Eduvest – Journal of Universal Studies
Volume 5 Number 02, February, 2025
p- ISSN 2775-3735- e-ISSN 2775-3727

RELATIONSHIP OF COGNITIVE FUNCTION ON MEDICATION ADHERENCE AND CLINICAL OUTCOMES OF GERIATRIC PATIENTS WITH DIABETIC NEUROPATHY

M. Andhika Fauzi[1], Nadia Farhanah Syafhan[2*], Taufan Harun Habibie[3]
Fakultas Farmasi, Universitas Indonesia, Indonesia [1,2]
RSUD Tebet, Jakarta Selatan, Indonesia [3]
Email: mandhikafauzi90@gmail.com; nadia.farhanah@farmasi.ui.ac.id; taufanhabibie@gmail.com

ABSTRACT

Diabetic neuropathy is a common complication of diabetes mellitus that significantly impacts quality of life and is also prone to cognitive decline exacerbated by diabetes complications. Medication adherence has been shown to slow or prevent cognitive decline. Neuropathy symptoms, neuropathic pain, and sensory disturbances can worsen cognitive function. This study aimed to assess the relationship between cognitive function and medication adherence, as well as clinical outcomes of neuropathy symptoms in geriatric patients with diabetic neuropathy. This observational cross-sectional study involved 217 geriatric patients at RSUD Tebet from June to September 2024. Cognitive function was assessed using the MoCA-Ina questionnaire, and adherence was measured through questionnaires, medical records, and direct observation (MARS-5, MPR, and Pill Count) as well as DNS scoring to assess clinical outcomes of neuropathy symptoms. This study found that women (71,5%) were more likely to experience cognitive decline than men (28,5%). The study found that medication adherence varied by method. Triangulation showed 64.6% non-adherence in cognitive decline versus 35.4% in normal function (OR 1.774, 95% CI: 1.001-3.144). Caregiver presence significantly affected adherence (p=0.011), with a 2.8 times higher risk of non-adherence and a 2.4 times higher risk of neuropathy symptoms in patients without caregivers.

KEYWORDS *geriatrics, diabetic neuropathy, cognitive function, medication adherence, neuropathy symptoms.*

How to cite: M. Andhika Fauzi, et al. (2025). Relationship of Cognitive Function on Medication Adherence and Clinical Outcomes of Geriatric Patients with Diabetic Neuropathy. *Journal Eduvest. 5*(2), 1577-1589
E-ISSN: 2775-3727

INTRODUCTION

The global increase in the elderly population is accompanied by a rise in life expectancy, posing significant challenges in managing degenerative diseases. In Indonesia, the percentage of the elderly population reached 11.75% in 2022, a 4% increase from 2010. This demographic shift is associated with a higher prevalence of chronic conditions such as diabetes mellitus, which affected 19.46 million adults aged 20-79 years in 2021 ((Badan Pusat Statistik, 2023) .Diabetes mellitus is often complicated by diabetic neuropathy, with incidence rates in various studies ranging from 6% to 51%, and a reported rate of 17.6% in Indonesia in 2021 (International diabetes federation, 2021). Diabetic neuropathy leads to a spectrum of clinical manifestations, from asymptomatic conditions to severe neuropathic pain, increasing cardiovascular morbidity and mortality, as well as the risk of foot ulcers and amputations (Hicks & Selvin, 2019; Jermendy et al., 2023).

Effective management of diabetic neuropathy involves pharmacotherapy including anticonvulsants, serotonin and norepinephrine reuptake inhibitors, tricyclic antidepressants, opioids, and topical analgesics, as recommended by the American Diabetes Association (ADA) (Bondar et al., 2021; Pop-Busui et al., 2022). The Diabetic Neuropathy Symptom (DNS) scoring instrument is utilized to predict neuropathy symptoms in diabetic patients (Meijer et al., 2003; Z. Yang et al., 2018). Medication adherence remains a critical determinant of therapeutic success, with non-adherence impacting overall health outcomes. Studies indicate that only about 50% of patients with chronic diseases adhere to their medication regimens, highlighting a significant challenge in managing diabetes mellitus and its complications (Jose & Bond, 2021, Fernandez-Lazaro et al., 2019; Timar et al., 2016; H. Yang et al., 2020).

