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Research Article

Changes in the Prevalence of Diabetes in Bulgaria over an 18-Year Period (2006-2024)

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Abstract

The international medical community is increasingly aware that diabetes is a major global health threat and poses increasing challenges to public health and health systems worldwide. *Aim:* To compare the results of three national cross-sectional studies on diabetes prevalence in Bulgaria (2006, 2012 and 2024) and to assess the dynamics. *Material and Methods:* The three studies included 2396, 2033 and 936 subjects respectively. The United Nation / The International Diabetes Federation (2006) diagnostic criteria were applied, and the data were evaluated according to type of settlement and age. *Results:* Diabetes prevalence was 7.9% in 2006 and 9.55% in 2012 ($p = 0.06$). This difference is due to the greater rise in men (9.2% to 11.5%, $p = 0.09$) compared to women (6.9% to 7.7%, NS). In the next period, 2012 - 2024, the prevalence of diabetes in general, as well as the prevalence in men and women increased significantly. (Diabetes in general - from 9.6% to 15.7%, $p < 0.001$; diabetic men - from 11.5% to 21.2%, $p < 0.001$; diabetic women – from 7.8% to 10.4%, $p < 0.016$). The prevalence of diabetes nearly doubled, while the population decreased and its structure, lifestyle and diet changed. Obesity significantly increased over a 18-year period - 2024 vs. 2006 (33.3% vs. 26.7%, $p < 0.001$). The prevalence of diabetes increased with age, with significant rise in the 30-39 age group for 2012 - 2024, from 1.7% to 4.5% ($p < 0.047$) and more sharply when comparing 2006 - 2024 – from 0.9% to 4.5% ($p < 0.002$). There was a similar increase in the next age group. For the age 60-79, the prevalence reached 29.9%, i.e. every third person. As arterial hypertension is significantly more common in diabetics, its role as a risk factor is indisputable. *Conclusion:* The health care system should be readjusted according to the new reality for early diagnose of diabetes in risk groups and adequate modern care.

Keywords

Diabetes Prevalence, Diabetes Dynamic, Age, Obesity, Diabetes Epidemic

1. Introduction

Diabetes is a serious chronic disease characterized by an incresed blood sugar due to impaired β-cell biology and/or impaired insulin action [1-3].

The international medical community has become increasingly aware that diabetes is a major global health threat, posing challenges to public health and to the health systems

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worldwide. The World Health Organisation (WHO) has identified diabetes as one of three target diseases in its Global Plan for the Prevention and Control of Noncommunicable Diseases [4]. The Global Diabetes contract, established in 2021, aims to improve access to health care and better work with those living with diabetes. The United Nations (UN) considers diabetes care as indicator for the level of countries' health systems, aiming to achieve universal health coverage for reducing by a third the rate of premature death due to diabetes and other non-communicable diseases by 2030, as described in UN Sustainable Development Goal 3 [5, 6]. The prevalence of diabetes is almost entirely determined by type 2 diabetes, which accounted for more than 96% of diabetes cases worldwide in 2021, and the analyses focus mainly on this type of diabetes. Today it must be recognized that Diabetes mellitus is a significant global health problem with a high burden on the population and healthcare systems. Approximately 11% of the world population (537 million people), aged 20–79 lived with diabetes in 2021. This number is expected to increase to 783 million by 2045 [3]. In the last decade, the number of people living with diabetes aged 20–79 has increased by 62% globally. Monitoring diabetes trends is crucial for diabetes management and healthcare policy [3, 7]. World Health Organization (WHO) analyzes predict that almost 50% of the expected increased prevalence of diabetes will be due to changing demographic profiles, and therefore countries will need to invest in their health systems to cope with the expected increase in the number of diabetics [1].

The analysis of Centers for Disease Control and Prevention on the prevalence of diabetes in the world indicates shocking statistic data for a 34-year period (1980-2014) of the WHO, when 400% increase (from 109 to 422 million) in diabetes was reported worldwide [8].

The Bulgarian Society of Endocrinology carried out three population-based screening studies concerning the most common endocrine disorders, cardiovascular risk factors (obesity, arterial hypertension, dyslipidemia), and diabetes in 2006, 2012 and 2024 [9, 10].

The aim of the current study was to compare the data from the three nationwide cross-sectional studies of diabetes prevalence in Bulgaria (2006, 2012 and 2024) and to assess its dynamics and relationship with certain risk factors: age, gender, obesity and arterial hypertension.

2. Material and Methods

Precise criteria for the selection of the study participants were set in advance. The participants in the study were divided into groups by their age, gender and place of residence. This distribution was made according to the data from the population censuses in Bulgaria by the National Statistical Institute (NSI), documented in its regular reports and published in 2001, 2011 and 2022, the years before the relevant screenings in 2006, 2012 and 2024. Non-institutionalized individuals from the population were studied as advised in the Recommendations of NHANES (2022) [11].

Brief presentation of the three cross-sectional studies:

The first study of diabetes prevalence was carried out in January-February 2006. Twenty eight nests in six regions were organised, and 3813 subjects were selected randomly from the national population registry. A total of 2396 subjects (62.8%) who agreed to participate, signed an informed consent, and were included in the study. 1348 of them were females (55.8%) and 1068 were males (44.2%). The mean age of the participants was 47.7 ±14.8 years (from 20 to 79) [9]. The standardized diabetes prevalence data, as per the WHO recommendations, were published in the IDF Diabetes Atlas in 2009 as total prevalence and by age and gender as well [12-15].

