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Factors Influencing Medication Adherence in Patients with Type 2 Diabetes Mellitus in Japan

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A R T I C L E I N F O

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A B S T R A C T

Introduction. Diabetes mellitus (DM) is a chronic metabolic disease marked by persistent hyperglicemia. Type 2 diabetes mellitus (T2DM) is increasingly prevalent in Japan, affecting approximately 10% of adults with diabetes, according to the Ministry of Health, Labor and Welfare in 2020. Maintaining medication adherence is critical for T2DM management and complications prevention. This review aimed to synthesize factors influencing medication adherence in T2DM patients in Japan. **Methods**. This systematic review followed PRISMA-P guidelines, using the keywords The keywords “risk factors", "medication adherence", "diabetes mellitus", and "Japan”. After applying inclusion and exclusion criteria, five cross-sectional studies were selected for analysis. **Results**. Medication adherence among Japanese T2DM patients ranged from 65% to 85%. Positive factors linked to higher adherence included higher family income, knowledge of drug effect, absence of complication, increased number of medications, frequent healthcare utilization, structured lifestyle perception, and physical functionality. In contrast, variables such as gender, education level, and type of medication showed no significant influence in multiple studies. The use of validated scales highlighted correlations between high adherence and improved HbA1c outcomes. **Conclusion**. Medication adherence is multifactorial, driven by clinical and socio-behavioral determinants. Knowledge and perception-based interventions, combined with lifestyle modification and simplified therapy regimens, may enhance adherence in Japanese T2DM patients.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia or a persistent increase in blood glucose levels. This condition occurs due to disturbances in insulin secretion, insulin action, or both. Poorly managed DM contributes to severe complications including cardiovascular disease, nephropathy, retinopathy, and neuropathy. The prevalence of type 2 diabetes mellitus (T2DM) continues to rise globally. According to 2021 data from the International Diabetes Federation (IDF), approximately 537 million adults (aged 20-79 years) worldwide are living with diabetes, with T2DM accounting for the majority of these cases.[1] In Japan, the prevalence of T2DM is also showing an increase. Data from the Japanese Ministry of Health, Labour and Welfare in 2020 reported that approximately 10% of the adult population in Japan had diabetes with T2DM being the most common type.[2]

In Japan, the growing elderly population and lifestyle changes, such as increased consumption of high-fat diets and sedentary lifestyles, have accelerated the rise of T2DM prevalence. Despite Japan's highly developed healthcare infrastructure, challenges in controlling T2DM include low patient adherence to treatment and cost constraints in ongoing care, especially in the elderly who are dependent on fixed pensions. This is particularly concerning given that good adherence is associated with improved glycaemic control and reduced risk of complications.[3,4]

Medication adherence in Japan varies depending on the type of disease and the population studied. For example, a study published in 2020 examined the adherence of hypertensive patients in Japan and found that about 60% of patients showed a high level of adherence to their medication regimen. However, in patients with other chronic conditions, such as T2DM, adherence rates may be lower influenced by factors such as the complexity of the drug regimen, side effects, and the patient's perception of their disease.[5,6]

Management of T2DM involves a holistic approach that includes lifestyle changes, pharmacological therapy and close monitoring to achieve optimal glycaemic control and prevent long-term complications. Recommended lifestyle modifications include adopting a balanced, calorie-controlled diet low in saturated fats and rich in dietary fiber, along with engaging in regular physical activity to enhance insulin sensitivity and reduce the risk of diabetes-related complications.[7] If lifestyle changes are not enough, pharmacological therapies such as Metformin (starting with 500 mg once or twice daily, can be increased to 2000-2500 mg per day), sulfonylureas such as glibenclamide (2.5-20 mg per day), and glimepiride (1-8 mg per day), DPP-4 inhibitors such as sitagliptin (100 mg per day), GLP-1 agonists such as liraglutide (starting from 0.6 mg per day, can be increased to 1.8 mg per day), and SGLT2 inhibitors such as dapagliflozin (10 mg per day) can be used, with drug selection based on the patient's clinical condition. Regular monitoring of blood glucose levels and ongoing education on self-management are also critical to the successful management of T2DM, requiring multidisciplinary support from healthcare professionals.[7–9]

While global studies have explored general determinants of adherence, Japan presents a unique context due to its aging society, sociocultural norms, and healthcare access patterns. However, a systematic review focusing on factors influencing medication adherence specifically among Japanese T2DM patients remains limited. Understanding these context-specific determinants is crucial for developing targeted interventions to improve patient outcomes. This systematic review aims to identify and synthesize existing evidence on the risk factors influencing medication adherence in patients with T2DM in Japan.