Cognitive function plays a crucial role in medication adherence among elderly diabetic patients. Declining cognitive function, particularly in those over 65 years with uncontrolled glycemic levels and severe neuropathy, has been linked to poor adherence. Cognitive function encompasses various brain processes, including attention, memory, learning, and perception, which are essential for daily activities and health management. (Brognara et al., 2020; Rachman et al., 2022; Jiawei, 2019). Research has shown that patients with diabetes and peripheral neuropathy are more likely to experience cognitive impairment, further complicating disease management.(Huang et al., 2021; Mufidah, 2022; Palomo-Osuna et al., 2022)

Inconsistent findings in existing literature regarding the relationship between neuropathy and cognitive function underscore the need for focused studies on geriatric populations. Some studies report no significant correlation between cognitive function and neuropathy severity, while others highlight cognitive impairment as a contributing factor to non-adherence (Y. J. Lin et al., 2021; Moreira et al., 2015; Rahmawati & Hargono, 2018), This study aimed to assess the relationship between cognitive function and medication adherence in geriatric patients with diabetic neuropathy at RSUD Tebet, utilizing a triangulation method involving MARS questionnaires, pill counts, and medical records. The study seeks to provide insights into factors affecting medication adherence and clinical outcomes, contributing to enhanced patient management and the development of clinical pharmaceutical science in Indonesia.

RSUD Tebet, located in South Jakarta's densely populated Tebet District, serves as the primary healthcare facility for elderly patients, offering specialized geriatric clinics. This research, conducted from June to September 2024, will explore the characteristics of geriatric patients, the interplay between cognitive function and medication adherence, and other determinants influencing neuropathy outcomes. The findings are expected to inform better clinical practices and policies, ultimately improving the quality of care for geriatric patients with diabetic neuropathy.

RESEARCH METHOD

This study used a cross-sectional design to assess the influence of cognitive function on medication adherence and clinical outcomes of geriatric patients with diabetic neuropathy at RSUD Tebet, South Jakarta from June to September 2024. The study population consisted of geriatric patients with a diagnosis of diabetic neuropathy who met inclusion criteria, such as age ≥ 60 years, receiving antihyperglycemic therapy, and being able to communicate well

This research has been approved by the Medical and Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia, under the number KET- 572/UN2.F1/ETIK/PPM.00.02/2024 and also received permission from RSUD Tebet, South Jakarta. Data collection tools included the MoCA-Ina questionnaire to assess cognitive function, Medication Adherence Report Scale (MARS-5) for medication adherence, as well as the calculation of the Medication Possession Ratio (MPR) and pill count. The clinical outcome of neuropathy symptoms was assessed by a DNS questionnaire.

Data analysis included a univariate test for frequency distribution, bivariate analysis with the Chi-Square tests to test variable relationships, and multivariate analysis using binary logistic regression to evaluate the influence of confounding variables on medication adherence and neuropathy symptoms. This study was expected to provide insight into patient characteristics and factors that affect the management of diabetic neuropathy in geriatric service facilities.

RESULT AND DISCUSSION

Characteristics of Patient Based on Cognitive Function

In this study, we observed a total of 217 geriatric patients with diabetic neuropathy, with a higher proportion of females experiencing cognitive decline (71.5%) compared to males (28.5%). The gender difference was statistically significant ($p=0.012$), suggesting that females are at a higher risk for cognitive decline, potentially due to hormonal changes post-menopause affecting brain health (Bell et al., 2022; Russell et al., 2019). The average age of subjects with cognitive decline was significantly higher at 69.62 years compared to 64.98 years in those with normal cognitive function ($p<0.001$). Older age was associated with greater cognitive decline, consistent with previous research identifying aging as a primary risk factor for cognitive impairment due to neurodegenerative and vascular processes (Wang et al., 2017; Zhang et al., 2019).

Educational level showed a significant association with cognitive function ($p<0.001$), where subjects with more than 12 years of education were

predominantly in the normal cognitive function group (79.3%). Higher education may enhance cognitive reserve, providing resilience against cognitive decline, and is associated with better access to health information and resources (Hoffmann & Lutz, 2019; Matyas et al., 2019; Zhong et al., 2024).

