Jurnal Kesehatan
Volume 17, Number 2, August 2026
ISSN 2086-7751 (*Print*), ISSN 2548-5695 (*Online*)
http://ejurnal.poltekkes-tjk.ac.id/index.php/JK

Risk Factors of Peripheral Neuropathy in Diabetic and Non-Diabetic Populations: A Systematic Review

I Made Putra Biantara*, I Wayan Tunjung
Medical Education Study Program, Faculty of Medicine, Universitas Islam Al-Azhar, Mataram, Indonesia

Corresponding author: madeputrabiantara01@gmail.com

ARTICLE INFO

Article history

Submitted:
29 September 2025

Revised:
18 April 2026
7 May 2026

Accepted:
18 August 2026

Keywords:

Chemotherapy-induced peripheral neuropathy;
Diabetes mellitus;
Glycemic control;
Hypertension;
Metabolic syndrome.

ABSTRACT

Peripheral neuropathy (PN) is a common neurological complication associated with substantial morbidity, disability, and reduced quality of life. Although numerous studies have identified risk factors for PN, findings remain heterogeneous across diabetic and non-diabetic populations, and comprehensive evidence synthesizing these determinants, particularly in the Indonesian context, is still limited. This study aims to identify and compare the major risk factors associated with peripheral neuropathy in diabetic and non-diabetic populations through a systematic literature review. A systematic review was conducted in accordance with PRISMA guidelines. Literature searches were performed in PubMed and Google Scholar using keywords related to peripheral neuropathy and risk factors. Articles published between 2020 and 2025 in English or Indonesian were screened through identification, eligibility assessment, and inclusion stages. Twelve studies meeting the predefined criteria were included and analyzed qualitatively. The most consistently reported risk factors were poor glycemic control and advanced age. Additional determinants were grouped into metabolic factors (hypertension, dyslipidemia, obesity), lifestyle factors (physical inactivity and smoking), clinical factors (longer diabetes duration and male sex), treatment-related factors (taxane-based chemotherapy, oxaliplatin, and beta-blockers), and sociodemographic factors (race, low educational level, and urban residence). These findings indicate that PN is a multifactorial condition influenced by metabolic, clinical, therapeutic, lifestyle, and social determinants. Peripheral neuropathy is associated with a broad range of modifiable and non-modifiable risk factors, with poor glycemic control and advanced age emerging as the most consistent determinants. Early identification of these factors may support targeted screening, prevention strategies, and risk reduction interventions in clinical practice and public health settings. Future longitudinal studies are needed to clarify causal relationships and improve risk prediction models.
Term.

INTRODUCTION

Peripheral neuropathy (PN) is a disorder resulting from damage to peripheral nerves that manifests through sensory, motor, and autonomic dysfunction. The condition may arise from various etiologies, with diabetes mellitus representing the most common cause, leading to diabetic peripheral neuropathy (DPN). In non-diabetic populations, one of the most prevalent forms is chemotherapy-induced peripheral neuropathy (CIPN), which develops as a consequence of neurotoxic cancer treatment. Regardless of its etiology, PN is associated with substantial morbidity, functional impairment, reduced quality of life, and increased mortality risk (Zhu et al., 2024; Sun et al., 2020; Rodriguez-Saldana et al., 2024).

Peripheral neuropathy constitutes a significant global health burden. Its prevalence in the general adult population is estimated at 10–15%, while approximately 30% of individuals with diabetes experience neuropathy, with lifetime prevalence reaching nearly 50% in some

populations (Savelieff et al., 2025). In oncology settings, CIPN represents one of the most common adverse effects of chemotherapy, with approximately 41% of patients reporting chronic neuropathic pain following treatment (D'Souza et al., 2025). These findings indicate that PN affects diverse patient populations and contributes significantly to the global healthcare burden.

The burden of peripheral neuropathy is also evident in Indonesia. Previous studies have reported a high prevalence of CIPN among cancer patients, with institutional studies documenting prevalence rates ranging from 30% to 54%, while national-level analyses have reported substantially higher estimates in specific cohorts (Susanti et al., 2025). These findings highlight the need for improved screening, prevention, and early detection strategies to reduce disease burden and long-term complications.

