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Using the Medication Adherence Reasons Scale (MAR-Scale) to Identify the Reasons for Medication Non-Adherence among Type 2 Diabetes, Migraine, and Depression Medication Users in Japan

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Introduction

- Diabetes, headache disorders, and depressive disorders are among the top ten health problems that cause the most disability in Japan. [1]
- 7.9% of the Japanese population have diabetes, 12.2% have depression, and 6.0% have migraine. [2, 3, 4]
- Koynagi (2016) reported that more than 40% of patients have a target HbA1c level of less than 7%, and a non-adherence rate of 58% with oral antidiabetic drugs.[5]
- A recent claims-based cohort study on DPP-4 inhibitors demonstrated that 12-month persistence rates with once-daily regimens were 66.3%, 64.7% with twice-daily, and 38.8% with once-weekly regimens.[6]
- For migraine, 62.2% discontinued initial prophylactic treatment after an average of 61.2 days (SD 65.3) of persistent treatment.[7]
- This calls for the need to understand the reasons for non-adherence from the patients' perspective.

Background

Medication Adherence Reasons Scale (MAR-Scale)

- A comprehensive self-report measure that assesses the different aspects of non-adherence, such as reasons and frequency.
- The scale has demonstrated acceptable reliability and validity in 17 disease areas.[8]
- Previous exploratory factor analyses have found that the MAR-Scale has 4 domains:
  - Non-adherence due to logistic issues (8 items), e.g., Difficulty swallowing
  - Non-adherence due to belief issues (4 items), e.g., Skip medicine to see if it is still needed
  - Non-adherence due to forgetfulness issues (4 items), e.g., Forgetfulness due to a busy schedule
  - Non-adherence due to long-term concerns (3 items), e.g., Concern about the potential side effects from the medicine

Objectives

- To use the MAR-Scale to determine the extent and reasons for non-adherence with medicines used to treat type 2 diabetes (T2D), migraine, and depression in Japan.
- To determine the reliability of the MAR-Scale in T2D, migraine, and depression in a Japanese population.

Methods and Sample

- Data from the 2019 National Health and Wellness Survey (NHWS), a self-administered, annual, internet-based cross-sectional survey of Japanese adults (age 18+) was used.
- NHWS uses a random-stratified sampling framework (sex and age) to ensure that it is representative of the demographic composition of the Japanese adult population, based on data from the International Data Base of the U.S. Census Bureau and Organization for Economic Cooperation and Development.
- The NHWS has been approved by Pearl IRB (Indianapolis, IN, USA).
- Respondents who self-reported a physician diagnosis of T2D, migraine, or depression and reported taking daily prescription medication(s) to treat their T2D, migraine, and/or depression were given the MAR-Scale.

Medication Adherence Reasons Scale (MAR-Scale)

- The scale has 19 specific reasons for non-adherence and one global item.
  - Respondents were shown the 19 items from the MAR-Scale and were asked to select all the items that were reasons for their non-adherence in the past week. For the items chosen by the respondent, they then selected the number of days, using a 7-point scale (1 day to 7 days), in which that reason was a cause of their non-adherence.

For the following questions, please think about your **DAILY** medicine or medicines for **<condition>** (i.e., medicine prescribed for use every day). These medications include:
Over the last **7 days**, which of the following were reasons you did **NOT** take the medicine or medicines above as prescribed? **MULTI SELECT**

1	I had side effects from the medicine.
2	I did not have money to pay for the medicine.
3	I was not comfortable taking it for personal reasons (e.g., tired of taking medicine, too sick, my religious beliefs).

- The global item provides an overall estimate of the frequency of medication adherence. Respondents use an 8-point scale (0 days to 7 days) to report the number of days they took the medicine as prescribed in the past week.

Over the last **7 days, how many days** were **YOU ABLE TO** take your **DAILY** medicine or medicines for **<condition>** exactly as prescribed? These medications include:

0 days (have not taken the medicine or medicines in the last 7 days)	1 day	2 days	3 days	4 days	5 days	6 days	7 days (took the medicine or medicines on all of the 7 days)
0	1	2	3	4	5	6	7

Statistical Analysis

- Descriptive statistics included count and percentages for categorical variables and means and standard deviations for continuous variables.
- Cronbach alpha's were used to provide an estimate of reliability. A cut-off of ≥ 0.70 was used.[8]

Respondent Demographics

- Sample size:
  - T2D medication daily use (n=889)
  - Migraine medication daily use (n=156)
  - Depression medication daily use (n=790)
- Males were more likely to be on medication for T2D and depression, and females were more likely to be on medication for migraine.
- Over 50% of those with T2D and depression reported an annual household income over < ¥5,000,000.
- Majority of respondents had some college education and medical insurance.