HbA1c levels did not show a significant relationship with cognitive decline (p=0.376), contrary to some studies suggesting a link between poor glycemic control and cognitive impairment (Alkethiri et al., 2021). Similarly, no significant association was found between the duration of diabetes mellitus and cognitive decline (p=0.159), though long-standing diabetes has been implicated in vascular and neurodegenerative complications affecting cognitive function (Gonzales et al., 2022; Randväli et al., 2024). While the presence of comorbidities was high among subjects with cognitive decline (95.4%), it was not significantly associated with cognitive function (p=0.676). However, obesity was significantly related to cognitive decline (p=0.046), supporting evidence that midlife obesity increases risks for cognitive impairment (Randväli et al., 2024).

Most subjects prescribed more than four types of medication were in the cognitive decline group (95.4%) compared to the normal cognitive function group (92.0%). In contrast, only 4.6% of the cognitive decline group and 8.0% of the normal function group were prescribed four or fewer medications. There was no significant difference in the number of prescribed medications between the groups (p=0.452). Polypharmacy in older age can impair cognitive function (Rhalimi et al., 2018; Umegaki, 2020).Caregiver support significantly impacted cognitive function (p=0.002), with high social support associated with better self-efficacy and medication adherence, thereby reducing cognitive impairment risk (Huang et al., 2021; Ma et al., 2024; Pillemer & Holtzer, 2016). The characteristics of patients based on cognitive function can be seen in **Table 1** below.

Table 1. Demographic characteristics and clinical data of research subjects based on cognitive function

Variable	Cognitive Function		Total	*p-value*
	Declined (n=130)	Normal (n=87)		
	N (%)	N (%)	N (%)	
Demographics				
Gender				
Male	37 (28,5)	40 (46,0)	77 (35,5)	0,012
Female	93 (71,5)	47 (54,0)	140 (64,5)	
Age				
Mean ± SD	69,62 ± 6,65	64,98 ± 3,98	67,76 ± 6,16	<,001
60-69 years	67 (51,5)	78 (89,7)	145 (66,8)	<,001
70-79 years	52 (40)	8 (9,2)	60 (9,2)	
≥80 years	11 (8,5)	1 (1,1)	12 (5,5)	
Education Level				
>12 years	53 (40,8)	69 (79,3)	122 (56,2)	<,001

Variable	Cognitive Function		Total	*p-value*
	Declined (n=130)	Normal (n=87)		
	N (%)	N (%)	N (%)	
≤12 years	77 (59,2)	18 (20,7)	95 (43,8)	
DM- Related Factors				
HbA1c Level (%)				
Median (min-max)	7.1 (5,00 - 14.30)	6.9 (5,6-13,5)	6,9 (5-14,3)	0,580
HbA1c ≥ 7	66 (50,8)	38 (43,7)	104 (47,9)	0,376
HbA1c < 7	64 (49,2)	49 (56,3)	113 (52,1)	
DM Duration				
≤ 5 years	49 (37,7)	42 (48,3)	91 (41,9)	0,159
> 5 years	81 (62,3)	45 (51,7)	126 (58,1)	
Comorbidities				
Yes	124 (95,4)	81 (93,1)	205 (94,5)	0,676
No	6 (4,6)	6 (6,9)	12 (5,5)	
BMI kg/m2				
Median (min-max)	24,79 (18,71-68,44)	25.71 (18,65-35,71)	25,00 (18,65-68,44)	0,500
Underweight-Normal	73 (56,2)	36 (41,4)	109 (50,2)	0,046
Overweight-Obese	57 (43,8)	51 (58,6)	108 (49,8)	
Number of Prescribed Drigs				
≤ 4	6 (4,6)	7 (8,0)	13 (6,0)	0,452
> 4	124 (95,4)	80 (92,0)	204 (94,0)	
Caregiver				
Yes	29 (22,3)	5 (5,7)	34 (15,7)	0,002
No	101 (77,7)	82 (94,3)	183 (84.3)	