Although numerous studies have investigated risk factors associated with PN, findings remain heterogeneous across populations and study settings. Reported determinants include metabolic factors such as poor glycemic control, obesity, dyslipidemia, and hypertension; clinical factors such as age and disease duration; lifestyle-related factors including smoking and physical inactivity; and sociodemographic characteristics. Furthermore, evidence from diabetic and non-diabetic populations is often reported separately, making it difficult to obtain an integrated understanding of the factors contributing to PN development. Variations in diagnostic approaches across studies further complicate comparisons and interpretation of findings.

Identification of major risk factors is essential because delayed recognition of individuals at risk may lead to serious complications, including chronic pain, impaired mobility, foot ulceration, and lower-limb amputation (Chew et al., 2025). A comprehensive understanding of both modifiable and non-modifiable determinants can support risk stratification, targeted prevention strategies, and evidence-based clinical decision-making.

To date, no comprehensive synthesis has integrated evidence regarding risk factors for peripheral neuropathy across both diabetic and non-diabetic populations, particularly in a manner relevant to the Indonesian context. This gap limits the development of comprehensive prevention and screening strategies. Therefore, this systematic review identifies, synthesizes, and compares the major risk factors associated with peripheral neuropathy across diverse populations. By integrating evidence from multiple clinical settings and etiological backgrounds, this study aims to provide a comprehensive overview that may inform future research, clinical practice, and public health policy.

METHOD

This study employed a systematic review design conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review aimed to identify and synthesize evidence regarding risk factors associated with peripheral neuropathy across diabetic and non-diabetic populations.

Literature searches were performed in PubMed and Google Scholar, selected because of their broad coverage of biomedical and health-related literature. The search strategy combined keywords and Boolean operators, including: ("peripheral neuropathy" OR "diabetic peripheral neuropathy" OR "chemotherapy-induced peripheral neuropathy") AND ("risk factors" OR determinants OR predictors). The final literature search was conducted in June 2025. The search was restricted to articles published between January 2020 and June 2025 to include the most recent evidence.

Studies were eligible if they: (1) investigated risk factors associated with peripheral neuropathy; (2) included patients with peripheral neuropathy, diabetic peripheral neuropathy, or chemotherapy-induced peripheral neuropathy; (3) used observational study designs, including cross-sectional, cohort, or case-control studies; (4) were published in English or Indonesian; and (5) provided full-text access. Studies were excluded if they were conference abstracts, editorials, commentaries, review articles, duplicate publications, or did not report relevant risk-factor data.

The study population included individuals with peripheral neuropathy from diverse clinical settings, including patients with diabetes mellitus, cancer survivors receiving chemotherapy, and community-based adult populations. Data extracted from eligible studies included author,

publication year, country, study design, sample size, study population, diagnostic methods, and reported risk factors.

Article selection followed the PRISMA process consisting of identification, screening, eligibility assessment, and final inclusion. Duplicate and irrelevant records were removed during screening. Eligible full-text articles were subsequently assessed against the predefined inclusion and exclusion criteria. The selection process is presented in the PRISMA flow diagram (Figure 1).

Methodological quality was evaluated through critical appraisal of study design, sample characteristics, and reporting completeness to assess potential sources of bias. Potential publication and selection bias were considered during data interpretation.

Due to substantial heterogeneity in study populations, diagnostic criteria, and reported outcomes, quantitative meta-analysis was not performed. Instead, data were analyzed using a narrative synthesis approach. Identified risk factors were grouped into major categories, including metabolic, clinical, lifestyle, treatment-related, and sociodemographic factors. Patterns were then summarized based on their frequency of occurrence and consistency across studies.

As this study was based exclusively on published literature and did not involve direct human participation, ethical approval was not required.