The second study was carried out in January–February 2012. Thirty-six nests in 12 regions were organized, and 3450 adult subjects were randomly selected from the national population registry. A total of 2033 subjects (58.8%) agreed to participate, signed an informed consent, and were included in the study. 1076 of them were females (52.9%) and 957 were males (47.1%). The mean age of the participants was 49.3 ± 14.7 years (20–79) [16, 17]. The age structure of the samples in both studies was planned according to the IDF methodology for diabetes prevalence assessment in adults [18].

The third study was carried out from 25-th March to 16-th May 2024 in 16 regions with 51 nests. 1352 individuals aged from 20 to 79, randomly selected from regional population registers according to age, gender and place of residence were invited. A total of 936 persons (69.2%) agreed to participate, signed an informed consent, and were included in the study - 479 women (51.2%) and 457 men (48.8%). The mean age of the participants was 50.5 ±13.6 years (from 20 to 79).

The participants in the three studies were further divided in age groups by decades (20–29; 30–39; 40–49; 50–59; 60–69; 70-79). The three sets of data were compared in view of type of settlement and age.

It should be noted that during this 18-year period there was a considerable change in the number of the population (decrease of more than 20%), as well as a change in its structure - age, sex, place of residence, financial capabilities. According to the reports of the National Statistical Institute (NSI) of Bulgaria, the country's population of 20 years of age or older was 6,168,000 (31 December 2005), 6,011,713 (February 2011) and 4,904,382 (December 2022) [19-21].

The age structure of the samples in the studies was planned according to the IDF methodology for diabetes prevalence assessment in adults and the comprehensive guide to designing a research protocol, offering a step-by-step approach by J. Cimino and C. Braun, 2023 [18, 22].

The studied groups were devided by gender, age, and type of place of residence according to the NSI reports. The three studies were cross-sectional. The sample size was calculated with the expectation of at least 6% prevalence of the studied variable among the target population, 95 % confidence level, and 5% absolute precision The geographic regions, the nests,

the gender and age distribution of the sample were planned to represent the adult general population (from 20 to 79 years). All participants signed an informed consent approved by the local ethics committee at the University Hospital of Endocrinology, and the research was conducted in accordance with the Declaration of Helsinki. The participants filled in a questionnaire containing demographic data, current health status, medical history, family history for cardiovascular and thyroid disorders and diabetes, past history and therapies, menstrual status for the females, and current smoking. Height, body weight and sitting arterial pressure on the arm were measured. Hypertension was defined according to the IDF consensus for diabetes type 2 recommending arterial pressure levels up to 130/80 mmHg [23] and the same recommendation in the last Guideline of European Society of Hypertension (ESH) 2023 [24].

Laboratory analysis

After a 12-hour overnight fast, a. cubitalis venipuncture blood samples were taken to determine baseline blood sugar. The participants had a standard oGTT with 75 g glucose in 200 ml of water and glycemia was tested at 120 minutes. An exception was made only for persons who presented evidence of existing diabetes. Two individuals refused to perform the oGTT and dropped out of the study. Venous blood was drawn at 0, 60 and 120 minutes in plasma tubes, containing Na2EDTA and NaF, as an inhibitor of glycolysis for stability of glucose in the samples. The samples were transported to the laboratory after centrifugation. All of the samples were analysed in one Central laboratory on the day of the blood sampling. Glucose was quantitatively determined using enzymatic reference method with hexokinase (Roche reagent) on Cobas e501 analyzer. The results were in mmol/L. Established precision using human samples and controls: 1) Intra assay: Level 1 (n=6) CV=1.12%; Level 2 (n=6) CV=0.42%; 2) Inter assay: Level 1 (n=30) CV=1.25%; Level 2 (n=30) CV=1.58%; 3) Two levels Intralaboratory quality control on a daily basis was performed.

The Laboratory participates in two EQA systems – Bulgarian EQAS and INSTAND and has certificates for this parameter.

Venous blood was taken separately in a special tube with the anticoagulant EDTA for the determination of HbA1c by immunoturbidimetric method after hemolysis of a whole blood sample. The method was certified following the National Program for Standardization of Glycated Hemoglobin (NGSP) and standardized according to the Diabetes Control and Complications Trial (DCCT) [25].

The analysis was conducted on the basis of the WHO (1994) and United Nation / IDF (2006) criteria to analyze the rate of increase of Diabetes in the Bulgarian population for a period of 18 years (2006 - 2024) [26, 27]. It should be noted that the first two screenings for diabetes in Bulgaria reported the prevalence of diabetes according to the above criteria, which necessitated that the current screening be analyzed precisely on the basis of the same criteria, in order to make it possible to assess the dynamics of diabetes in the country for the specified period. Diabetes was diagnosed after the United Nation / International Diabetes Federation (2006) diagnostic criteria were applied: Diabetes was diagnosed when fasting glucose ≥ 7.0 mmol/L or at 120 minutes glucose ≥ 11.1 mmol/L was measured; IGT was diagnosed when glucose level at 120 minutes was 7.8 - 11.0 mmol/L and at 0 minute glucose was < 7.0 mmol/L; IFG was diagnosed when glucose level at 0 minute was 6.1 - 6.9 mmol/L and at 120 minute glucose was < 7.8 mmol/L [27].