The Relationship of Cognitive Function to Medication Adherence

In this study, medication adherence was measured using the MARS-5 questionnaire, Medication Possession Ratio (MPR), and Pill Count method. While no significant differences were found in adherence measured by MARS-5 and MPR between patients with cognitive decline and normal cognitive function (p=0.234 and p=0.651 respectively), the Pill Count method showed a significant difference (p=0.036). Patients with cognitive decline were 3.16 times more likely to be non-adherent compared to those with normal cognitive function. These findings highlight the influence of cognitive function on medication adherence and the importance of using multiple assessment methods to obtain a comprehensive understanding (Anghel et al., 2019; Choo et al., 2021; Hansen et al., 2009). Using the triangulation method from three medication adherence measurements, it was

found that 71.5% of patients with cognitive decline were non-adherent, compared to 58.6% of those with normal cognitive function. This difference was not statistically significant (p=0.068). However, the odds ratio (OR) of 1.774 (95% CI: 1.001-3.144) suggests that patients with cognitive decline have a 1.77 times higher risk of non-adherence. Previous studies have shown that poor cognitive function negatively impacts medication adherence, leading to irregular medication consumption and reduced therapy effectiveness (Austin et al., 2017; Chudiak et al., 2018).

Table 2. Relationship between cognitive function and medication adherence

	Cognitive Function			
Variable	**Declined (n=130)**	**Normal (n=87)**	***p-value***	**OR (95% CI)**
	N (%)	**N (%)**		
Medication Adherence				
MARS-5 Category				
Non- Adherent	82 (63,6)	47 (36,4)	0,234	Ref
Adherent	48 (54,5)	40 (45,5)		1,454(0,837-2,525)
MPR Method				
Non- Adherent	30 (63,8)	17 (36,2)	0,651	Ref
Adherent	100 (58,8)	70 (41,2)		1,235 (0,633-2,411)
Pill Count Method				
Non- Adherent	21 (80,8)	5 (19,2)	0,036	Ref
Adherent	109 (57,1)	82 (42,9)		3,160 (1,143-8,732)
Overall Adherence (MARS-5+MPR+Pill Count)				
Non- Adherent	93 (64,6)	51 (35,4)	0,068	Ref
Adherent	37 (50,7)	36 (49,4)		1,774 (1,001-3,144)

The Relationship of Cognitive Function to Clinical Outcomes of Neuropathy Symptoms

This study assessed clinical outcomes of diabetic neuropathy using the Diabetic Neuropathy Symptom (DNS) scoring. Among patients with cognitive decline, 73.1% had neuropathy, while 26.9% did not. In patients with normal cognitive function, 75.9% had neuropathy, and 24.1% did not. The p-value of 0.763 indicates that this difference is not statistically significant. The Odds Ratio (OR) of 1.158 (95% CI: 0.619-2.164) suggests no significant difference in neuropathy risk between patients with cognitive decline and those with normal cognitive function. Cognitive dysfunction is common in diabetic patients (Ba-Tin et al., 2011) and does not seem to affect the presence of microvascular complications like neuropathy. However, other studies found a significant negative correlation between cognitive performance and the severity of peripheral neuropathy (Y.-J. Lin et al., 2021).

.

Table 3. Relationship between Cognitive Function and Clinical Outcomes of Neuropathy Symptoms (DNS Scoring)

	Cognitive Function			
Variable	**Decreased (n=130)**	**Normal (n=87)**	***p-value***	**OR (95% CI)**
	N (%)	**N (%)**		
Clinical Outcomes Symptoms of Neuropathy (DNS Scoring)				
No	35 (62,5)	21 (37,5)	0,763	Ref
Yes	95 (59,0)	66 (41,0)		1,158 (0,619-2,164

The Relationship between Cognitive Function and Other Variables with Medication Adherence

Researchers conducted a multivariate analysis to examine the relationships between multiple variables and identify potential effects when analyzed collectively. The analysis aimed to evaluate the impact of cognitive function and other confounding variables on medication adherence using logistic regression with the enter method. Variables with p <0.25, such as education level, BMI category, and presence of a caregiver, were included in the analysis. The OR value for BMI category was less than 10%, indicating it is not a confounding variable. In contrast, education and caregiver presence showed OR changes above 10%, indicating they are confounding variables affecting the relationship between cognitive function and medication adherence.

