Original Article

Proportional Hazards Model for Predictors of Type 2 Diabetes Mellitus among the Elderly

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ABSTRACT

OBJECTIVE: To find the prevalence and prognostic characteristics of type 2 diabetes mellitus (T2DM) in older adults.

METHODOLOGY: This study's quantitative observational approach utilized the Cox proportional hazards model. This study was conducted from January to June 2024 in Manado City's urban regions. Data was collected at nearby community health centres and senior care institutions to guarantee participant accessibility and convenience.

This study included older adults aged 60 or older living in urban settings. Based on power estimates, a sample size of 550 participants was chosen to guarantee adequate statistical power to identify significant correlations between predictive factors and the occurrence of T2DM. Medical examination (BMI, HbA1c and fasting plasma glucose) and structured interviews were used. The participants willing to provide informed consent were included, while exclusions included severe comorbidities and cognitive impairment. The studies were conducted using SPSS version 25.

RESULTS: In the study population, T2DM was prevalent in 45% of cases. The key prognostic factors discovered included dietary habits, degree of physical activity, body mass index, and family history of Diabetes. T2DM was found to be predicted by unhealthy eating habits (HR = 1.62, 95% CI: 1.10-2.39), low physical activity (HR = 1.54, 95% CI: 1.02-2.33), high body mass index (HR = 1.87, 95% CI: 1.25-2.80), and a family history of Diabetes (HR = 2.15, 95% CI: 1.42-3.25).

CONCLUSION: The high incidence of Diabetes in older adults makes it essential to intervene in diet, physical activity and weight control.

KEYWORDS: Diabetes, Dietary Habits, Elderly, Family History, Physical Activity, Predictors

INTRODUCTION

Diabetes is a problem for world health. It is linked to a high death rate, elevated health risks, exorbitant medical expenses, and a low quality of life [1]. In prediabetes, normal glucose metabolism gives way to Diabetes, as evidenced by impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)[2]. Many people do not realize they have prediabetes because prediabetic persons do not exhibit any of the symptoms or indicators of diabetes[3]. People with prediabetes are more likely to develop Diabetes, obesity, hypertension, dyslipidaemia, cardiovascular disease, cancer, and dementia. Preventing and managing prediabetes lowers the chance of developing Diabetes and its associated problems[4].

The World Health Organisation (WHO) reported an increase in prediabetes and diabetes prevalence worldwide in 2017. The survey made it clear that sedentary lifestyles, poor diets, and obesity were significant contributing factors to the rise in diabetes incidence. It also highlights how urgent preventive measures and better access to healthcare services are needed for people with Diabetes. According to the research, low- and middle-income countries are disproportionately affected by Diabetes, and these nations may have restricted access to healthcare and resources for controlling the condition[5]. Finding the signs that might accurately forecast the onset of prediabetes is crucial; this will support better patient monitoring and intervention quality [6].

T2DM is a chronic metabolic disease characterized by insulin resistance and hyperglycemia[7]. T2DM is becoming more commonplace worldwide, and age-related physiological changes and lifestyle variables disproportionately impact the senior population. Targeted public health interventions are necessary, as evidenced by the significant rise in T2DM in older persons reported in previous studies[8–10].

The study's justification is the pressing need to comprehend the risk factors for T2DM in older adults to develop more potent preventative and treatment plans. Numerous risk factors have been identified by earlier research, such as poor diet, obesity, sedentary lifestyle, and genetic predisposition. Several studies have found strong correlations between these risk factors and T2DM. However, other investigations have produced contradictory findings, underscoring the complexity of the disease's aetiology. The gap was identified in the literature regarding the inconsistent results from previous studies, highlighting

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the need for further research to clarify the relationship between these risk factors and T2DM in the elderly population. At 10.8%, Indonesia has one of the highest rates of Type 2 Diabetes Mellitus (T2DM) among the top 10 nations. The distinctive characteristics of type 2 diabetes in Indonesia are still unknown[11].

