.[3]
- The annual economic burden of migraine in the US is approximately $78 billion with a total mean annual direct all-cause healthcare costs of $11,010 and indirect costs of $11,294.[4,5]
- The Migraine Impact Model projected approximately 60,000 to 686,000 annual workdays to be affected by lost productive time due to migraine.[6]
- In one study conducted between 2012 and 2013, 35.5% of the respondents reported discontinuing the use of acute prescription medication for migraine.[7]
  - One-third of respondents who discontinued treatment exhibited moderate to severe depression (33.0%) and/or moderate to severe anxiety (30.0%).
  - The most common reason (45.5%) associated with acute prescription medication discontinuation was the decision to switch away from prescription medication to over-the-counter or alternative treatment options. This was followed by concerns about lack of efficacy (28.2%), safety/tolerability (24.9%), headaches had improved (21.3%), and financial concerns (19.4%).

Objective

- To utilize the Medication Adherence Reasons Scale (MAR-Scale) to determine the extent and reasons for non-adherence in individuals with migraine.
- To compare non-adherence between the years 2019 and 2021 through the US National Health and Wellness Survey in patients with migraine.

Methods

Data Source

- This study utilized data collected from the US National Health and Wellness Survey (NHWS), a self-administered, internet-based cross-sectional survey of adults in 2019 and 2021 (not necessarily mutually exclusive samples).
- NHWS ensures representativeness through quota sampling of age, sex, and race/ethnicity categories that match the demographic composition of the US adult population, based on data from US Census Bureau.
- NHWS has been granted exemption status by Pearl IRB (Indianapolis, IN, USA).
- Respondents eligible for this study who self-reported taking daily prescription medication(s) to treat migraine answered the 20 items in the MAR-Scale in the NHWS. The MAR-Scale measures non-adherence "in the past 7 days" and uses an 8-point scale ranging from 0 days to 7 days.
- Questions around switching behavior were used to determine reasons respondents switched their prior prescription medication.
- COVID-19 vaccination rate was included in this analysis to determine if there is relationship between healthy habits such as vaccination and medication adherence.

Statistical Analyses

- Descriptive statistics included count and percentages for categorical variables and means and standard deviations for continuous variables.
- Frequencies for each year's respondents were reported to illustrate the reasons for non-adherence.
- Chi-square tests and ANOVA were used to test differences between groups for categorical variables and continuous variables, respectively.

Results

Differences in Demographics

- There were a greater proportion of males (approximately 8.3%), married respondents (5.1%), college-educated (7.6%), current smokers (8.7%), reported alcohol drinkers (4.1%), those taking steps to lose weight (3.9%), and fewer respondents in the low-income bracket (10.6%) in 2021 than 2019.
- Adherent individuals were older, white, retired, and overweight/obese with low annual income.
- A significantly greater proportion of individuals reporting non-adherence were smokers, drank alcohol, and trying to lose weight.
- A higher proportion of respondents in the adherent group had received a COVID-19 vaccine compared to the non-adherent group (62.71% vs. 48.36%, p <0.05).

Trends of Non-Adherence

- There was a significant increase in non-adherence between 2019 and 2021, for all classes of migraine medicines.
- The mean number of missing days increased from 1.99 to 2.41 between 2019 and 2021.
- For both 2019 and 2021, the reasons for missing the most number of days of the medication were:
  - Don't think the medicine is needed anymore.
  - Don't think the medicine is working.
  - Did not consider taking this medicine as a high priority in life.
- The greatest proportion of non-adherence was found in patients who took opioids for migraine.
- In 2021, side-effects from the medicine was the major reason for non-adherence for all classes of medicines, except, NSAIDS.
- The overall non-adherence rate for all medicines was 50.3% in 2019 and 57.61% in 2021. The lowest non-adherence was with anticonvulsants and the highest was with opioids.
- The 2019 top 3 reasons for non-adherence:
  - Concerned about long-term side-effects from the medicine.
  - Concerned about possible side-effects from the medicine.
  - Simply missed the medicine.
- The 2021 top 3 reasons for non-adherence:
  - Side-effects from the medicine.
  - Sometimes skip the medicine to see if it is still needed.
  - Concerned about long-term effects from the medicine.
- Reasons for switching medication among non-adherent respondents:
  - Doctor's recommendation was the most common reason for switching medications for both 2019 (64.60%) and 2021 (57.58%). In 2021, a greater proportion of non-adherent respondents reported switching medications due to cost (35.02% vs. 24.78%, p <0.05) and dosing convenience (15.82% vs. 7.96%, p <0.05).