Multivariate analysis showed no statistically significant relationship between cognitive decline and medication adherence (p=0.087) after controlling for education and caregiver presence, with a 0.5 times risk of non-adherence compared to normal cognitive function. Caregiver presence was significant (p=0.011), indicating a strong influence on medication adherence. Patients without caregivers had a 2.8 times higher risk of non-adherence compared to those with caregivers. Strong social support from caregivers, especially family members, is crucial in enhancing patient adherence to medication (Scheurer et al., 2012).

Table 4. Relationship of cognitive function and other variables to medication adherence

Model	**Confounding Variable**	**Category**	**p- value**	**OR**	**95% CI (lower-upper)**
Crude	Cognitive Function	Declined	0,049	0,564	0,318-0,999
		Normal			
Multivariat	Cognitive Function	Declined	0,108	Ref	0,309-1,122
		Normal		0,589	
	Education	>12 years	0,122	Ref	0,870-3,256
		<=12 years		1,684	

	BMI	Underweight-normal	0,110	Ref	0,334-1,116
		Overweight-obese		0,616	
	Caregiver	Yes	0,09	Ref	1,309-6,674
		No		2,953	
Adjusted	Cognitive Function	Declined	0,087	Ref	0,300-1,084
		Normal		0,570	
	Education	>12 years	0,082	Ref	0,928-3,438
		<=12 years		1,786	
	Caregiver	Yes	0,011	Ref	1,275-6,410
		No		2,859	

The Relationship between Cognitive Function and Other Variables with Clinical Outcomes of Neuropathy Symptoms

Multivariate analysis was conducted on cognitive function and clinical outcomes of neuropathy symptoms, considering confounding variables like comorbidities and the presence of a caregiver. Comorbidities were not confounding variables as their OR value change was less than 10%. However, the caregiver variable showed an OR change above 10%, indicating it is a confounding factor.

The analysis revealed no statistically significant relationship between cognitive decline and clinical outcomes of neuropathy symptoms (p=0.405) when controlled for the caregiver variable. Patients without a caregiver had a 2.4 times higher risk of experiencing neuropathy symptoms compared to those with a caregiver.

Table 5. Relationship between cognitive Function and other variables with clinical outcomes of neuropathy symptoms

Model	Confounding Variable	Category	p- value	OR	95% CI (lower-upper)
Crude	Cognitive Function	Declined	0,646	0,864	0,462-1,614
		Normal			
Multivariat	Cognitive Function	Declined	0,447	Ref	0,407-1,488
		Normal		0,778	
	Comorbidity	Yes	0,999	Ref	0,0-
		No		<0,001	
	Caregiver	Yes	0,089	Ref	0,873-6,842
		No		2,444	
Adjusted	Cognitive Function	Declined	0,405	Ref	0,402-1,445
		Normal		0,762	
	Caregiver	Yes	0,088	Ref	0,876-6,744
		No		2,430	

Cognitive decline may be linked to factors such as education, glycemic control, diabetes duration, and comorbidities, affecting patients' ability to manage their health. Pharmacists play a crucial role in providing education, support, and monitoring medication adherence. They can offer information on the importance of medication adherence, counseling, early detection of neuropathy symptoms, and coordinate care with healthcare teams. Further research is needed to explore these relationships and design effective interventions, including those involving pharmacists, for diabetic patients at high risk of neuropathy

.

Research Limitations

This study had several weaknesses. First, the observational design limited the ability to draw causal conclusions between the variables studied. Second, non-random sample selection reduced the generalizability of the results. Third, the sampling was only conducted at one location, RSUD Tebet in South Jakarta, which could not represent the entire population of geriatric patients with diabetic neuropathy in Indonesia.