The aim was to use the Cox Proportional Hazards Model to analyze the predictors of T2DM in the older population and to ascertain its prevalence. Comprehending these determinants can facilitate the creation of focused therapies and prophylactic tactics for this susceptible cohort. Applying the Cox Proportional Hazards Model offers a more sophisticated understanding of the temporal dynamics and the risk factors linked to T2DM.

METHODOLOGY

The Cox proportional hazards model was utilized in this study's quantitative observational approach to find important determinants of T2DM. The data for the cross-sectional research were gathered all at once. This study was conducted from January to June 2024 in Manado City's urban regions. Data was collected at nearby community health centres and senior care institutions to guarantee participant accessibility and convenience.

Population and Sample Size Determination

The target demographic consisted of senior citizens living in cities. Based on power estimates, a sample of 550 participants was chosen to guarantee adequate statistical strength and identify significant correlations between predictive factors and T2DM. A 25% calculated frequency of T2DM was considered when calculating the sample size for older adults, with a margin of error of 5% and a 95% confidence level. The participants were randomly chosen from community centres and retirement homes spread across several urban regions to provide a varied representation of the senior population. Various health and socioeconomic backgrounds were included in the study to offer a more complete picture of the variables impacting the incidence of T2DM in older urban populations. Older adults sixty years of age or older who lived in urban areas were included in this study. Inclusion criteria were those willing to engage in the trial could give informed consent. Meanwhile, Exclusion criteria were severe comorbidities that could limit research participation and cognitive impairment.

Data Sources and Data Collection Techniques / Instruments

Medical examinations and structured interviews were used to gather data. The study collected demographic data, medical history, lifestyle factors, and family diabetes history using a standardized questionnaire. It measured BMI (Body mass index), fasting plasma glucose, and HbA1c (Glycated haemoglobin) values during medical exams.

Measurements

Body Mass Index is the result of dividing body weight by height (kg/m2) and is determined using a calibrated scale and stadiometer. Body mass index is taken from samples of the designated research area by measuring the weight and height of the sample using a stadiometer.

HbA1c and Plasma Glucose Levels during Fasting: Blood samples and conventional laboratory procedures are carried out after fasting overnight to determine fasting plasma glucose and HbA1c levels. We work with skilled and certified Health workers to measure HbA1c Levels. Health workers will take blood samples through the arm; then, the blood samples will be examined in the laboratory.

Statistical methods

The studies were conducted using SPSS version 25, a statistical software. Descriptive statistics were used to gather the clinical and demographic characteristics of the study population. Means and standard deviations were displayed for continuous variables, whereas percentages and frequencies were displayed for categorical variables.

Critical factors for type 2 diabetes were identified by using the Cox proportional hazards model. The model considered the following variables: food preferences, degree of physical exercise, BMI (Body mass index), and family history of Diabetes. Schoenfeld residuals were employed to test the proportional hazard assumption. The hazard ratios (HR) and 95% confidence intervals (CI) were calculated for each predictor. At $P < 0.05$, statistical significance was established.

Multiple imputations were employed to manage missing values and guarantee the robustness of the results in the event of missing data. Sensitivity analyses were used to evaluate how the results were affected by imputation. P values were published to three decimal places for every statistical test. The CONSORT statement's guidelines were followed in this investigation to guarantee the reproducibility and transparency of the research findings.

This study was approved by the Poltekkes Kemenkes Manado Institutional Review Board (IRB). It was conducted per the ethical principles outlined in the Declaration of Helsinki (Approval Number: IRB-2024-01), ensuring that all protocols followed the moral guidelines for researching human subjects.

Before enrolment, each participant received a comprehensive explanation of the study's objectives, procedures, potential risks, and benefits. This information was given to us verbally and in writing. Participants in the study were informed that their participation was completely voluntary and that they could withdraw without incurring any penalties.

We obtained each participant's informed consent before collecting any data. Written informed consent forms were signed by each participant and filed in compliance with IRB regulations. The consent form explained the study's objectives, how the data would be used exclusively for research, and how their information would be kept private.