Table 1. Top Reasons for Medication Non-Adherence in Patients with Migraine

Reason	Patients Taking Migraine Prescription Medication																			
	2019 Total n=1705		2021 Total n=1848		2019 Triptans n=629		2021 Triptans n=689		2019 Opioids n=487		2021 Opioids n=553		2019 Anticonvulsants n=582		2021 Anticonvulsants n=621		2019 NSAIDs n=465		2021 NSAIDs n=545	
% of Patients Who Missed/Mean # of Days Missed	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#
Non-adherence – aggregated score from 19 reasons	50.3%	1.99	**57.6%**	**2.41**	52.2%	2.17	**58.8%**	**2.63**	63.9%	2.82	**75.4%**	**3.49**	36.9%	1.38	**46.1%**	**2.01**	60.0%	2.49	**66.2%**	**2.88**
Side-effects from the medicine	21.8%	3.41	**31.4%**	3.24	25.9%	3.56	**35.9%**	3.59	31.2%	3.45	**50.1%**	3.24	14.3%	3.61	**25.3%**	3.47	23.4%	3.40	**33.9%**	3.30
Sometimes skip the medicine to see if it is still needed	21.6%	3.38	**30.7%**	3.33	20.5%	3.74	**30.6%**	3.70	33.3%	3.53	**42.7%**	3.53	11.7%	3.53	**22.5%**	3.64	29.0%	3.35	**36.2%**	3.34
Concerned about long-term effects from the medicine	24.2%	3.46	**29.2%**	3.50	24.6%	3.57	**30.2%**	3.74	35.1%	3.66	**41.6%**	3.69	16.5%	3.47	**22.7%**	3.62	31.0%	3.38	**37.3%**	3.48
Simply missed the medicine	21.9%	3.03	**26.6%**	**3.31**	23.1%	3.02	**29.3%**	**3.61**	31.2%	3.55	**38.7%**	3.56	17.0%	2.66	**23.8%**	**3.28**	25.6%	2.96	28.4%	**3.53**
Concerned about possible side-effects from the medicine	23.0%	3.54	**26.3%**	3.57	23.1%	3.72	**28.0%**	3.65	33.3%	3.75	38.2%	3.76	16.2%	3.41	**22.1%**	3.85	27.1%	3.53	**33.2%**	3.49
Missed it because of busy schedule/change in routine	17.0%	3.25	**23.8%**	3.46	17.0%	3.21	**27.1%**	3.63	27.9%	3.44	**36.9%**	3.72	10.8%	2.71	**18.4%**	**3.30**	19.8%	2.98	**26.2%**	3.42
Not comfortable taking it for personal reasons	16.5%	3.55	**23.4%**	3.44	19.2%	3.74	**25.3%**	3.81	25.9%	3.76	**36.7%**	3.61	11.2%	3.80	**18.5%**	3.46	20.0%	3.77	**25.7%**	3.49
Don't think need the medicine anymore	14.4%	3.89	**23.4%**	3.78	16.2%	4.20	**28.5%**	4.10	22.2%	4.06	**38.3%**	3.83	8.4%	3.78	**16.9%**	4.05	17.0%	3.86	**27.0%**	4.05