An analysis was made for the prevalence of diabetes in 2024 in the country based on updated data from the WHO / IDF Report (2016) [28] to determine the current status of diabetes in the country and the data were published separately.

Statistical analysis

A. Descriptive and evaluation methods

Variance analysis of quantitative variables – mean, median, standard deviation, standard error of the mean, 95% confidence interval of the mean and median, minimum, maximum.

Frequency analysis of qualitative variables (nominal and rank), which includes absolute frequencies, relative frequencies (in percentages), cumulative relative frequencies (in percentages).

B. Hypothesis Testing Methods

Chi-square test or Fisher's exact test - search for a relationship between two qualitative variables.

Logistic regression analysis for odds ratios (OR).

The statistical analysis was performed using IBM SPSS Statistics 25. The critical significance level we used was $\alpha = 0.05$. The corresponding null hypothesis is rejected when the P-value is less than α.

3. Results

Table 1 shows the dynamics in the prevalence of diabetes in total for the period 2006 - 2024, as well as among both sexes and for each age decade.

Table 1. *Trends in the prevalence of diabetes - overall, for both sexes and by decade over an 18-year period (2006 - 2024).*

Groups	2006	2012	p-value	2006	2024	p-value	2012	2024	p-value
Total	7,9%	9,6%	0,06	7,9%	15,7%	< 0,001	9,6%	15,7%	< 0,001
Females	6.9%	7,8%	0,43	6.9%	10,4%	< 0,002	7,8%	10,4%	< 0,016

Groups	2006	2012	p-value	2006	2024	p-value	2012	2024	p-value
Males	9.2%	11,5%	0,09	9.2%	21,2%	< 0,001	11,5%	21,2%	< 0,001
20-29	0%	0,6%	0,247	0%	1.5%	0,058	0,6%	1.5%	0,466
30-39	0.9%	1,7%	0,295	0.9%	4,5%	< 0,002	1,7%	4,5%	< 0,047
40-49	5.8%	4,9%	0,527	5.8%	9,9%	0,058	4,9%	9,9%	< 0,020
50-59	9.4%	15,7%	< 0,005	9.4%	18,9%	< 0,001	15,7%	18,9%	0,323
60-69	19%	17,5%	0,865	19%	29,9%	< 0,001	17,5%	29,9%	< 0,001
70+	24.6%	18,9%	0,174	24.6%	27%	0,692	18,9%	27%	0,168

First of all, it should be noted that for the first period 2006 - 2012, the prevalence of diabetes in general increased from 7.9% to 9.6%, p = 0.06. This difference was due to greater increase in men (9.2% to 11.5%, p = 0.09) compared to women (6.9% to 7.7%, NS). In this period, certain trends emerge, although they are not very distinct.

In the following period, 2012-2024, the prevalence of diabetes in general, as well as the incidence in men and women significantly increased (Diabetes in general - from 9.6% to 15.7%, p < 0.001; diabetic men - from 11.5% to 21.2%, p < 0.001; diabetic women – from 7.8% to 10.4%, p < 0.016).

The difference in the prevalence of the risk factors that contribute to diabetes (age, BMI, arterial hypertension) was explored. Table 2 shows comparison of the prevalence of the risk factors in the studied population.

Table 2. *Distribution of arterial hypertension, normal, overweight and obesity in diabetics and general population in 2006, 2012, 2024.*

2006			2012		2024	
	Diabetics	Population	Diabetics	Population	Diabetics	Population
	Number/%	Number/%	Number/%	Number/%	Number/%	Number/%
Hypertension	153/190 (80.5%)	1053/2396 (43.9%)*	164/194 (84.5%)***	1002/2020 (49.6%)*/**	115/153 (74.2%)***	419/936 (44.8%)**
Body Mass Index (BMI kg/m^2)						
< 25	17/190 (8.9%)	863/2396 (36.0%)	22/194 (11.5%)	609/2021 (30.1%)	18/154 (11.7%)	294/931 (31.6%)
25-30	89/190 (46.8%)	889/2396 (37.1%)	73/194 (37.6%)	751/2021 (37.2%)	51/154 (33.1%)	327/931 (35.1%)
> 30	84/190 (44.2%)	640/2396 (26.7%)	99/194 (51.0%)	661/2021 (32.7%)	85/154 (55.2%)	310/931 (33.3%)

*p < 0.001; **p < 0.014; ***p < 0.017

In the general population, the dynamics of hypertension showed a significant increase in the first period (2006 - 2012) - from 43.9% to 49.6%, p < 0.001. In the next period (2012 - 2024), the incidence of hypertension declines and returns almost to its 2006 levels.

The diabetic group, had much higher level of hypertension compared to the general population – 80.5% vs. 43.9%, 84.5% vs. 49.6%, and 74.2% vs. 44.8% (for all p < 0.01). This trend of hypertension, observed in the general population in the period 2012-2024, is also demonstrated in diabetics, but at a higher level.