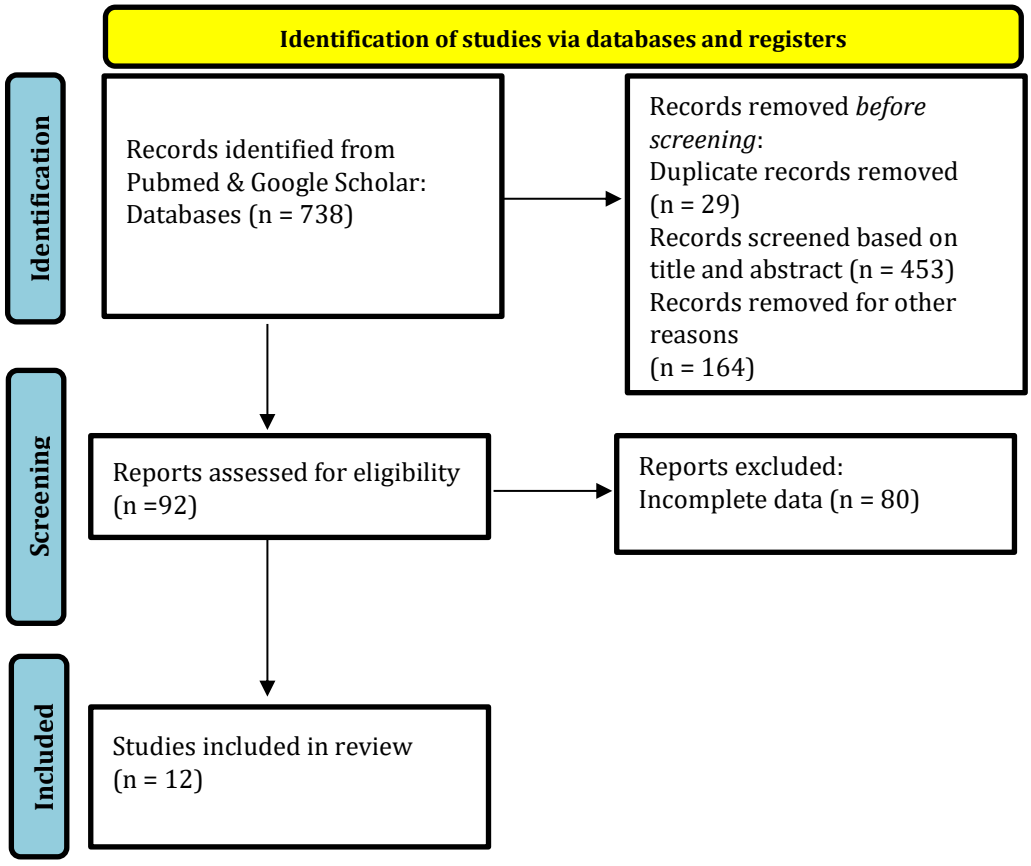


Figure 1. Prisma method

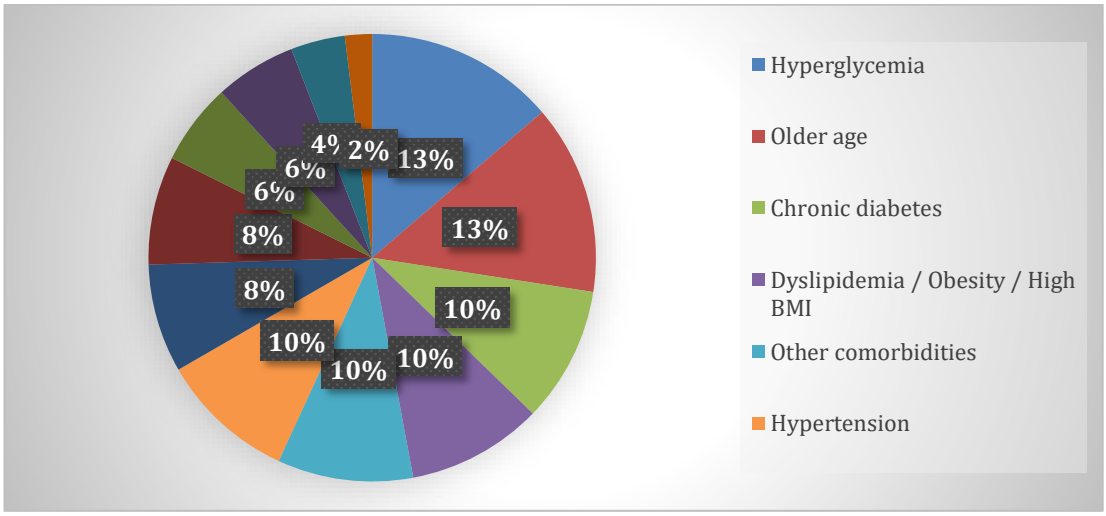
Articles meeting the final criteria were analyzed qualitatively. Each risk factor identified in the publications was recorded and analyzed narratively, grouping findings based on their occurrence and alignment with previous literature. Final conclusions were drawn from patterns and the frequency of risk factor occurrence in the systematically reviewed articles.