Don't think medicine is working	16.8%	3.87	**21.9%**	3.89	20.7%	3.92	**27.1%**	4.16	24.2%	3.91	**33.1%**	4.09	11.5%	4.01	**18.7%**	4.28	19.1%	3.91	**25.7%**	3.99
Difficulty opening the container or getting the injection ready to use	13.8%	3.69	**21.2%**	3.66	16.1%	3.87	**26.7%**	3.84	22.6%	3.99	**36.2%**	3.79	8.9%	3.44	**15.9%**	3.90	14.8%	3.75	**24.0%**	3.67
Trouble managing all the medicines I have to take	12.5%	3.68	**21.1%**	3.64	14.2%	3.97	**24.7%**	3.98	20.5%	3.67	**34.9%**	3.83	7.2%	3.43	**15.8%**	3.82	13.3%	3.50	**23.9%**	3.63
Do not consider taking the medicine as a high priority in my daily routine	14.4%	3.87	**21.1%**	3.87	16.9%	3.98	**26.1%**	3.92	24.6%	4.14	**33.8%**	3.92	9.6%	3.89	**14.2%**	4.33	18.9%	3.74	**24.0%**	3.95
Difficulty swallowing/applying/inhaling/injecting the medicine	12.8%	3.70	**20.6%**	3.76	13.8%	3.76	**24.7%**	4.05	23.2%	3.76	**35.6%**	3.85	7.2%	3.40	**14.8%**	3.97	14.4%	3.34	**21.1%**	3.76
Pharmacy/provider was out of this medicine, out of refills, or the mail order did not arrive in time	14.1%	3.67	**20.5%**	3.61	18.0%	3.87	**25.1%**	3.79	21.8%	3.88	**30.7%**	3.74	9.1%	3.57	**14.5%**	3.76	15.1%	3.44	**23.1%**	3.65
Difficulty remembering things in daily life	15.3%	3.44	**20.2%**	3.55	16.2%	3.55	**23.1%**	3.82	25.1%	3.82	30.4%	3.85	10.7%	3.32	**15.6%**	3.58	17.6%	3.35	22.2%	3.58
Not comfortable taking it for social reasons	13.8%	3.54	**19.1%**	3.54	14.6%	3.68	**21.0%**	3.83	21.6%	3.54	**31.5%**	3.66	7.7%	3.51	**13.7%**	3.71	13.6%	3.30	**20.4%**	3.55
Didn't have a way to get to the pharmacy/provider	13.0%	3.73	**18.8%**	3.73	13.7%	3.99	**22.1%**	3.88	21.2%	3.78	**31.1%**	3.81	7.6%	3.75	**12.1%**	3.71	14.6%	3.47	**21.3%**	3.89
Don't have money to pay for the medicine	15.4%	3.60	**18.0%**	3.51	16.7%	4.05	20.9%	3.77	23.0%	3.92	**29.7%**	3.55	9.5%	3.89	**14.2%**	3.72	18.7%	3.77	22.2%	3.49
Not sure how to take this medicine	10.4%	3.82	**16.1%**	3.68	13.0%	4.17	**20.5%**	3.89	17.9%	3.74	**27.3%**	3.82	6.9%	3.85	**11.4%**	4.15	11.6%	4.11	**16.7%**	4.00