In the three years analyzed (2006-2012-2024), comparisons in terms of BMI showed that:

1) among the general population, obesity significantly increased in 2012 vs. 2006 (32.7% vs. 26.7%, p < 0.001) and in 2024 vs. 2006 (33.3% vs. 26.7%, p < 0.001).
2) obesity is significantly more common in diabetics compared to that of the population of the corresponding year of study [44.2% v.s. 26.77% (2006 y); 51% vs. 32.7% (2012 y); 55.2% vs. 33.3% (2024 y)], p < 0.001 for the three groups.
3) among the groups of diabetics, a significant increase in

the proportion of obese diabetics was noted - from 44.2% to 51% and resp. to 55.2%, with significant difference only in 2024, compared with 2006 (55.2% v.s. 44.2%, p < 0.043).

To sum up, obesity has increased progressively, both in the general population and in the diabetic group over the 18-year period.

In a logistic regression model, age, gender and BMI were included as factors and diabetes as a dependent variable. Each of these three factors has a significant effect on the presence of diabetes as shown in table 3.

Table 3. *Logistic regression analysis of odds ratio for the independent action of each risk factor for diabetes.*

Independent variables (factors)	Odds ratio (action of a single factor)	P - value
Male v.s. female gender	2,089 (95%CI: 1,462-2,984)	<0.001
45-59 years vs. 20-44 years	5,238 (95%CI: 2,847-9,636)	<0.001
60-79 years vs. 20-44 years	9,734 (95%CI: 5,390-17,578)	<0.001
Overweight vs. normal weight	2,833 (95%CI: 1,614-4,973)	<0.001
Obesity vs. normal weight	5,793 (95%CI: 3,382 -9,922)	<0.001

4. Discussion

First of all, it should be noted that the prevalence of diabetes during the 18 years studied (2006 - 2024), increased progressively as shown in Table 1. Following the national data for the total population and the adult population (20-79 years) from NSI documented in its regular reports, an assessment was made of the number of diabetics in the country through the three regular cross-sectional studies (2006, 2012, 2024), shown in table 4.

Table 4. *Extrapolated number of diabetics according to national diabetes prevalence data.*

Screening conducted (year)	Prevalence of Diabetes	Number of population 20-80 years (NSI)	Extrapolated number of diabetics
2006	7.9%	6 168 000	487 272
2012	9.6%	6 011 713	577 056
2017-Follow-up 2012*	12.5%	6 011 713	751 464
2024	15.7%	4 904 382	769 987

*In 2017 i.e. 5 years after the 2012 screening, persons with fasting blood glucose above 5.6 - 6.0 mmol/L and persons with proven prediabetes (after oGTT-75 g glucose) were examined. After a new oGTT-75 g conducted in 2017, 61 more diabetics were discovered. It turns out that 5 years later, 50% of those with prediabetes in 2012 had become diabetic, as had 25% of those with fasting blood glucose above 5.6 - 6.0 mmol/L [29].

158 % increase in the number of diabetics was established over a period of 18 years. In comparison, the data of the IDF Diabetes Atlas (2021) show that in 2007 the total number of diabetics in the world was 246 million, while in 2021 it reached 537 million, i.e. an absolute increase of 218% which is double increase [3]. According to the population of the country, there is an increase in diabetics by 199%, i.e. doubling. A specific feature for Bulgaria is the decreasing number of the population. In parallel with this, during this long period of 18 years, significant demographic changes developed - migration of mainly young population out of the country, migration of workable population to the big cities, financial problems for a significant part of the population with subsequent selection of unhealthy foods, as well as lack of education and traditions of doing physical activity. Research by some scientists indicates that low- and middle-income populations are rapidly shifting from traditional homemade food to processed fast food, which causes a significant increase in diet-related diabetes [30]. A number of authors in the last 30 years (1990 - 2021) reported major behavioral changes in food systems - preference for high-calorie products, increased consumption of fat and sugar, and at the same time limited

financial opportunities which do not allow provision of healthy food [31]. There is an increasing trend worldwide for the prevalence of type 2 DM. The aging of the population, the rise of the middle class, and the spread of urbanization are all factors that contribute to the rise of obesity – a major risk factor for developing diabetes [32].

Khunti K., Valabhji J. (2023) analysis of risk factors for diabetes indicates that obesity is the leading cause of type 2 diabetes in 60% of cases. High BMI (52.2%), non-dietary foods (25.7%), environmental or occupational stress (19.6%), smoking (12.1%), insufficient exercise (7.4%) and use of alcohol (1.8%) are among the significant risk factors [33]. Added to this is the reduced physical activity with modern transport options and the lack of traditions and education for systematic physical activity as part of a healthy lifestyle [34].

In this study assessment is that obesity plays a significant role in the onset of diabetes. The research demonstrated that in the population as a whole, the prevalence of normal weight decreased over the years by about 5% (NS), while obesity increased by 6 percent in 2012 vs. 2006 (32.7% vs. 26.7%, $p < 0.001$) and by 6,6 percent in 2024 vs. 2006 (33.3% v.s. 26.7%, $p < 0.001$).

In the groups of diabetics, the dynamics in the prevalence of overweight and obesity is much more pronounced. The trend for overweight is downward, with a 9.2% decrease for the period 2006-2012 and a further 4.5% decrease for the following period 2012 - 2024, or a total of 13.7% over an 18-year period ($p < 0.05$). At the same time, the trend of obesity is upward, increasing by 6.8% for the period 2006 - 2012 and for the next period 2012-2024 there is a rise of another 4.2%, or a total of 11.0% for the period 2006 - 2024 ($p < 0.043$).