Table 1. The summary of the reviewed articles

No	Author & year	Paper title	Sample	Results
1	(Yildirim & Cengiz, 2020)	Predictive clinical factors of chronic peripheral neuropathy induced by oxaliplatin	186 colorectal cancer patients	Old age, gender, poor ECOG status, mucinous carcinoma histopathology type, high GGT and glucose levels, low levels of vitamin D, hemoglobin, albumin, and magnesium.
2	(Wu et al., 2021)	Study on risk factors of peripheral neuropathy in type 2 diabetes mellitus and establishment of prediction model	612 T2DM patients	Combination of variables in the C & D model (7 main factors, including clinical, biochemical, and medical record data – specific details according to the variables in the model).
3	(Pfannkuche et al., 2020)	Prevalence and risk factors of diabetic peripheral neuropathy in a diabetics cohort: Register initiative "diabetes and nerves"	141 T1D patients & 844 T2D patients	Older age, longer duration of diabetes, history of severe hypoglycemia with loss of consciousness (T1D), cardiovascular-metabolic profile (obesity, hypertension, low HDL, high triglycerides, low physical activity, limited mobility) in T2D, as well as comorbidities of diabetic nephropathy, retinopathy, and peripheral arterial disease.
4	(Lu et al., 2020)	Prevalence and Risk Factors for Diabetic Peripheral Neuropathy in Type 2 Diabetic Patients From 14 Countries: Estimates of the INTERPRET-DD Study	2,733 T2DM patients	Longer duration of diabetes, poor glycemic control (high HbA1c), history of hypertension, cardiovascular disease, and symptoms of depression.
5	(Kamgar et al., 2021)	Prevalence and predictors of peripheral neuropathy after breast cancer treatment	2,420 female breast cancer survivors	Type of therapy (chemotherapy vs. no therapy), taxane-based chemotherapy (paclitaxel, docetaxel), and the use of paclitaxel is riskier than docetaxel.
6	(Hicks et al., 2021)	Prevalence of peripheral neuropathy determined by monofilament insensitivity in middle-aged and older adults in two US cohorts	5,200 participants (40–85 years old) & 3,362 participants (70–89 years old)	Diabetes (more severe at a younger age), male gender, black race, greater height, high body mass index, peripheral artery disease, and low education level.
7	(Hicks et al., 2020)	Peripheral neuropathy and all-cause and cardiovascular mortality in us adults: A prospective cohort study	7,116 participants (≥40 years)	Diabetes mellitus, peripheral neuropathy (PN), advanced age, cardiovascular factors, demographic status (age, gender, race)

No	Author & year	Paper title	Sample	Results
8	(Levitt et al., 2021)	Risk factors for diabetic peripheral neuropathy in adolescents and young adults with type 2 diabetes: Results from the current study	674 T2DM adolescents	High HbA1c, male, older age, high BMI
9	(Gebabo et al., 2021)	Determinants of peripheral neuropathy among diabetic patients under follow-up in chronic care clinics of public hospitals at Gamo and Gofa zones, southern Ethiopia	528 patients	Living in urban areas, DM ≥10 years, high blood sugar, late glucose control, hypertension, family history of DM complications, lack of physical activity, waist circumference ≥40 in
10	(Cheng et al., 2022)	Determinants of Diabetic Peripheral Neuropathy and Their Clinical Significance: A Retrospective Cohort Study	1,262 patients	Age >66 years, hypertension, HbA1c >7.7%, high lymphocytes; protective: high neutrophils, high FT3
11	(Braffett et al., 2020)	Risk factors for diabetic peripheral neuropathy and cardiovascular autonomic neuropathy in the Diabetes Control and Complications Trial/Epidemiology of Diabetes interventions and Complications (DCCT/EDIC) study	1,441 patients	High HbA1c, advanced age, long duration of DM, height, albuminuria, high pulse rate, use of β-blockers, high blood pressure, eGFR <60, smoking
12	(Abdissa et al., 2020)	Prevalence and Determinants of Peripheral Neuropathy among Type 2 Adult Diabetes Patients Attending Jimma University Medical Center, Southwest Ethiopia, 2019, an Institutional-Based Cross-Sectional Study	366 patients	Age >40 years, duration of DM >5 years, physical inactivity, smoking