CONCLUSION

Women (71,5%) were more likely to experience cognitive decline than men (28,5%). Medication adherence varied by method. MARS-5 showed 63,6% non-adherence in cognitive decline versus 36.4% in normal cognitive function (p=0,234). MPR indicated 58,8% adherence in cognitive decline versus 41,2% in normal function (p=0,651). Pill Count revealed a significant difference (p=0,036) with 80,8% non- adherence in cognitive decline versus 19,2% in normal function (OR 3,160, 95% CI: 1,143-8,732). Triangulation showed 64,6% non-adherence in cognitive decline versus 35,4% in normal function (OR 1,774, 95% CI: 1,001-3,144).

Acknowledgements

The author would like to extend heartfelt thanks to apt. Nadia Farhanah Syafhan, M.Si., Ph.D., and dr. Taufan Harun Habibie, Sp.PD, for their invaluable guidance, support, and suggestions throughout this research. Appreciation is also extended to all parties who contributed to the completion of this original research..

REFERENCES

Alkethiri, K., Almtroudi, T., Jurays, A. bin, Abanumay, F., Aldammas, M., AlKhodheer, M., Iqbal, M., Habib, S. S., & Bashir, S. (2021). The relationship between type 2 diabetes mellitus with cognitive functions. *Heliyon*, *7*(3), e06358. https://doi.org/10.1016/j.heliyon.2021.e06358

Anghel, L. A., Farcas, A. M., & Oprean, R. N. (2019). An overview of the common methods used to measure treatment adherence. *Medicine and Pharmacy Reports*. https://doi.org/10.15386/mpr-1201

Austin, J., Klein, K., Mattek, N., & Kaye, J. (2017). Variability in medication taking is associated with cognitive performance in nondemented older adults.

Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, *6*(1), 210–213. https://doi.org/10.1016/j.dadm.2017.02.003

Badan Pusat Statistik. (2023). Statistik Penduduk Lanjut Usia 2023. *Badan Pusat Statistik*, *20*, 1–326.

Ba-Tin, L., Strike, P., & Tabet, N. (2011). Diabetic Peripheral Microvascular Complications: Relationship to Cognitive Function. *Cardiovascular Psychiatry and Neurology*, *2011*, 1–7. https://doi.org/10.1155/2011/723434

Bell, T., Franz, C. E., & Kremen, W. S. (2022). Persistence of pain and cognitive impairment in older adults. *Journal of the American Geriatrics Society*, *70*(2), 449–458. https://doi.org/10.1111/jgs.17542

Bondar, A., Popa, A., Papanas, N., Popoviciu, M., Vesa, C., Sabau, M., Daina, C., Stoica, R., Katsiki, N., & Stoian, A. (2021). Diabetic neuropathy: A narrative review of risk factors, classification, screening and current pathogenic treatment options (Review). *Experimental and Therapeutic Medicine*, *22*(1), 690. https://doi.org/10.3892/etm.2021.10122

Brognara, L., Volta, I., Cassano, V. M., Navarro-Flores, E., & Cauli, O. (2020). The Association between Cognitive Impairment and Diabetic Foot Care: Role of Neuropathy and Glycated Hemoglobin. *Pathophysiology*, *27*(1), 14–27. https://doi.org/10.3390/pathophysiology27010003

Choo, E., Jung, M., Shin, J., & Lee, S. (2021). Comparing the Sensitivities of Measures of Adherence to Antihypertensive Drugs Using Korean National Health Insurance Claims Data. *Patient Preference and Adherence*, *Volume 15*, 1717–1728. https://doi.org/10.2147/PPA.S322745

Chudiak, A., Uchmanowicz, I., & Mazur, G. (2018). Relation between cognitive impairment and treatment adherence in elderly hypertensive patients. *Clinical Interventions in Aging*, *Volume 13*, 1409–1418. https://doi.org/10.2147/CIA.S162701

Gonzales, M. M., Garbarino, V. R., Pollet, E., Palavicini, J. P., Kellogg, D. L., Kraig, E., & Orr, M. E. (2022). Biological aging processes underlying cognitive decline and neurodegenerative disease. *Journal of Clinical Investigation*, *132*(10). https://doi.org/10.1172/JCI158453

Hansen, R. A., Kim, M. M., Song, L., Tu, W., Wu, J., & Murray, M. D. (2009). Adherence: Comparison of Methods to Assess Medication Adherence and Classify Nonadherence. *Annals of Pharmacotherapy*, *43*(3), 413–422. https://doi.org/10.1345/aph.1L496