2. Methods

This study was conducted as *systematic review* using *Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols* (PRISMA-P).. A literature search was carried out in PubMed**,** Google Scholar, and ScienceDirect to identify relevant articles published up to 2024. The search terms used were: *"risk factor"* AND *"medication adherence"* AND *"diabetes mellitus"* AND *"Japan"*. Additional references were identified by screening bibliographies of the selected articles.

Inclusion criteria comprised original research conducted in Japan, focused on T2DM patients, and reporting on medication adherence and its influencing factors. Only full-text articles in English or Japanese were considered. Studies were excluded if they were reviews, case reports, conference abstracts, or did not specifically assess adherence. The selection process began with 45 articles identified through the initial search. After removing duplicates and screening titles and abstracts, 13 articles remained for full-text review. Ultimately, five studies met all inclusion criteria and were included in the analysis. The article selection process is outlined in the PRISMA flow diagram (Figure 1).

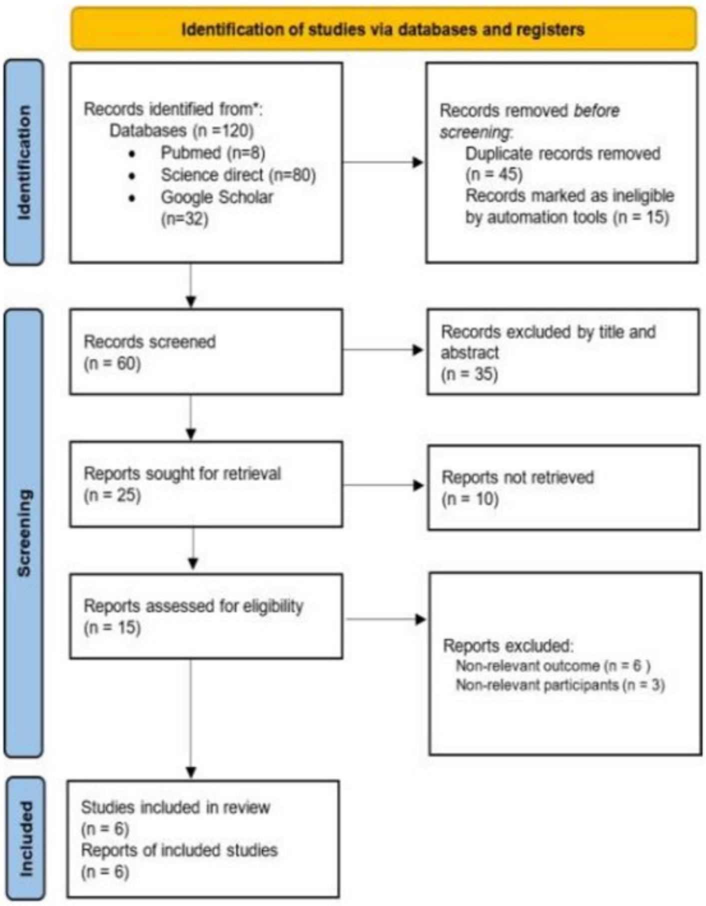

Figure 1. PRISMA diagram of article screening for systematic review

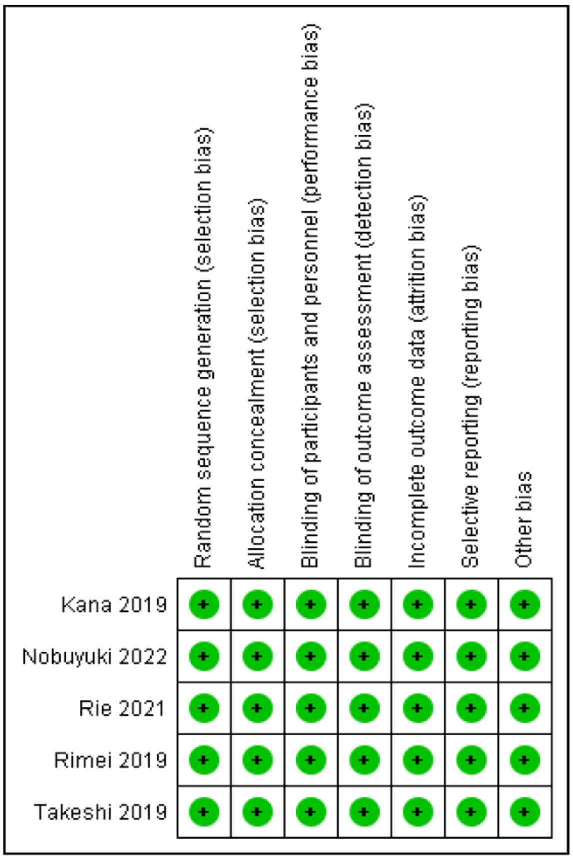

Figure 2. Risk of bias and applicability concerns from article findings using the review manager

Data from each study were extracted using a standardized form and included information such as study design, sample size, population characteristics, adherence measurement tools, and key findings. Risk of bias was assessed using a modified version of the Newcastle-Ottawa Scale for cross-sectional studies, and results were visualized using Review Manager (RevMan) software. All five included studies were considered to be of moderate to high methodological quality.

3. Results

Based on the search results, 5 journals were obtained that were in accordance with the research objectives regarding T2DM treatment adherence in Japan. All studies were cross sectional studies, including Rimei et al. (2019), Nobuyuki et al. (2022), Rie Nakajima et al. (2021), Takeshi et al. (2019), and Kana et al. (2019). Each article was analysed for risk of bias. Tools used to assess compliance scale included the Proportion of Days Covered (PDC), Morisky Medication Adherence Scale (MMAS-4), and other validated instruments.

4. Discussion

Medication adherence in patients with T2DM is crucial for effective glycaemic control and preventing long-term complications. Patients who adhere to treatment with oral antidiabetic drugs show significant improvements in HbA1c level control, thereby reducing the risk of microvascular complications, as well as improving quality of life and reducing costs burden. In contrast, non-adherence to treatment often leads to glycaemic instability, triggering chronic complications. Contributing factors to non-adherence include side effects, complexity of the therapy regimen, and lack of social support and education.[10–14]