RESULTS



Picture 1. Distribution of peripheral neuropathy risk factors identified across 12 studies

Analysis of the 12 included articles found that the most frequently reported risk factors for peripheral neuropathy were poor glycemic control and older age, each reported in seven studies. Other important factors included longer diabetes duration, hypertension, and a poor metabolic profile (dyslipidemia, obesity, low physical activity), which appeared in five studies. Furthermore, male gender, an unhealthy lifestyle (smoking, physical inactivity), and certain therapies or medications (chemotherapy, β-blockers, oxaliplatin) were consistently reported across several studies. Several studies also highlighted laboratory biomarkers (e.g., GGT, albumin, magnesium, hemoglobin, FT3 levels) and sociodemographic factors (race, low education, urban residence). Interestingly, one study found an association between depression and an increased risk of neuropathy. This variety of risk factors suggests that PN is influenced not only by classic factors such as hyperglycemia, age, and disease duration, but also by other clinical, biological, and social determinants.

DISCUSSION

This systematic review identified poor glycemic control and advanced age as the most consistently reported risk factors for peripheral neuropathy, each appearing in seven of the twelve included studies. Lu et al. (2020), Levitt et al. (2021), Cheng et al. (2022), Braffett et al. (2020), Gebabo et al. (2021), and other included studies reported poor glycemic control as a major determinant of neuropathy development. Similarly, advanced age was consistently associated with increased neuropathy risk in studies by Yildirim and Cengiz (2020), Pfannkuche et al. (2020), Hicks et al. (2020), Hicks et al. (2021), Levitt et al. (2021), Cheng et al. (2022), and Abdissa et al. (2020). These findings suggest that both metabolic dysregulation and aging-related physiological changes play central roles in peripheral nerve damage.

Longer diabetes duration was another frequently reported determinant. Studies by Pfannkuche et al. (2020), Lu et al. (2020), Gebabo et al. (2021), Braffett et al. (2020), and Abdissa et al. (2020) demonstrated that prolonged exposure to hyperglycemia increases the likelihood of neuropathy. Hypertension was also consistently identified as a risk factor in several studies, including those by Lu et al. (2020), Gebabo et al. (2021), Cheng et al. (2022), Pfannkuche et al. (2020), and Braffett et al. (2020), highlighting the contribution of vascular dysfunction to nerve injury.

Metabolic and lifestyle-related factors also emerged as prominent. Pfannkuche et al. (2020), Hicks, Wang, Windham, et al. (2021), Levitt et al. (2021), and Gebabo et al. (2021) reported obesity, dyslipidemia, low physical activity, and elevated body mass index. Braffett et al. (2020) and Abdissa et al. (2020) identified smoking as a significant factor. Collectively, these findings indicate that peripheral neuropathy is influenced not only by glycemic status but also by broader metabolic and behavioral determinants.

Treatment-related factors were particularly evident among patients with cancer. Yildirim and Cengiz (2020) reported oxaliplatin-associated neuropathy, whereas Kamgar et al. (2021) identified taxane-based chemotherapy, particularly paclitaxel, as a significant predictor of neuropathy. Additionally, Braffett et al. (2020) found an association between beta-blocker use and neuropathy risk. These findings demonstrate that therapeutic exposures may contribute substantially to neuropathy development in specific patient populations.

Several studies also highlighted sociodemographic and psychosocial determinants. Hicks, Wang, Windham, et al. (2021) reported associations with race and lower educational attainment, while Gebabo et al. (2021) identified urban residence as a risk factor. Furthermore, Lu et al. (2020) found that depressive symptoms were associated with diabetic peripheral neuropathy. These observations suggest that social and psychological factors may influence neuropathy risk alongside biological and clinical determinants.

.

CONCLUSION

This systematic review identified poor glycemic control and advanced age as the most consistently reported risk factors for peripheral neuropathy across both diabetic and non-diabetic

populations. Additional determinants included longer disease duration, hypertension, obesity, dyslipidemia, physical inactivity, smoking, treatment-related factors such as chemotherapy and beta-blockers, and several sociodemographic characteristics. These findings demonstrate that peripheral neuropathy is a multifactorial condition influenced by metabolic, clinical, lifestyle, therapeutic, and social factors.