Hicks, C. W., & Selvin, E. (2019). Epidemiology of Peripheral Neuropathy and Lower Extremity Disease in Diabetes. *Current Diabetes Reports*, *19*(10), 86. https://doi.org/10.1007/s11892-019-1212-8

Hoffmann, R., & Lutz, S. U. (2019). The health knowledge mechanism: evidence on the link between education and health lifestyle in the Philippines. *The European Journal of Health Economics*, *20*(1), 27–43. https://doi.org/10.1007/s10198-017-0950-2

Huang, J., Ding, S., Xiong, S., & Liu, Z. (2021). Medication Adherence and Associated Factors in Patients With Type 2 Diabetes: A Structural Equation Model. *Frontiers in Public Health*, *9*. https://doi.org/10.3389/fpubh.2021.730845

International diabetes federation. (2021). Indonesia diabetes report 2000 — 2045. In *IDF Diabetes Atlas 10 edition 2021* (p. 1).

Jermendy, G., Rokszin, G., Fábián, I., Kempler, P., & Wittmann, I. (2023). Morbidity and mortality of patients with diabetic neuropathy treated with pathogenetically oriented alpha-lipoic acid versus symptomatic pharmacotherapies – A nationwide database analysis from Hungary. *Diabetes Research and Clinical Practice*, *201*, 110734. https://doi.org/10.1016/j.diabres.2023.110734

Jose, J., & Bond, C. (2021). Medication Adherence: Still a problem. *International Journal of Pharmacy Practice*, *29*(2), 93–95. https://doi.org/10.1093/ijpp/riaa019

Lin, Y. J., Kao, T. W., & Chen, W. L. (2021). Relationship between peripheral neuropathy and cognitive performance in the elderly population. *Medicine (United States)*, *100*(20), E26071. https://doi.org/10.1097/MD.0000000000026071

Lin, Y.-J., Kao, T.-W., & Chen, W.-L. (2021). Relationship between peripheral neuropathy and cognitive performance in the elderly population. *Medicine*, *100*(20), e26071. https://doi.org/10.1097/MD.0000000000026071

Ma, T., Liao, J., Ye, Y., & Li, J. (2024). Social support and cognitive activity and their associations with incident cognitive impairment in cognitively normal older adults. *BMC Geriatrics*, *24*(1), 38. https://doi.org/10.1186/s12877-024-04655-5

Matyas, N., Keser Aschenberger, F., Wagner, G., Teufer, B., Auer, S., Gisinger, C., Kil, M., Klerings, I., & Gartlehner, G. (2019). Continuing education for the prevention of mild cognitive impairment and Alzheimer's-type dementia: a systematic review and overview of systematic reviews. *BMJ Open*, *9*(7), e027719. https://doi.org/10.1136/bmjopen-2018-027719

Meijer, J.-W. G., Bosma, E., Lefrandt, J. D., Links, T. P., Smit, A. J., Stewart, R. E., van der Hoeven, J. H., & Hoogenberg, K. (2003). Clinical Diagnosis of Diabetic Polyneuropathy With the Diabetic Neuropathy Symptom and Diabetic Neuropathy Examination Scores. *Diabetes Care*, *26*(3), 697–701. https://doi.org/10.2337/diacare.26.3.697

Moreira, R. O., Soldera, A. L., Cury, B., Meireles, C., & Kupfer, R. (2015). Is cognitive impairment associated with the presence and severity of peripheral neuropathy in patients with type 2 diabetes mellitus? *Diabetology and Metabolic Syndrome*, *7*(1), 1–4. https://doi.org/10.1186/s13098-015-0045-0

Mufidah, B. (2022). Hubungan Neuropati Diabetik dengan Fungsi Kognitif pada Pasien Diabetes Melitus Tipe 2 di RSUD Prof. Dr. Margono Soekarjo. *Skripsi Thesis, Universitas Jenderal Soedirman.Http://Repository.Unsoed.Ac.Id/13195/*.