In 2006, the ratio between overweight and obesity was slightly in favor of overweight (by 2.6%). In 2012, the ratio sharply reversed and obesity dominated with 13.4% over overweight, and in 2024 this difference still increased and reached 22.1%. Therefore, BMI > 25 kg/m2 in diabetics is maintained within very close limits (91-88.1%), but with a reversal of the ratio between obesity: overweight in favor of the more severe disorder, i.e. of obesity. Thus, in 2024, more than half of diabetics (55.7%) are obese, which emphasizes the direct strong correlation between obesity and diabetes.

There was also an inverse relationship, with an increased prevalence of diabetes among obese individuals, and the prevalence of this phenomenon was estimated in the NHANES analysis (2021). As BMI increases, so does the prevalence of diabetes. While the prevalence of diabetes is 6.6% with normal weight, it is 10.3% with overweight and 23.3% with obesity. Men have a higher prevalence of diabetes than women in all three BMI categories i.e. not dependent on BMI [35]. Table 5 presents the NHANES data (2021) for the obesity-diabetes correlation - total and in both sexes.

Table 5. *Relationship between obesity and prevalence of diabetes /general/ and in both sexes.*

Indicator	Under 25 kg/m^2	25-30 kg/m^2	Above 30 kg/m^2
Total (%)	6.6	10.3	23.3
Women (%)	4.9	7.4	22.8
Men (%)	9	12.7	24

The three Bulgarian analyses, as well as the NHANES analysis (2021), show that men are more likely to have diabetes than women. In the today's study, an increase in diabetes was observed: in total for the period 2006 - 2012 from 7.9% to 9.6%, $p = 0.06$, with a distinct increase in men (9.2% to 11.5%, $p = 0.09$) compared to women (6.9% to 7.7%, NS). In the following period, 2012 - 2024, the incidence of diabetes in general, as well as the incidence in men and women, significantly increased (Diabetes in general - from 9.6% to 15.7%, $p < 0.001$; diabetic men - from 11.5% to 21.9%, $p < 0.001$; diabetic women – from 7.8% to 11.7%, $p < 0.016$), and again the increase is mostly for men. The higher prevalence of diabetes in men versus women of the same age group could be related to the impact of obesity, socioeconomic factors, biological and hormonal differences. It is believed that men with a lower BMI threshold can develop Diabetes because their insulin resistance is more pronounced [36].

The role of age is essential for the appearance of diabetes and this is proven in the study. The relationship between age and diabetes is very strong and definite for all studied periods. It should stress the fact that the average age of those examined in 2006 was 47.72 ±14.82 years, and in 2012 – 49.30 ±14.7 years ($T = 3.559$, $p < 0.001$). The average age of those examined in 2024 was even higher, 50.56 ± 13.6 years, and the difference was significant in 2012 ($T = 2.254$, $p < 0.05$), and also in 2006 ($T = 5.289$, $p < 0.001$). The data confirmed that the population was not only decreasing over the 18-year period by about 21%, but it was also "aging", which may have played an important role for the increase in diabetes. Further analysis by decade of the three groups of participants from 2006, 2012, 2024 showed many interesting changes in this 18-year period (Table 1).

In 2006, there was not a single case of diabetes in the 20-29 age group, but in the following decades the incidence of diabetes progressively increased to 19% for 60-69 years and resp. 24.6% for the 70+ group.

In 2012, in the 20-29 age group, there were already 0.6% cases of diabetes, which increased with age and reached 17.5% for 60-69 age group, resp. 18.9% for the 70+ age group.

In 2024, the 20-29 age group had 2.5 times more cases of diabetes than in 2012 y, and the incidence in the following age groups was higher than in previous periods, reaching its highest levels of 29.9% for 60-69 age group, respectively 27% for the 70+ age group.

This recurrence in all three studied periods (2006, 2012, 2024)

reinforces the direct relationship between advancing age and increase in the prevalence of diabetes. The particularities of the dynamics in the prevalence of diabetes in individual decades for this 18-year period should be specially noted. While for the first 6-year period (2006 - 2012) only for the 50-59 age group there was a significant increase in the prevalence of diabetes (from 9.2% to 11.5%, $p = 0.09$), in the second 12-year period (2012 - 2024) dramatic changes took place and a "rejuvenation" of diabetes has occurred. Its frequency increased significantly in the 30-39 age group (for 2012 - 2024, from 1.7% to 4.5%, $p < 0.047$) and much more sharply when comparing 2006 - 2024 - from 0.9% to 4.5%, $p < 0.002$. Diabetes significantly increased in the 40-49 age group (from 4.9% to 9.9%, $p < 0.02$). The rise in the 50-59 age group was confirmed, with increased frequency for the period 2012 - 2024 (from 15.7% to 18.9%, NS), and more significantly in 2024 against 2006 (from 9.4% to 18.9 %, $p < 0.001$). During the second 12-year period (2012 - 2024) for the 60-69 age group the prevalence of diabetes significantly increased (from 17.5% to 29.9%, $p < 0.001$) and practically every third after the age of 60 has diabetes.