Given the possible susceptibility of the older population, extra care was taken to ensure that participants understood the purpose of the study and what their cooperation would entail. Before getting a signature or thumbprint from participants with low literacy, the consent material was read aloud, and understanding was verified through conversation.

RESULTS

Age, Gender, smoking status, physical activity, unhealthy dietary habits, and family history of Diabetes were measured using a questionnaire adapted from the Ministry of Health of the Republic of Indonesia. All data collected were then entered into SPSS version 25. specifically, they were first concluded and changed into nominal data for physical activity and dietary habits, making it easier to test SPSS. Meanwhile, BMI data still uses ratio data. At the same time, other data are already in nominal form and need to be directly analyzed. More details can be seen in Tables I, II, and III.

Participants in the study with and without type 2 diabetes were surveyed. The participants' average age was 72.4 years; there were 266 men (48%), 284 females (52%), and a standard deviation of 6.7 years. According to the study, the participants' average BMI was 25.8, that of the older adults with T2DM was 27.6, and that of people without Diabetes was 24.9. Of the participants, 46% were smokers, making up most of the group. The individuals' physical activity levels varied, with 52% inactive and 48% not in the condition.

Table I reveals significant differences in age, BMI, and smoking status between individuals with and without T2DM, with older patients having higher BMI and smoking. In contrast, no significant differences were found in physical activity or sex. These findings suggest that age, BMI, and smoking status may be essential factors in the development of T2DM.

TABLE I: DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

Characteristics	Total (N=550/ 100%)	Diabetic (N=248/ 45%)	Non-Diabetic N=302/55%	Homogeneity between groups
Age (years)	72.4 ± 6.8	73.6 ± 6.9	71.8 ± 6.7	0.045
Gender				
Male (%)	266(48%)	122 (49%)	144 (48%)	0.754
Female (%)	284(52%)	126 (51%)	158 (52%)	0.754
BMI (kg/m²)	25.8 ± 4.2	27.6 ± 4.5	24.9 ± 3.8	0.761
Smoking Status				
Smokers (%)	245(44%)	120 (48%)	125 (41%)	0.030
Non-Smokers(%)	305(46%)	128 (52%)	177 (59%)	0.030
Physical Activity				
Active (%)	263(48%)	116 (47%)	147 (49%)	0.119
Inactive (%)	287(52%)	132 (53%)	155 (51%)	0.119

The statistical analysis of the study participants' prognostic indicators for T2DM is shown in **Table II**. For every factor under investigation, The risk of type 2 diabetes increases with age, particularly in those with higher BMIs and smoking. There is no significant difference in risk based on Gender or physical activity. Controlling BMI and quitting smoking is crucial to reducing the risk of developing type 2 diabetes in older adults.

The Cox proportional hazards model, shown in Table 3, has found several vital predictors of T2DM. A high body mass index, little physical activity, bad eating habits, and a family history of Diabetes were significant predictors. According to the research, the risk of acquiring T2DM was considerably higher in older adults with a high BMI (≥30 kg/m²) (HR = 1.87, 95% CI: 1.25-2.80, p<0.001). Similarly, a lower level of physical activity was linked to a higher risk of T2DM (HR = 1.54, 95% CI: 1.02-2.33, p = 0.039). A substantial increase in risk was also observed with unhealthy eating behaviours (HR = 1.62, 95% CI: 1.10 -2.39, p = 0.015). The most significant predictor, with a hazard ratio of 2.15 (95% CI: 1.42-3.25, p<0.001), was a family history of Diabetes. **Table III**

TABLE II: PREDICTIVE FACTORS FOR T2DM

Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Age	1.04	1.01 - 1.08	0.038
Gender (Male)	1.13	0.58 - 2.18	0.731
BMI	1.15	1.06 - 1.24	<0.001
Smoking Status	2.13	1.10 - 4.12	0.025
Physical Activity	0.60	0.29 - 1.23	0.158