Consistent to WHO's five-domain model (2003), the American Diabetes Association (ADA) identify the same broad categories including patient-related (e.g. age), socioeconomic (e.g. medication cost), condition-related (e.g. present of complication), therapy-related (e.g. adverse effect), and health-system-related (e.g. continuity care) as key determinants of medication non-adherence.[15,16] Furthermore, the Japan Diabetes Society (JDS) emphasizes patient-centered care and lifestyle support as integral to promoting long-term treatment success.[17] In addition, technology-based interventions such as medication reminder apps have been shown to effectively improve adherence by helping patients remember schedules and providing medication-related information, contributing to better glycaemic control.[18]

Findings from several Japanese studies underscore key individual and systemic barriers to adherence. Nishimura et al. (2019) identified the complexity of therapy regimens and the experience of adverse drug effects are key factors that reduce patient's likelihood of to adhere to their medication.[19] Social support and education also found to be strong predictors of adherence, aligning with the Health Belief Model, which suggests that perceived barriers and benefits, along with cues to action, influence health behaviors such as medication-taking.[20]

This study used Proportion of Days Covered (PDC) as the measurement scale for treatment adherence, where patients were considered adherent if PDC reached ≥80%. The results showed that high adherence to therapy, especially with the use of dipeptidyl peptidase-4 inhibitor (DPP-4i), was positively associated with better diabetes management.[19]

Research by Nobuyuki Wakui et al. (2022) further emphasized risk factors particularly among elderly patients. These factors include proper medication storage, knowledge of medication effects and side effects, and physical functioning of the patient. The relationship between these factors and diabetes mellitus treatment is evident in the way that a strong understanding of medication effects enhances patients' motivation to adhere to therapy, as diabetes is a chronic condition that often lack noticeable symptoms, patients may feel less compelled to continue taking medication. This study used a medication adherence measurement scale that included medication storage status and knowledge of drug effects, and used the 12-Item Short Form Survey (SF-12) to assess patient's quality of life. The results showed that knowledge of drug effects had the strongest association with medication adherence, emphasising the importance of patient education.[21]