Early identification and management of modifiable risk factors are essential to reduce neuropathy progression and prevent complications such as chronic pain, functional impairment, foot ulceration, and amputation. Clinicians should incorporate routine risk assessment and preventive interventions into patient care, particularly among high-risk populations.

Future studies with larger and more diverse populations, standardized diagnostic criteria, and longitudinal designs are recommended to strengthen the evidence base and improve risk prediction strategies for peripheral neuropathy.

AUTHOR'S DECLARATION

Authors' contributions and responsibilities

IMPB: Conceptualization, literature search, study selection, data extraction, data synthesis, formal analysis, visualization, and writing-original draft preparation; **IWT**: Methodological supervision, validation of study selection and data interpretation, critical review of the manuscript, and writing-review and editing. Both authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Availability of data and materials

All data analyzed in this study were obtained from publicly available published articles included in the systematic review. Additional information regarding the extracted data is available from the corresponding author upon reasonable request.

Competing interests

The authors declare no competing interests.

Additional information

Ethical approval was not required because this study was based exclusively on published literature and did not involve human participants, patient data, or animal subjects.

ACKNOWLEDGEMENT

The authors thank Al-Azhar Islamic University for academic support during the preparation of this manuscript. Special thanks to reviewers and colleagues for their valuable feedback.

REFERENCES

Abdissa, D., Hamba, N., Kene, K., Bedane, D.A., Etana, G., Muleta, D., & Gerbi, A. (2020). Prevalence and Determinants of Peripheral Neuropathy among Type 2 Adult Diabetes Patients Attending Jimma University Medical Center, Southwest Ethiopia, 2019: An Institution-Based Cross-Sectional Study. *Journal of Diabetes Research*, *2020*(1), 9562920. https://doi.org/https://doi.org/10.1155/2020/9562920

Braffett, B. H., Gubitosi-Klug, R., Albers, J., Feldman, E., Martin, C., White, N., Orchard, T., Lopes-Virella, M., Lachin, J., Pop-Busui, R., & Group, the DR (2020). Risk Factors for Diabetic

Peripheral Neuropathy and Cardiovascular Autonomic Neuropathy in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study. *Diabetes, 69*(5), 1000–1010. https://doi.org/10.2337/db19-1046

Cheng, Y., Cao, W., Zhang, J., Wang, J., Liu, X., Wu, Q., & Lin, Q. (2022). Determinants of Diabetic Peripheral Neuropathy and Their Clinical Significance: A Retrospective Cohort Study. *Frontiers in Endocrinology*, *Volume 13*. https://doi.org/10.3389/fendo.2022.934020

Chew, S. M., Dua Avinashi, S., & Venkataraman, K. (2025). Predictors of incident diabetic peripheral neuropathy: a systematic review of longitudinal studies in patients with diabetes mellitus. *Reviews in Endocrine & Metabolic Disorders*, *26*(4), 659–677. https://doi.org/10.1007/s11154-025-09973-6

D'Souza, R.S., Saini, C., Hussain, N., Javed, S., Prokop, L., & Her, Y.F. (2025). Global estimates of prevalence of chronic painful neuropathy among patients with chemotherapy-induced peripheral neuropathy: systematic review and meta-analysis of data from 28 countries, 2000-24. *Regional Anesthesia and Pain Medicine.* https://doi.org/10.1136/rapm-2024-106229

Gebabo, T.F., Zewdie, T., Shagaro, SS, & Haile, F. (2021). Determinants of peripheral neuropathy among diabetic patients under follow-up in chronic care clinics of public hospitals at Gamo and Gofa zones, southern Ethiopia. *PLOS ONE*, *16*(2), e0246722. https://doi.org/10.1371/journal.pone.0246722

Hicks, C.W., Wang, D., Matsushita, K., Windham, B.G., & Selvin, E. (2021). Peripheral Neuropathy and All-Cause and Cardiovascular Mortality in US Adults: A Prospective Cohort Study. *Annals of Internal Medicine*, *174*(2), 167–174. https://doi.org/10.7326/M20-1340