TABLE III: COX PROPORTIONAL HAZARDS MODEL FOR PREDICTORS OF T2DM

Predictors	Hazard Ratio (HR)	95% Confidence Interval (CI)	p-value
High BMI (≥30 kg/m²)	1.87	1.25 - 2.80	<0.001
Low Physical Activity	1.54	1.02 - 2.33	0.039
Unhealthy Dietary Habits	1.62	1.10 - 2.39	0.015
Family History of Diabetes	2.15	1.42 - 3.25	<0.001

DISCUSSION

Using the Cox Proportional Hazards Model, this study sought to ascertain the prevalence and prognostic characteristics of T2DM in the senior population. The primary findings indicated that T2DM affected 45% of the study population and that significant risk factors for the condition were a high body mass index, low physical activity, bad eating habits, and a family history of the condition. These findings are consistent with past research showing that genetic

predisposition, poor diet, obesity, and sedentary lifestyle were significant risk factors for T2DM [12,13]. The onset of type 2 diabetes is closely linked to factors such as smoking, physical inactivity, ethnicity, dyslipidaemia, hypertension, sleep quantity and quality, and family history of Diabetes. Individuals with a family history of Diabetes are at a higher risk of developing type 2 diabetes due to genetic predisposition[14].

Our findings show that the risk of type 2 diabetes increases with age, particularly in those with higher BMIs and smoking. The age range of older persons with type 2 diabetes is diverse and complex. For all medical professionals, whether they are specialists or primary care physicians, managing Diabetes in later life continues to be a significant clinical problem. An individualized patient-centred glycaemic target is necessary to achieve glycaemic control and prevent severe hypo- and hyperglycaemic episodes since elderly diabetes patients often exhibit frailty and/or numerous comorbidities[15].

Our research showed that Gender is not directly related to Diabetes. The biological and psychosocial risk factors, pathophysiology, complications, treatment, and treatment adherence are all included in the differences between sexes and genders in type 2 diabetes. Women with type 2 diabetes typically have a higher risk of cardiovascular complications [16]. According to another research, Diabetes primarily impacted women and individuals between the ages of 61 and 65. Obesity, being overweight, and having a family history of Diabetes raise the risk of developing type 2 diabetes[17].

Obesity has been repeatedly demonstrated to increase the risk of developing T2DM because it is linked to inflammation and insulin resistance [18,19]. Insulin resistance can worsen by eating a poor diet, especially one heavy in processed foods and added sugars[20,21]. T2DM has been demonstrated to be more susceptible to particular gene variants, suggesting that genetic predisposition may be a significant factor in the development of the condition. Early intervention and lifestyle changes to address these modifiable risk factors are critical to preventing and managing type 2 diabetes[22]. Elative inactivity, smoking, and a sedentary lifestyle are important risk factors that contribute to the onset of type 2 diabetes. A balanced diet, frequent exercise, and quitting smoking are among the healthy decisions that can help lower the chance of acquiring these illnesses[23,24].

When determining the probability of acquiring T2DM, genetic predisposition should be considered in addition to lifestyle factors[25–27]. People with high genetic risk can take proactive steps to prevent or control the disease using routine testing and early identification[28]. People who have a family history of Diabetes should be cognisant of their genetic susceptibility to the disease and adopt appropriate measures[29]. People can more effectively control their overall risk of acquiring T2DM by combining modifications to lifestyle with genetic risk assessment [30–33]. Diabetes prevention and management techniques that are more individualized and successful may result from an all-encompassing strategy[34–36]. Furthermore, seeking advice from medical experts regarding genetic testing and lifestyle modifications can help people lower their chance of contracting the illness[37].

A healthy weight and frequent exercise are two other lifestyle changes that can help lower the chance of acquiring T2DM [38]. People can proactively prevent this chronic illness by including physical activity in daily routines and adopting a balanced diet[39]. To prevent T2DM from developing, it can also be helpful to regularly check blood sugar levels and seek medical guidance to identify and treat pertinent risk factors [40]. The chance of acquiring this illness can be considerably decreased by adopting an informed lifestyle and a proactive attitude to health[41,42].