Note: Cells outlined in blue with bold font indicate a statistically significant difference, p<0.05.

Table 2. Demographic and Lifestyle Characteristics

Characteristic	US 2019 – Migraine			US 2021 – Migraine		
	Total (n=1,705)	Adherent (n=847)	Non-Adherent (n=858)	Total (n=1,848)	Adherent (n=783)	Non-Adherent (n=1,065)
Male (%)	26.80	19.13	**34.38**	35.12	19.54	**46.57**
18-34 years old (%)	33.49	23.26	**43.59**	30.19	22.48	**35.87**
35-44 years old (%)	23.34	21.37	25.29	29.87	22.48	**35.31**
45-54 years old (%)	20.88	**25.74**	16.08	19.64	22.09	17.84
55-64 years old (%)	15.37	**20.07**	10.72	14.07	**22.35**	7.98
65+ years old (%)	6.92	**9.56**	4.31	6.22	**10.60**	3.00
Age (mean) years	42.51	**46.26**	38.81	42.3	**46.66**	39.09
Married (%)	50.09	48.17	51.98	55.19	50.83	**58.40**
Single, never married (%)	25.34	23.73	26.92	22.46	22.22	22.63
Retired (%)	10.09	**14.17**	6.06	9.47	**15.96**	4.69
College graduate (four-year) or more (%)	44.93	39.79	**50.00**	52.49	45.85	**57.57**
White (%)	70.50	**76.86**	64.22	69.48	**77.39**	63.66
Non-White (%)	29.50	23.14	**35.78**	30.52	22.61	**36.34**
Annual household income < $50K (%)	44.57	**49.35**	39.86	33.93	**38.19**	30.80
Overweight/obese^ (%)	64.55	**69.93**	58.99	62.73	**70.62**	56.55
Currently smoke cigarettes (%)	26.98	19.95	**33.92**	35.71	21.07	**46.48**
Drink alcohol (%)	68.50	62.22	**74.71**	72.62	62.58	**80.00**
Mean days exercising (past month)	7.42	7.08	7.77	8.08	7.58	8.44
Currently taking steps to lose weight (%)	59.41	55.02	**63.75**	63.26	57.60	**67.42**
Received COVID-9 vaccine (%)	-	-	-	54.44	**62.71**	48.36

Note: Red, bold font indicates a statistically significant difference, p <0.05. ^Base differs.

Table 3. Prescription Medication Switches

Medication Summary	Patients Taking Migraine Prescription Medication					
	Total		Adherent		Non-Adherent	
	US 2019 (n=1,705)	US 2021 (n=1,848)	US 2019 (n=847)	US 2021 (n=783)	US 2019 (n=858)	US 2021 (n=1,065)
Received Medication* Prior to Current Medication (%)						
No	65.63	60.77	72.61	71.39	**58.74**	52.96
Yes	34.37	39.23	27.39	28.61	41.26	**47.04**
Did Current Medication Replace Previous Medication* OR Was It Added On? (%)						
Not sure	7.51	6.48	6.90	5.80	7.91	6.79
Added on to my existing medication*	28.50	30.62	28.88	23.21	28.25	33.93
Replaced my existing medication*	63.99	62.90	64.22	70.98	63.84	59.28
Reason Current Medication Replaced Previous Medication* (%)						
Doctor's recommendation	64.00	59.43	63.09	62.89	64.60	57.58
To reduce side-effects	26.67	30.70	20.81	23.90	30.53	34.34
Lower cost	18.13	25.22	8.05	6.92	24.78	**35.02**
Not responding to the previous treatment	38.40	37.72	42.95	50.94	35.40	30.64
Dosing of the current Rx is more convenient	5.87	10.96	2.68	1.89	7.96	**15.82**
Mode of administration is more convenient	4.27	4.17	2.68	2.52	5.31	5.05
Other	5.33	4.17	8.72	5.66	3.10	3.37

Note: Red, bold font indicates a statistically significant difference, p <0.05. *Medication, treatment, or therapy.

Discussion

- Non-adherence rate significantly increased from 2019 to 2021.
- Health habits were not compared between 2019 and 2021; however, drinking and smoking are directionally higher amongst non-adherent patients in 2021 vs. 2019.
- In the 2021 US NHWS respondents, a higher proportion of those in the adherent group had received a COVID-19 vaccine.
- There may be many factors to help explain why reasons for non-adherence changed, including fewer respondents reporting "simply missing." This could indicate better self-awareness of medication post-COVID pandemic or may be unrelated.
- Further studies should explore if there are differences in reasons for adherence in other migraine medications, including those with newer administrations such as injections and intranasal sprays.

Limitations

- The data analyzed for this study is self-reported data.
- The NHWS estimates one cross-section of time; as such, adherence behavior over time is not captured.
- The MAR-Scale was used only for daily medications and did not include the option to report for non-daily migraine medications that could have been available and impact adherence differently than those reported.

Conclusions

Self-reported **adherence to medications has changed from 2019 to 2021** among patients who have migraine. **Exploration of adherence to all types of migraine medications is warranted** to further investigate differences within this patient population.

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