Research by Rie Nakajima et al. (2021) identified behavioral contributors to non-adherence, showing that smoking, alcohol consumption, unhealthy diet, and lack of physical activity were all significantly associated with non-adherence both unintentionally and intentionally. This study used a measurement scale to assess medication non-adherence that distinguishes between unintentional and intentional non-adherence, with lower scores indicating higher levels of non-adherence. The results showed that patients who had unhealthy living habits and experienced difficulties in taking medication tended to have lower levels of adherence. The importance of interventions that focus on increasing health awareness and lifestyle changes to improve medication adherence.[22]

Table 1. List of articles and journals related to T2DM treatment adherence in Japan

No	Author/Research Design	Sample Quantity	Observation Duration (Months)	Compliance Scale	Scale Validation	Definition of Compliance	Compliance Level
1.	Rimei et al., 2019/Cross Sectional	131.329	4 years	Proportion of Days Covered (PDC)	Patients are considered compliant if PDC ≥ 80%	Proportion of days on which the patient has a prescribed medicine in the period.	High (82.5%) Low (17.5%)
2.	Nobuyuki et al., 2022/Cross Sectional	47	7 months	MMAS-4 (Medication Management Situation) and SF-12v2	Norm-based scoring (NBS)	Ability to take prescribed medications correctly as directed by the doctor and proper understanding of the timing of taking medications.	High (77.3%) Low (22.7%)
3.	Rie Nakajima et al., 2021/Cross Sectional	599	4 days	Unintentional and Intentional Non-Adherence Scale	NA	The rate at which patients follow treatment recommendations given by a healthcare professional	High (65%) Low (35%)
4.	Takeshi et al., 2019/Cross Sectional	884	3 years	Proportion of Days Covered (PDC)	PDC was calculated based on the number of days the patient had medication compared to the total days in the observation period; PDC ≥ 0.8 was considered to be adherent	The degree to which the patient follows the treatment regimen as prescribed by the healthcare provider	High (79.6%) Low (20.4%)
5.	Kana et al., 2019/Cross Sectional	157	2 years	MMS (Medication Management Situation) and SF-12v2	Norm-based scoring (NBS)	Ability to take prescribed medication correctly as directed by the doctor and with proper understanding about the time to take medicine	High (85%) Low (15%)

Table 2. Characteristics of the analysed research

No	Researcher Name	Influential factors (*p-value*)	Factors that have no effect (p-value)
1.	Rimei et al., 2019	1. Monthly family income >50 USD: AOR = 5.00, $p < 0.001$ 2. No diabetes-related complications: AOR = 1.66, p = 0.003 3. Using a health facility more than once a month: AOR = 2.87, $p < 0.001$ 4. Following a specialised diet for diabetes: AOR = 1.81, p = 0.008 5. No alcohol consumption: AOR = 13.67, p = 0.001	1. Marital status: p = 0.051 2. Education: p = 0.067 3. Frequency of measuring weight: p = 0.056 4. Frequency of checking blood pressure: p = 0.407 5. Smoking: p = 0.691 6. Knowledge score: p = 0.180
2.	Nobuyuki et al., 2022	1. Drug storage: p = 0.01 2. Knowledge of drug effects: $p < 0.001$ 3. Knowledge of side effects: p = 0.026 4. Physical functioning (SF-12 subscale): p = 0.045	1. Gender: p = 1.00 2. Duration of diabetes: p = 0.32 3. Type of drugs used: p = 0.37 4. Drug management status: p = 0.64 5. Treatment satisfaction score (DTSQ): p = 0.52 6. Other SF-12 subscales: $p > 0.05$
3.	Rie Nakajima et al., 2021	1. Current smoking: β = 0.280, $p < 0.001$ 2. Alcohol consumption more than three days a week: β = 0.147, p = 0.020 3. Unhealthy eating habits: β = -0.136, p = 0.034 4. Lack of exercise: β = -0.151, p = 0.020 5. Insufficient sleep: β = 0.164, p = 0.002	1. Age: p = 0.62 2. Gender: p = 0.88 3. Food: p = 0.077
4.	Takeshi et al., 2019	1. Number of drugs (3–4): OR = 1.68, p = 0.024 2. Number of drugs (≥5): OR = 2.74, p = 0.004 3. Gender (male): OR = 0.45, p = 0.022 4. Age (50–<60 years): OR = 2.15, p = 0.016 5. Number of visits (≥17): OR = 29.9, $p < 0.001$	1. HbA1c (≥7.0%): p = 0.214 2. BMI (≥25): p = 0.446 3. Use of DPP-4 inhibitors: p = 0.370 4. Use of α-GI: p = 0.473 5. Glinide use: p = 0.526 6. Biguanide use: p = 0.096 7. Thiazolidine use: p = 0.123
5.	Kana et al., 2019	1. Body Mass Index (BMI): p = 0.031 2. Family history of diabetes: p = 0.002 3. Diabetes knowledge: p = 0.033 4. Patient perception (organised living): p = 0.001	1. Gender: p = 0.821 2. Age: p = 0.217 3. Duration of diabetes: p = 0.053 4. HbA1c: p = 0.658 5. Complications: $p > 0.05$ for all types of complications tested