The risk variables that have been discovered can help with the creation of more focused and efficient preventive measures[43]. Furthermore, thoroughly comprehending the disease's temporal dynamics can yield crucial information for improving the quality of life for those with T2DM [44]. The Cox proportional hazards model allows for a clear understanding of how various factors influence the chance of getting T2DM over time. Risk factors for T2DM include being overweight, sedentary, and deficient eating habits; this implies that a deeper comprehension of the risk factors influencing this disease can lead to more effective preventative measures. Therefore, patients' quality of life can benefit from efforts to avoid and manage this disease.

Several mechanisms could explain the observed connections. Increased adiposity and inflammatory processes brought on by a high BMI impede glucose metabolism and lead to insulin resistance[45]. Insulin resistance deteriorates, and muscle glucose absorption decreases with low physical exercise. Bad eating practices raise the risk of T2DM by causing obesity and metabolic dysregulation[46]. A genetic predisposition, maybe involving polymorphisms in the genes linked to insulin production and action, is suggested by a family history of Diabetes. These elements work together to raise the chance of T2DM [47]. Maintaining a healthy lifestyle with regular exercise and a balanced diet is essential to preventing this disease.

This study significantly impacts public health initiatives aimed at the senior citizen demographic. The necessity for all-encompassing measures to address the characteristics identified as significant predictors of T2DM is highlighted by the identification of high body mass index, low physical activity, bad food habits, and family history. Prioritizing weight control programs, encouraging physical activity, and making dietary adjustments can help lower the prevalence of type 2 diabetes in older adults. Furthermore, screening people with a family history of Diabetes for

T2DM may help with early detection and intervention. Regular diabetes screenings and preventive education can lessen the impact of the disease on the senior population, thereby enhancing their quality of life and cutting down on medical expenses connected to treating complications from Diabetes.

Limitation

A limitation of this study is that it did not account for potential confounding variables such as socioeconomic status or comorbidities that may influence the risk of developing T2DM. Future studies should consider using objective measures of dietary habits and physical activity levels to reduce bias. Furthermore, including a more comprehensive set of potential confounding variables in the analysis would provide a more accurate assessment of the predictors of T2DM; this would help strengthen the validity of the findings and provide a clearer understanding of the relationship between lifestyle factors and T2DM risk. In addition, exploring the influence of socioeconomic status and comorbidities in future studies may offer valuable insights into the complex nature of T2DM development.

CONCLUSION

According to this study, T2DM is very common in older adults. A family history of the condition, a high body mass index, a low level of physical activity, and poor eating habits are all significant risk factors for the illness. These results highlight the critical need for focused interventions to help older adults manage their weight, increase physical activity, and support good eating practices to lower the likelihood that they will acquire type 2 diabetes. To enable early detection and intervention, public health policies should concentrate on these areas and incorporate routinely checking for type 2 diabetes, particularly in people with a family history of the disease. More long-term studies are required to validate these results and investigate other variables impacting the risk of T2DM in older adults. Additionally, implementing educational programs in community settings can help raise awareness about the importance of healthy lifestyle choices in preventing Diabetes. Furthermore, collaboration between healthcare providers and public health officials is essential to ensure comprehensive care for older adults at risk for T2DM.

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Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Tumurang MN: Writing Manuscript, Design and Modelling, Data Analysis, Supervised, Conceptual Framework.
Lalangpuling IE: Writing Manuscript, Data analysis.