Hicks, C.W., Wang, D., Windham, B.G., Matsushita, K., & Selvin, E. (2021). Prevalence of peripheral neuropathy determined by monofilament insensitivity in middle-aged and older adults in two US cohorts. *Scientific Reports*, *11*(1), 19159. https://doi.org/10.1038/s41598-021-98565-w

Kamgar, M., Greenwald, M., Assad, H., Hastert, T., McLaughlin, E., Reding, K., Paskett, E., Bea, J., Shadyab, A., Neuhouser, M. L., Nassir, R., Crane, T. E., Sreeram, K., & Simon, MS (2021). Prevalence and predictors of peripheral neuropathy after breast cancer treatment. *Cancer Medicine*, *10* (19), 6666–6676. https://doi.org/https://doi.org/10.1002/cam4.4202

Levitt Katz L, White N, Ghormli L, Chan C, Copeland K, Lipman T, Marcus M, ZP (2021). Risk Factors for Diabetic Peripheral Neuropathy in Adolescents and Young Adults With Type 2 Diabetes: Results From the TODAY Study. *Diabetes Care*, *45*(5), 1065–1072. https://doi.org/10.2337/dc21-1074

Lu, Y., Xing, P., Cai, X., Luo, D., Li, R., Lloyd, C., Sartorius, N., & Li, M. (2020). Prevalence and Risk Factors for Diabetic Peripheral Neuropathy in Type 2 Diabetic Patients From 14 Countries: Estimates of the INTERPRET-DD Study. *Frontiers in Public Health, 8* (October), 1–8. https://doi.org/10.3389/fpubh.2020.534372

Pfannkuche, A., Alhajjar, A., Ming, A., Walter, I., Piehler, C., & Mertens, P.R. (2020). Prevalence and risk factors of diabetic peripheral neuropathy in a diabetics cohort: Register initiative "diabetes and nerves." *Endocrine and Metabolic Science*, *1*(1), 100053. https://doi.org/10.1016/j.endmts.2020.100053

Rodriguez-Saldana, J., Mijangos, J.H.S., Hancock, C.N., Ramsey, D.L., & Weiser, L.-K. (2024). Prevalence and disease burden of peripheral neuropathy in the general population in Mexico city: a cross-sectional epidemiological study. *Current Medical Research and Opinion, 40*(6), 977–987. https://doi.org/10.1080/03007995.2024.2352852

Savelieff, M.G., Elafros, M.A., Viswanathan, V., Jensen, T.S., Bennett, D.L., & Feldman, E.L. (2025). The global and regional burden of diabetic peripheral neuropathy. *Nature Reviews. Neurology*, *21*(1), 17–31. https://doi.org/10.1038/s41582-024-01041-y

Sun, J., Wang, Y., Zhang, X., Zhu, S., & He, H. (2020). Prevalence of peripheral neuropathy in patients with diabetes: A systematic review and meta-analysis. *Primary Care Diabetes*, *14*(5), 435–444. https://doi.org/10.1016/j.pcd.2019.12.005

Susanti, I., Seraph, N., Edward, M., & Burhan, A. (2025). National Trends in the Prevalence of Diabetic Peripheral Neuropathy Among Diabetes Mellitus Patients in Indonesia (2010–2024): A Pooled Meta-Analysis of 46 Studies with 2,808 Participants. *Java Nursing Journal*, *3* , 2988–4152. https://doi.org/10.61716/jnj.v3i2.103

Wu, B., Niu, Z., & Hu, F. (2021). Study on Risk Factors of Peripheral Neuropathy in Type 2 Diabetes Mellitus and Establishment of Prediction Model. *Dmj*, *45*(4), 526–538. https://doi.org/10.4093/dmj.2020.0100

Yildirim, N., & Cengiz, M. (2020). Predictive clinical factors of chronic peripheral neuropathy induced by oxaliplatin. *Supportive Care in Cancer*, *28*(10), 4781–4788. https://doi.org/10.1007/s00520-020-05319-x

Zhu, J., Hu, Z., Luo, Y., Liu, Y., Luo, W., Du, X., Luo, Z., Hu, J., & Peng, S. (2024). Diabetic peripheral neuropathy: pathogenetic mechanisms and treatment. *Frontiers in Endocrinology*, *Volume 14 - 2023*. https://doi.org/10.3389/fendo.2023.1265372