Palomo-Osuna, J., Dueñas, M., Naranjo, C., De Sola, H., Salazar, A., & Failde, I. (2022). Factors related to cognitive function in type-2 diabetes and neuropathic pain patients, the role of mood and sleep disorders in this relationship. *Scientific Reports*, *12*(1), 15442. https://doi.org/10.1038/s41598-022-18949-4

Pillemer, S. C., & Holtzer, R. (2016). The differential relationships of dimensions of perceived social support with cognitive function among older adults. *Aging & Mental Health*, *20*(7), 727–735. https://doi.org/10.1080/13607863.2015.1033683

Pop-Busui, R., Ang, L., Boulton, A., Feldman, E., Marcus, R., Mizokami-Stout, K., Singleton, J. R., & Ziegler, D. (2022). Diagnosis and Treatment of Painful Diabetic Peripheral Neuropathy. *ADA Clinical Compendia*, *2022*(1), 1–32. https://doi.org/10.2337/db2022-01

Rachman, A., Sauriasari, R., Syafhan, N. F., Prawiroharjo, P., & Risni, H. W. (2022). Cognitive Function in Type 2 Diabetes Mellitus Patients Taking Metformin and Metformin-Sulfonylurea. *Kesmas*, *17*(4), 270–278. https://doi.org/10.21109/kesmas.v17i4.6303

Rahmawati, A., & Hargono, A. (2018). Dominant Factor of Diabetic Neuropathy on Diabetes Mellitus Type 2 Patients. *Jurnal Berkala Epidemiologi*, *6*(1), 60. https://doi.org/10.20473/jbe.v6i12018.60-68

Randväli, M., Toomsoo, T., & Šteinmiller, J. (2024). The Main Risk Factors in Type 2 Diabetes for Cognitive Dysfunction, Depression, and Psychosocial Problems: A Systematic Review. *Diabetology*, *5*(1), 40–59. https://doi.org/10.3390/diabetology5010004

Rhalimi, M., Rauss, A., & Housieaux, E. (2018). Drug-related problems identified during geriatric medication review in the community pharmacy. *International Journal of Clinical Pharmacy*, *40*(1). https://doi.org/10.1007/s11096-017-0571-y

Russell, J. K., Jones, C. K., & Newhouse, P. A. (2019). The Role of Estrogen in Brain and Cognitive Aging. *Neurotherapeutics*, *16*(3), 649–665. https://doi.org/10.1007/s13311-019-00766-9

Scheurer, D., Choudhry, N., Swanton, K. A., Matlin, O., & Shrank, W. (2012). Association between different types of social support and medication adherence. *The American Journal of Managed Care*, *18*(12), e461-7.

Umegaki, H. (2020). Association of polypharmacy with decline in quality of life in mild cognitive impairment and mild dementia. *Geriatrics & Gerontology International*, *20*(9), 840–842. https://doi.org/10.1111/ggi.13988

Wang, L., Gao, P., Zhang, M., Huang, Z., Zhang, D., Deng, Q., Li, Y., Zhao, Z., Qin, X., Jin, D., Zhou, M., Tang, X., Hu, Y., & Wang, L. (2017). Prevalence and Ethnic Pattern of Diabetes and Prediabetes in China in 2013. *JAMA*, *317*(24), 2515. https://doi.org/10.1001/jama.2017.7596

Yang, Z., Chen, R., Zhang, Y., Huang, Y., Hong, T., Sun, F., Ji, L., & Zhan, S. (2018). Scoring systems to screen for diabetic peripheral neuropathy. *Cochrane Database of Systematic Reviews*, *2018*(7). https://doi.org/10.1002/14651858.CD010974.pub2

Zhang, L., Yang, J., Liao, Z., Zhao, X., Hu, X., Zhu, W., & Zhang, Z. (2019). Association between Diabetes and Cognitive Function among People over 45 Years Old in China: A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*, *16*(7), 1294. https://doi.org/10.3390/ijerph16071294

Zhong, T., Li, S., Liu, P., Wang, Y., & Chen, L. (2024). The impact of education and occupation on cognitive impairment: a cross-sectional study in China. *Frontiers in Aging Neuroscience*, *16*. https://doi.org/10.3389/fnagi.2024.1435626