REFERENCES

1. Tomic D, Shaw JE, Magliano DJ. The burden and risks of emerging complications of Diabetes mellitus. Nat Rev Endocrinol. 2022; 18(9): 525-39.
2. Blond MB, Færch K, Herder C, Ziegler D, Stehouwer CDA. The prediabetes conundrum: striking the balance between risk and resources. Diabetologia. 2023; 66(6): 1016-23.
3. Moradpour F, Rezaei S, Piroozi B, Moradi G, Moradi Y, Piri N et al. Prevalence of prediabetes, Diabetes, diabetes awareness, treatment, and its socioeconomic inequality in west of Iran. Sci Rep. 2022; 12(1): 17892.
4. Lawal Y, Bello F, Kaoje YS. Prediabetes Deserves More Attention: A Review. Clin Diabetes. 2020; 38(4): 328-38.
5. Roglic G, World Health Organization. Global report on Diabetes. 2016th ed. 2016. P. 1-86.
6. Liberty IA, Septadina IS, Rizqie MQ, Ananingsih ES, Hasyim H, Sitorus RJ. Predictors of Prediabetes Among Communities Without a Family History of Type 2 Diabetes Mellitus: A Case-Control Study. Cureus. 2023; 15(8): e44131. doi: 10.7759/cureus.44131.
7. Dilworth L, Facey A, Omoruyi F. Diabetes Mellitus and Its Metabolic Complications: The Role of Adipose Tissues. Int J Mol Sci. 2021; 22(14): 7644. doi: 10.3390/ijms22147644.
8. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM et al. Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2022; 45(11): 2753-2786. doi: 10.2337/dci22-0034.
9. Randväli M, Toomsoo T, Šteinmiller J. The Main Risk Factors in Type 2 Diabetes for Cognitive Dysfunction, Depression, and Psychosocial Problems: A Systematic Review. Diabetology. 2024; 5(1): 40-59. doi: 10.3390/diabetology50 10004.
10. Sugandh F, Chandio M, Raveena F, Kumar L, Karishma F, Khuwaja S et al. Advances in the Management of Diabetes Mellitus: A Focus on Personalized Medicine. Cureus. 2023; 15(8): e43697. doi: 10.7759/cureus.43697.
11. Soeatmadji DW, Rosandi R, Saraswati MR, Sibarani RP, Tarigan WO. Clinicodemographic Profile and Outcomes of Type 2 Diabetes Mellitus in the Indonesian Cohort of DISCOVER: A 3-Year Prospective Cohort Study. J ASEAN Fed Endocr Soc. 2023; 38(1): 68-74. doi: 10.15605/jafes.