Table 1. Respondent Demographics

Demographics	T2D (n=889)	Migraine (n=156)	Depression (n=790)
Age (mean / SD)	66.13 / 9.89	44.01 / 15.05	45.22 / 13.31
Male (gender) (%)	78.18	37.82	56.33
Annual Household Income < ¥5,000,000 (%)	50.73	46.15	52.66
Education			
Less than high school (%)	2.81	4.49	4.81
High school (%)	37.12	35.26	33.04
2-year college (%)	8.55	18.59	13.29
4-year college (%)	50.96	41.67	46.96
Declined to answer (%)	0.56	–	1.90
Marital Status			
Married (%)	73.79	51.92	41.39
Single, never married (%)	12.60	32.69	44.56
All other (net) (%)	13.61	15.38	14.05
Types of Medical Insurance			
National Health Insurance (%)	54.56	48.72	48.99
Social Insurance (%)	27.67	42.95	37.85
Late-Stage Elderly Insurance (%)	14.85	3.21	0.89
Other (%)	2.47	3.85	8.23
None of the above (%)	0.45	1.28	4.05

Respondent Lifestyle Demographics

- Over 40% of those with T2D were overweight or obese. However, they only exercised an average of 7 days a month.
- Those with migraine and depression took more steps to lose weight than those with T2D.
- Those with depression reported more smoking.
- Over 50% of respondents drank alcohol which was even higher in those with T2D.

Table 2. Lifestyle Demographics

Lifestyle Demographics	T2D (n=889)	Migraine (n=156)	Depression (n=790)
Overweight/Obese (%)^	41.88	23.68	34.12
Currently Smoke Cigarettes (%)	19.69	27.56	27.97
Drink Alcohol (%)	67.49	53.21	56.58
Mean Days Exercising in the Past Month	7.22	4.46	4.57
Currently Taking Steps to Lose Weight (%)	27.00	33.97	35.32

Note: ^Differing base size – respondents didn't provide weight.

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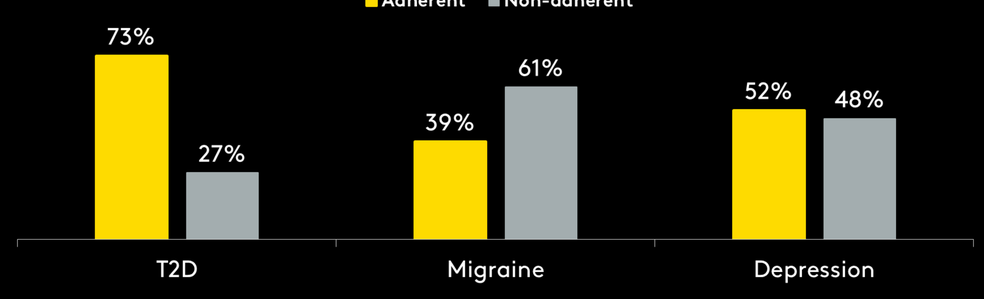
Results

Non-Adherence

- The overall medication non-adherence rate was 27% in T2D, 61% in migraine, and 48% in depression (based on the 19 items).

Figure 1. Non-Adherence Rates for T2D, Migraine, and Depression



Top Reasons for Medication Non-Adherence in T2D, Migraine, and Depression

- The most common reasons for non-adherence across all three diseases were concern about long-term effects, concern about possible side effects, and simply missing the medicine.
- The reason for missing the medicine for more days in the past week was side effects for T2D (3.89 days); lack of belief in the necessity of medicine for migraine (4.33 days); and difficulty opening the container for depression (3.86 days).

Figure 2. Top Reasons for Medication Non-Adherence in T2D, Migraine, and Depression

Reasons	T2D (n=889)		Migraine (n=156)		Depression (n=790)	
	% of Patients Who Missed	Mean # Days Missed	% of Patients Who Missed	Mean # Days Missed	% of Patients Who Missed	Mean # Days Missed
Concerned about long-term effects from the medicine	12.5%	1.9	34.0%	3.2	29.1%	2.7
Simply missed the medicine	10.0%	1.7	17.3%	3.0	18.6%	2.3
Concerned about possible side effects from the medicine	8.9%	1.9	23.1%	3.0	22.9%	2.7
Do not consider taking the medicine as a high priority in my daily routine	8.2%	2.1	19.9%	3.5	10.8%	2.9
Missed the medicine because of busy schedule/change in routine	4.4%	2.1	14.1%	3.5	9.8%	2.9
Don't think that the medicine is working for them	2.8%	1.6	12.8%	2.9	12.3%	2.9
Skip the medicine to see if it is still needed	2.0%	2.1	23.1%	3.7	14.1%	3.0
Don't think that they need the medicine anymore	1.8%	2.3	17.3%	4.3	6.1%	3.8
Did not have money to pay for the medicine	1.5%	2.7	9.6%	2.9	5.1%	3.9
Not comfortable taking it for personal reasons	1.4%	2.0	13.5%	3.6	9.2%	2.8
Not comfortable taking it for social reasons	1.4%	1.7	8.3%	3.2	6.1%	3.0
Difficulty opening the container	1.4%	2.9	9.0%	3.6	4.4%	3.9
Trouble managing all the medicines they have to take	1.2%	3.3	9.6%	3.7	4.7%	3.3
Difficulty swallowing the medicine or inhaling the medicine	1.1%	2.4	8.3%	3.7	4.6%	3.4
Missed the medicine because the pharmacy was out of this medicine/out of refills/mail order did not arrive in time	1.1%	2.5	9.6%	4.0	5.8%	3.5
Side effects from the medicine	1.0%	3.9	10.9%	3.1	9.4%	3.3
Forgetfulness due to cognitive issues	1.0%	2.3	9.0%	3.3	6.7%	3.3
Missed the medicine because they didn't have a way to get to the pharmacy/provider	0.8%	3.0	10.9%	3.7	5.2%	3.4
Not sure how to take this medicine	0.6%	3.0	5.8%	3.8	3.0%	3.4