Horii et al. (2019) provided further insight into how polypharmacy and demographic factors associated with medication adherence in T2DM patients in Japan. Interestingly, while polypharmacy is often associated with poor adherence, the authors found that a higher number of medications was correlated with better adherence. They suggested that this may be because patients taking multiple medications are more likely to have severe disease or complications, which increases their awareness of the condition and motivates them to adhere to treatment. Another key finding related to demographic factor was that male gender and age between 50-59 years demonstrated higher adherence. This study used Proportion of Days Covered (PDC) as the measurement scale for medication adherence, where patients were considered adherent if PDC reached ≥80%. The results showed that high adherence was positively associated with better haemoglobin A1c (HbA1c) values, emphasising the importance of interventions to improve adherence in diabetes management.[23]

Hashimoto et al. (2019) examined psychological and perceptual factors associated with medication adherence in T2DM patients in Japan. The study identified body mass index (BMI), family history of diabetes, knowledge of diabetes, and patient perception of living a regular life as significant factor. Patients who perceived themselves as leading a regular and structured life were more likely to adhere to their medication regiment. This suggest that psychological aspect is positively associated with medication adherence, emphasising the importance of interventions focusing on changing perceptions to improve adherence in diabetes management. This study utilised the medication adherence measurement scale developed by Ueno et al. which includes several subscales to assess different aspects of adherence.[24]

This study has several limitations that may influence the interpretations of its findings. The small number of included studies and all were cross sectional design, limits the ability to draw causal inferences regarding the relationship between identified factors and medication adherence. Differences in adherence measurement tools across studies may also reduce the comparability of results. Additionally, the literature search was limited to English and Japanese-language publications, raising the possibility that relevant studies in other languages were overlooked. Since all the included studies were conducted within the context of Japan's healthcare system, the findings may not be fully generalizable to other countries with differing cultural or systemic healthcare frameworks.

5. Conclusion

This review found that medication adherence among patients with T2DM in Japan is shaped by the factors such as patient knowledge, perception of illness, treatment complexity, lifestyle, and socioeconomic status. These findings highlight the need for tailored interventions, emphasizing both clinical and socio-behavioral determinants, to improve adherence. Future research should adopt longitudinal or interventional designs to better understand causality and evaluate targeted strategies within Japan's unique healthcare context. Standardizing adherence measurement tools would also enhance comparability across studies.

6. Author Contribution

The conceptualization was carried out by Nuzla Emira Ramadhany, Viona Olivia, Nabila Azzahra Putri, and Brian Jordan Yuwono. Data curation was performed by Nuzla Emira Ramadhany, Viona Olivia, Nabila Azzahra Putri, and Brian Jordan Yuwono. Data analysis was conducted by Nuzla Emira Ramadhany, Viona Olivia, Nabila Azzahra Putri, and Brian Jordan Yuwono. Supervision and review were provided by Eka Handayani Oktharina and Raissa Nurwany. All authors contributed to the preparation of the manuscript and approved the final version for submission to this journal.

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