038.01.10. Epub 2023 Jan 25.
12. Schnurr TM, Jakupović H, Carrasquilla GD, Ängquist L, Grarup N, Sørensen TIA et al. Obesity, unfavourable lifestyle and genetic risk of type 2 diabetes: a case-cohort study. Diabetologia. 2020; 63(7): 1324-32. doi: 10.1007/s00125-020-05140-5. Epub 2020 Apr 15.
13. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB et al. Pathophysiology of Type 2 Diabetes Mellitus. Int J Mol Sci. 2020; 21(17): 6275. doi: 10.3390/ijms21176275.
14. Ismail L, Materwala H, Al Kaabi J. Association of risk factors with type 2 diabetes: A systematic review. Comput Struct Biotechnol J. 2021; 19(1): 1759-85. doi: 10.1016/j.csbj.2021.03.003.
15. Longo M, Bellastella G, Maiorino MI, Meier JJ, Esposito K, Giugliano D. Diabetes and Aging: From Treatment Goals to Pharmacologic Therapy. Front Endocrinol (Lausanne). 2019; 10: 45. doi: 10.3389/fendo.2019.00045.
16. Kautzky-Willer A, Leutner M, Harreiter J. Sex differences in type 2 diabetes. Diabetologia. 2023; 66(6): 986-1002. doi: 10.1007/s00125-023-05891-x. Epub 2023 Mar 10.
17. Asiimwe D, Mauti GO, Kiconco R. Prevalence and Risk Factors Associated with Type 2 Diabetes in Elderly Patients Aged 45-80 Years at Kanungu District. J Diabetes Res. 2020; 2020(1): 1-5. doi: 10.1155/2020/5152146.
18. Ruze R, Liu T, Zou X, Song J, Chen Y, Xu R et al. Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. Front Endocrinol (Lausanne). 2023; 14: 1161521. doi: 10.3389/fendo.2023.1161521.
19. Wondmkun YT. Obesity, Insulin Resistance, and Type 2 Diabetes: Associations and Therapeutic Implications. Diabetes Metab Syndr Obes. 2020; 13: 3611-6. doi: 10.2147/DMSO.S275898.
20. Valicente VM, Peng CH, Pacheco KN, Lin L, Kielb EI, Dawoodani E et al. Ultraprocessed Foods and Obesity Risk: A Critical Review of Reported Mechanisms. Adv Nutrition. 2023; 14(4): 718-38. doi: 10.1016/j.advnut.2023.04.006. Epub 2023 Apr 18.
21. Malik VS, Hu FB. The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases. Nat Rev Endocrinol. 2022; 18 (4): 205-18. doi: 10.1038/s41574-021-00627-6. Epub 2022 Jan 21.
22. Ligthart S, Hasbani NR, Ahmadizar F, van Herpt TTW, Leening MJG, Uitterlinden AG et al. Genetic susceptibility, obesity and lifetime risk of type 2 diabetes: The ARIC study and Rotterdam Study. Diabetic Medicine. 2021; 38(10): e14639. doi: 10.1111/dme.14639. Epub 2021 Aug 2.
23. Galaviz KI, Narayan KMV, Lobelo F, Weber MB. Lifestyle and the Prevention of Type 2 Diabetes: A Status Report. Am J Lifestyle Med. 2018; 12(1): 4-20. doi: 10.1177/1559827615619159.
24. Kovács N, Shahin B, Andrade CAS, Mahrouseh N, Varga O. Lifestyle and metabolic risk factors, and diabetes mellitus prevalence in European countries from three waves of the European Health Interview Survey. Sci Rep. 2024; 14(1): 11623. doi: 10.1038/s41598-024-62122-y.
25. Tremblay J, Hamet P. Environmental and genetic contributions to Diabetes. Metabolism. 2019; 100S: 153952. doi: 10.1016/j.metabol.2019.153952.
26. Sirdah MM, Reading NS. Genetic predisposition in type 2 diabetes: A promising approach toward a personalized management of Diabetes. Clin Genet. 2020; 98(6): 525-47. doi: 10.1111/cge.13772.
27. Piko P, Werissa NA, Fiatal S, Sandor J, Adany R. Impact of Genetic Factors on the Age of Onset for Type 2 Diabetes Mellitus in Addition to the Conventional Risk Factors. J Pers Med. 2020; 11 (1): 6. doi: 10.3390/jpm11010006.
28. Haverfield E V., Esplin ED, Aguilar SJ, Hatchell KE, Ormond KE, Hanson-Kahn A et al. Physician-directed genetic screening to evaluate personal risk for medically actionable disorders: a large multi-center cohort study. BMC Med. 2021; 19(1): 199. doi: 10.1186/s12916-021-01999-2.
29. Sękowski K, Grudziąż-Sękowska J, Pinkas J, Jankowski M. Public knowledge and awareness of diabetes mellitus, its risk factors, complications, and prevention methods among adults in Poland—A 2022 nationwide cross-sectional survey. Front Public Health. 2022; 10: 1029358. doi: 10.3389/fpubh.2022.1029358.
30. Tieu S, Koivusalo S, Lahti J, Engberg E, Laivuori H, Huvinen E. Genetic risk of type 2 diabetes modifies the association between lifestyle and glycemic health at 5 years postpartum among high-risk women. BMJ Open Diabetes Res Care. 2024; 12(2): e003942.
31. Huvinen E, Lahti J, Klemetti MM, Bergman PH, Räikkönen K, Orho-Melander M et al. Genetic risk of type 2 diabetes modifies the effects of a lifestyle intervention aimed at the prevention of gestational and postpartum Diabetes. Diabetologia. 2022; 65(8): 1291-301.
32. Dietrich S, Jacobs S, Zheng J, Meidtner K, Schwingshackl L, Schulze MB. Gene□lifestyle interaction on risk of type 2 diabetes: A systematic review. Obesity Reviews. 2019; 20(11): 1557-71.
33. Raghavan S, Jablonski K, Delahanty LM, Maruthur NM, Leong A, Franks PW, et al. Interaction of Diabetes genetic risk and successful lifestyle modification in the Diabetes Prevention Programme. Diabetes Obes Metab. 2021; 23(4): 1030-40.
34. Jones A, Bardram JE, Bækgaard P, Cramer-Petersen CL, Skinner T, Vrangbæk K et al. Integrated personalized diabetes management goes Europe: A multi-disciplinary approach to innovating type 2 diabetes care in Europe. Prim