Lifestyle Demographics by Adherence

- Among T2D respondents, adherent respondents are more likely to make healthier lifestyle choices than non-adherent respondents.
- Among migraine respondents, adherent respondents have a higher rate of smokers, drinkers, and overweight/obese.
- Among depression respondents, adherent respondents are making healthier choices though they are more likely to be overweight/obese and are less like to drink alcohol than non-adherent respondents.

Table 3. Lifestyle Demographics by Adherence

Lifestyle Demographics by Adherence	T2D		Migraine		Depression	
	Adherent (n=653)	Non-Adherent (n=236)	Adherent (n=61)	Non-Adherent (n=95)	Adherent (n=408)	Non-Adherent (n=382)
Overweight/Obese (%)^	40.97	44.40	26.67	21.74	36.57	31.52
Currently Smoke Cigarettes (%)	18.68	22.46	31.15	25.26	25.49	30.63
Drink Alcohol (%)	67.38	67.80	55.74	51.58	53.19	60.21
Mean Days Exercising in the Past Month	7.59	6.20	3.92	4.81	4.39	4.76
Currently Taking Steps to Lose Weight (%)	27.41	25.85	31.15	35.79	36.52	34.03

Note: ^Differing base size – respondents didn't provide weight.

Scale Reliability

- The scale demonstrated acceptable reliability statistics in T2D, migraine, and depression.

Table 4. Reliability Statistics

Reliability Statistics	T2D Medication	Migraine Medication	Depression Medication
Cronbach Alpha	0.869	0.939	0.937

Strengths and Limitations

Strengths

- National database with various quality control measures
- Large sample size for a self-reported study for diabetes and depression
- Detailed insight and quantification of the various reasons for non-adherence

Limitations

- Analyses are based on self-report data of adherence measures. Recall bias may introduce error in addition to overestimation and/or underestimation of adherence.
- However, keeping in mind that self-reported adherence data are often skewed, correction factors should be applied to data for further analysis.
- Cross-sectional studies account for only one point in time and do not capture adherence behavior over time. Replicating these results with a longitudinal study would be beneficial.

Discussion

- Non-adherence rate with migraine and depression were higher compared to that with T2D.
  - Lack of knowledge about the medications in migraine and depression can be a reason for this.
    - While only 12.5% of patients in T2D were non-adherent due to fear of long-term effects, this was 34.0% and 29.1% for migraine and depression.
    - While only 8.9% of patients in T2D were non-adherent due to fear of side effects, this was 23.1% and 22.9% for migraine and depression.
  - Another reason can be the symptomatic nature of migraine and depression.
    - 12.8% and 12.3% of the respondents don't think the medicine is working for them compared with 2.8% in T2D patients.
    - 23.1% and 14.1% of the respondents skipped the medicine to see if it is still needed compared with 2.0% in T2D patients.
    - 17.3% and 6.1% of the respondents didn't think they needed the medicine anymore compared with only 1.8% in T2D patients.
  - Stigma can be another reason for this high non-adherence in migraine and depression.
    - While only 1.4% did not take the medicine due to personal reasons in T2D, it was 13.5% and 9.2% in migraine and depression.
    - While only 1.4% did not take the medicine due to social reasons in T2D, it was 8.3% and 6.1% in migraine and depression.
- Overall, the reasons for non-adherence were quite varied and high for both migraine and depression demonstrating a clear need for further education and awareness raising.

Conclusions

- Reasons for non-adherence with T2D, migraine, and depression:
  - MAR-Scale identified the most common reasons for non-adherence in T2D, migraine, and depression medications.
  - MAR-Scale differentiated between the most frequent reason and most impactful (i.e., number of days) reason of non-adherence for T2D, migraine, and depression medications.
- Scale reliability and validity:
  - MAR-Scale provided an overall rate estimate for non-adherence.
  - MAR-Scale demonstrated acceptable reliability with T2D, migraine, and depression medications.
- Overall, the MAR-Scale can be used as a scale to measure adherence with T2D, migraine, and depression medications in the Japanese population.

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