The distribution of diabetes prevalence in the three age groups presented by NHANES (2021) is as follows: 20-39 age group - 4.4% (95%CI:2.9-6.2), 40-59 age group - 16.4% (95%CI:13.4-19.9) and over 60 age group - 30.0% (95% CI:27.2-32.9). Additional data for both sexes are presented in Table 6 [35].

Table 6. *NHANES (2021) diabetes prevalence data – total and in both sexes.*

Indicator	20-39y	40-59 y	> 60 y
Women (%)	4.7 (95%CI:3.1-6.9)	15.9 (95%CI:10.9-21.9)	24.4 (95%CI:19.4-30.1)
Men (%)	4 (95%CI:1.7-7.9)	17.1 (95%CI:12.8-22.1)	36.3 (95%CI:30.8-42.1

In the same NHANES (2021) statistical analysis, the relationship between age and obesity, and hence the impact on diabetes prevalence, was also considered. While in the 20-39 age group obesity was 39.8% (95%CI:35.3-44.3), in the 40-59 age group it was 44.3% (95%CI:41.3-47.4) and 41.5% in the 60 – over age group (95% CI:38.4-44.7) [35].

A model with all three factors simultaneously (sex, age, BMI) was additionally analyzed to estimate the odds ratio. Male gender was associated with OR=2.243 (95%CI:1.511-3.331), $p<0.001$; 45-59 age group was associated with OR=4.845 (95%CI:2.599-9.032), $p<0.001$; 60-79 age group was associated with OR=9.774 (95%CI:5.296-18.040), $p<0.001$; overweight was associated with OR=1.821 (95%CI:1.008-3.288), $p<0.047$; obesity was associated with OR=3.410 (95%CI:1.935-6.010), $p<0.001$. The analysis showed a direct strong correlation between the above risk factors and diabetes, which give the reason to create and conduct diabetes screening programs aimed mainly at males, adults over 44 and obese individuals**.**

The other risk factor for diabetes is hypertension, and its prevalence is closely related to both age and weight. The data of National Health Statistics Reports (2021) show that the prevalence of hypertension increases with age: 18-39 age group - 23.4% (95%CI:20.5-26.5), 40-59 age group - 52.4% (95%CI:48.7-56.2) and 60+ age group - 74.1% (95%CI:71.4-76.7); with weight gain: normal weight: 31.1% (95%CI:26.8-35.6), overweight: 40.6% (95%CI:37.9-43.3) and obese: 57.7% (95%CI:54.8-60.6) and was more common among men than among women – 48.7% (95%CI:44.8-52.6) compared to 41.2 % (95%CI:38.5-44.0) [35].

Hypertension is twice as common in diabetics as in those without diabetes. In addition, hypertensive patients often have insulin resistance and are at greater risk of diabetes than normotensive individuals [37]. According to Akalu Y. et al. Hypertension and T2DM share common risk factors and therefore usually co-occur. Approximately 58% of diabetics have arterial hypertension [38].

In this study, throughout the18-year period, a much higher prevalence of hypertension was permanently maintained in the diabetic group compared to the general population - 80.5% vs. 43.9%, 84.5% vs. 49.6%, and 74.2% vs. 44.8% (for all $p < 0.01$). It can be summarized that, in different periods, hypertension in diabetics is 50% to 83% more common compared to the general population. Insulin resistance is a common feature of both prediabetes and prehypertension and precedes progression to both disease states, particularly in individuals who gain weight over time [39]. Diabetes and hypertension are closely related due to the presence of similar risk factors, such as endothelial dysfunction, vascular inflammation, arterial remodeling, atherosclerosis, dyslipidemia, and obesity. They also share common mechanisms, such as RAAS activation, oxidative stress, inflammation, and probably all of these close the link between diabetes and hypertension [37]. Several longitudinal studies have shown that hypertension is an important risk factor for T2DM and may play a vital role in its prognosis [40].

It can be summarized that diabetes is a major public health threat worldwide due to its rapid growth and significant impact on health and quality of life [41].

5. Conclusion

The results of the present study show a rapid double in-

crease in the prevalence of diabetes in the last two decades. It is essential to understand better the disparities in risk factor profiles and diabetes burden on the population, to encourage strategies for successful control of diabetes risk factors. Age, obesity, hypertension and male gender are the leading risk factors for diabetes in our population. All this necessitates the introduction of preventive programs for early diagnosis in the country health care system, as well as for regulated adequate care aimed at risk groups of the population.