Care Diabetes. 2021; 15(2): 360-4.
35. Guan H, Tian J, Wang Y, Niu P, Zhang Y, Zhang Y et al. Advances in secondary prevention mechanisms of macrovascular complications in type 2 diabetes mellitus patients: a comprehensive review. Eur J Med Res. 2024; 29 (1): 152. doi: 10.1186/s40001-024-01739-1.
36. Sarani Rad F, Hendawi R, Yang X, Li J. Personalized Diabetes Management with Digital Twins: A Patient-Centric Knowledge Graph Approach. J Pers Med. 2024; 14(4): 359. doi: 10.3390/jpm14040359.
37. Diez de los Rios de la Serna C, Fernández-Ortega P, Lluch-Canut T. Lifestyle Behavior Interventions for Preventing Cancer in Adults with Inherited Cancer Syndromes: Systematic Review. Int J Environ Res Public Health. 2022; 19(21): 14098. doi: 10.3390/ijerph192114098.
38. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2022; 45(11): 2753-86.
39. Rippe JM. Lifestyle Medicine: The Health Promoting Power of Daily Habits and Practices. Am J Lifestyle Med. 2018; 12(6): 499-512.
40. Czupryniak L, Barkai L, Bolgarska S, Bronisz A, Broz J, Cypryk K et al. Self-Monitoring of Blood Glucose in Diabetes: From Evidence to Clinical Reality in Central and Eastern Europe-Recommendations from the International Central-Eastern European Expert Group. Diabetes Technol Ther. 2014; 16(7): 460-75.
41. Alowais SA, Alghamdi SS, Alsuhebany N, Alqahtani T, Alshaya AI, Almohareb SN et al. Revolutionizing healthcare: the role of artificial intelligence in clinical practice. BMC Med Educ. 2023; 23(1): 689. doi:10.1186/s12909-023-04698-z.
42. Ghodeshwar GK, Dube A, Khobragade D. Impact of Lifestyle Modifications on Cardiovascular Health: A Narrative Review. Cureus. 2023; 15(7): e42616. doi: 10.7759/cureus.42616.
43. Budreviciute A, Damiati S, Sabir DK, Onder K, Schuller-Goetzburg P, Plakys G et al. Management and Prevention Strategies for Non-communicable Diseases (NCDs) and Their Risk Factors. Front Public Health. 2020; 8: 574111. doi: 10.3389/fpubh.2020.574111.
44. Yau M, Maclaren NK, Sperling MA, Feingold KR, Anawalt B, Blackman MR et al. Etiology and Pathogenesis of Diabetes Mellitus in Children and Adolescents. In: Endotext[Internet]. South Dertmouth. (MA): MDTEXT.com, Inc.; 2000, 2021 Jun 19.
45. Arneth B. Mechanisms of Insulin Resistance in Patients with Obesity. Endocrines. 2024; 5(2): 153-65.
46. Chait A, den Hartigh LJ. Adipose Tissue Distribution, Inflammation and Its Metabolic Consequences, Including Diabetes and Cardiovascular Disease. Front Cardiovasc Med. 2020; 7: 22. doi: 10.3389/fcvm.2020.00022.
47. Yang J, Qian F, Chavarro JE, Ley SH, Tobias DK, Yeung E et al. Modifiable risk factors and long term risk of type 2 diabetes among individuals with a history of gestational diabetes mellitus: prospective cohort study. BMJ. 2022; 378: e070312. doi: 10.1136/bmj-2022-070312.