Abbreviations

WHO	World Health Organisation
UN	United Nation
NSI	National Statistical Institute
NHANES	National Health and Nutrition Examination Survey
IDF	International Diabetes Federation
ESH	European Society of Hypertension
oGTT	Oral Glucose Tolerance Test
NGSP	National Program for Standardization of Glycated Hemoglobin
DCCT	Diabetes Control and Complications Trial
IGT	Impaired Glucose Tolerance
IFG	Impaired Fasting Glucose
OR	Odds Ratio
IBM	International Business Machines Corporation
SPSS	Statistical Package for the Social Sciences
BMI	Body Mass Index
DM	Diabetes Mellitus
T2MD	Type 2 Diabetes Mellitus

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Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] WHO. (2019). Classification of diabetes mellitus. https://apps.who.int/iris/handle/10665/325182

[2] Chan, Juliana C N; Lim, Lee-Ling; Wareham, Nicholas J; Shaw, Jonathan E; Orchard, Trevor J; Zhang, Ping; Lau, Eric S H; Eliasson, Björn et al. The Lancet Commission on diabetes: using data to transform diabetes care and patient lives. Lancet 2021; 396, 10267, P2019–2082. https://doi.org/10.1016/S0140-6736(20)32374-6

[3] International Diabetes Federation. (2021). IDF Diabetes Atlas, 10th edn. Brussels: International Diabetes Federation. https://www.idf.org/e-library/welcome/

[4] WHO. Global action plan for the prevention and control of noncommunicable diseases 2013–2020. Nov 14, 2013. Geneva: World Health Organization.

[5] The GBD 2019 Universal Health Coverage Collaborators. Measuring universal health coverage based on an index of effective coverage of health services in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*, *396*(10258), 1250-1284. https://doi.org/10.1016/S0140-6736(20)30750-9

[6] UN. The Sustainable Development Goals Report 2020. New York, NY: (2020). United Nations.

[7] Pouya Saeedi, Inga Petersohn, Paraskevi Salpea, Belma Malanda, Suvi Karuranga, Nigel Unwin, Stephen Colagiuri, Leonor Guariguata et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract*; (2019). https://doi.org/10.1016/j.diabres.2019.107843

[8] CDC: Centers for Disease Control and Prevention, National Diabetes Statistics Report, 2024. https://www.cdc.gov/diabetes/php/data-research/index.html.

[9] Borissova Anna-Maria, Kovatcheva Roussanka, Shinkov Alexander, Atanasova Iliana, Vukov Martcho, Aslanova Nina, Vlahov Jordan, Dakovska Lilia. Cross-sectional study on the prevalence of diabetes mellitus in non-selected Bulgarian population. Endokrinologya 2007; 12: 42–49. ISSN 1310-8131.

[10] Borissova Anna-Maria, Shinkov Alexander, Vlahov Jordan, Dakovska Lilia, Blajeva Emilia, Todorov Todor. Prevalence of diabetes mellitus and prediabetes in Bulgaria today. Endokrinologya 2012; 17: 172–182. ISSN 1310-8131.

[11] Akinbami LJ, Chen TC, Davy O, Ogden CL, Fink S, Clark J, et al National Health and Nutrition Examination Survey, 2017–March 2020 Prepandemic File: Sample Design, Estimation, and Analytic Guidelines. Data Evaluation and Methods Research. NATIONAL CENTER FOR HEALTH STATISTICS. Vital and Health Statisticsp Series 2, Number 190 May 2022. https://dx.doi.org/10.15620/cdc:115434

[12] IDF. Diabetes Atlas. 4th ed. Belgium: International Diabetes Federation; (2009), page 98. ISBN-13: 978-2-930229-71-3.

[13] Ahmad OB, Boschi-Pinto C, Murray CJL, Lozano R, Inoue M. Age Standardization of Rates. A New WHO World Standard 2001. Geneva, Switzerland: WHO (2001).

[14] United Nations, Population Division. World Population Prospects. The 2006 Revision. Geneva: United Nations, Population Division, 2007.

[15] Shaw E, Sicree RA, Zimment PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010; 87: 4–14. https://doi.org/10.1016/j.diabres.2009.10.007

[16] Anna-Maria Borissova, Alexander Shinkov, Roussanka Kovatcheva, Jordan Vlahov, Lilia Dakovska and Todor Todorov. Changes in the Prevalence of Diabetes Mellitus in Bulgaria (2006–2012). Clinical Medicine Insights: Endocrinology and Diabetes. 2015; Volume 8, pages 41-45. https://doi.org/10.4137/CMED.S24742

[17] Anna-Maria Borissova, Alexander Shinkov, Jordan Vlahov, Lilia Dakovska, Todor Todorov. Higher Prevalence of Diabetes Mellitus and Impaired Glucose Tolerance Among the Rural Population in Bulgaria. J Endocrinol Metab. 2016; Volume 6, Number 2, pages 52-58. https://dx.doi.org/10.14740/jem334w

[18] Guariguata L, Whiting D, Weil C, Unwin N. The International Diabetes Federation Diabetes Atlas methodology for estimating global and national prevalence of diabetes in adults. Diab Res Clin Pract. 2011; 94: 322–332. http://dx.doi.org/10.1016/j.diabres.2011.10.040

[19] NSI. The population of Bulgarian Republic. National Statistical Institute. 2005. Available at: http://www.nsi.bg/Population/Population.htm

[20] NSI. 17th National population census in Bulgaria. National Statistical Institute. 2011. Available at: http://censusresults.nsi.bg/Census/Reports/2/2/R1.aspx

[21] NSI. National population census in Bulgaria. National Statistical Institute. December 2022. https://www.nsi.bg/sites/default/files/files/publications/StatBook_Census2021.pdf

[22] Jonathan Cimino and Claude Braun. Design a Clinical Research Protocol: Influence of Real-World Setting. Healthcare. 2023; 11, 2254. https://doi.org/10.3390/healthcare11162254

[23] International Diabetes Federation. Clinical Guidelines Task Force. Global Guideline for Type 2 Diabetes. Belgium, 2012.

[24] 2023 ESH Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Hypertension Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). Authors/Task Force Members: Giuseppe Mancia (Chairperson), Reinhold Kreutz (Co-Chair), Mattias Brunstrom, Michel Burnierd, Guido Grassie, Andrzej Januszewiczf et al. J. of Hypertension. 2023; Vol 41, Number 12. https://doi.org/10.1097/HJH.0000000000003480

[25] The Diabetes Control and Complications Trial Research Group: The relationship of glycemic exposure (A1C) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. Diabetes. 1995; 44: 968–983. https://doi.org/10.2337/db07-1618

[26] World Health Organization. Prevention of Diabetes mellitus. Report of a WHO study group Geneva: World Health Organization. 1994, No 844. PMID: 7941615.

[27] United Nation, International Diabetes Federation. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia. Geneva, Switzerland, 2006.

[28] World Health Organization and International Diabetes Federation. Definition and diagnosis of diabetes mellitus and Intermediate hyperglycaemia. Report of a WHO/IDF Consultation, Geneva, 2016.

[29] Borissova Anna-Maria, Vlahov Jordan, Shinkov Alexander, Dakovska Lilia, Trifonova Boiana. A 5-year follow-up of subjects with fasting plasma glucose above 5.6 mmol/l found in a screening study in the Bulgarian population (2012-2017). Clinical Medical Research. 2021; 10(3): 95-101. https://doi.org/10.11648/j.cmr.20211003.15

[30] Fahed AC, El-Hage-Sleiman AK, Farhat TI, Nemer GM. Diet, genetics, and disease: a focus on the middle East and north Africa region. J Nutr Metab 2012: 109037. https://doi.org/10.1155/2012/109037

[31] Delpino FM, Figueiredo LM, Bielemann RM, Da Silva BGC, Dos Santos FS, Mintem GC, Flores TR, Arcencio RA, Nunes BP. Ultra-processed food and risk of type 2 diabetes: a systematic review and metaanalysis of longitudinal studies. Int J Epidemiol. 2022; 51(4): 1120–1141. https://doi.org/10.1093/ije/dyab247

[32] Lovic D, Piperidou A, Zografou I, Grassos H, Pittaras A, Manolis A. The growing epidemic of diabetes mellitus. Curr Vasc Pharmacol. 2020; 18(2): 104-109. https://doi.org/10.2174/1570161117666190405165911

[33] Khunti K, Valabhji J, Misra S. Diabetes and the COVID-19 pandemic. Diabetologia 2023; Feb 66(2): 255-266. https://doi.org/10.1007/s00125-022-05833-z

[34] Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. Nutr Rev. 2012; 70: 3–21. https://doi.org/10.1111/j.1753-4887.2011.00456.x

[35] National Health and Nutrition Examination Survey 2017–March 2020 Prepandemic Data Files—Development of Files and Prevalence Estimates for Selected Health Outcomes Bryan Stierman, M. D., M. P. H.; Joseph Afful, M. S.; Margaret D. Carroll, M. S. P. H.; Te-Ching Chen, Ph.D.; Orlando Davy, M. P. H.; Steven Fink, M. A.; Cheryl D. Fryar, M. S. P. H.; Qiuping Gu, Ph.D.; Craig M. Hales, M. D., M. P. H.; Jeffery P. Hughes, M. P. H.; Yechiam Ostchega, Ph.D., R. N.; Renee J. Storandt, M. T. (A.S.C.P.), M. S. P. H.; and Lara J. Akinbami, M. D. National Health Statistics Reports, 2021; Number 158 ν June 14. http://dx.doi.org/10.15620/cdc:106273

[36] Kautzky-Willer A, Harreiter J, Pacini G. Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. Endocr Rev. 2016; 37: 278–316. https://doi.org/10.1210/er.2015-1137

[37] John R. Petrie, Tomasz J. Guzik, Rhian M. Touyz. Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. Canadian Journal of Cardiology. 2018; 34, 575e584. https://doi.org/10.1016/j.cjca.2017.12.005

[38] Akalu Yonas, Belsti Yitaych. Hypertension and its associated factors among type 2 diabetes mellitus patients at debre tabor general hospital, Northwest Ethiopia. Diabetes Metab Syndr Obes. 2020; 13: 1621–31. https://doi.org/10.2147/DMSO.S254537

[39] Vasilis Tsimihodimos, Clicerio Gonzalez-Villalpando, James B. Meigs, Ele Ferrannini. Hypertension and Diabetes Mellitus Coprediction and Time Trajectories. Hypertension. 2018; 71: 422-428. https://doi.org/10.1161/HYPERTENSIONAHA.117.10546

[40] Sinclair A, Saeedi P, Kaundal A, Karuranga S, Malanda B, Williams R. Diabetes and global ageing among 65-99-year-old adults: Findings from the International Diabetes Federation Diabetes atlas, 9(th) edition. Diabetes Res Clin Pract. 2020; 162: 108078. https://doi.org/10.1016/j.diabres.2020.108078

[41] Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of type 2 diabetes - global burden of disease and forecasted trends. J Epidemiol Glob Health. 2020; 10(1): 107–11. https://doi.org/10.2991/jegh.k.191028.001