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A Longitudinal Assessment of the Dynamics of Metabolic Syndrome

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Abstract: Background: Metabolic syndrome (MetS) is a combination of conditions including central obesity, high blood pressure, high sugar levels, and abnormal triglycerides and cholesterol, which together increase chances of heart diseases, diabetes, and even death. The rates of MetS are different around the world, with 20–30% in Europe and 21.8–23.9% in Kazakhstan. Because MetS changes over time, it is important to study the dynamics of their components to improve prevention and treatments. **Methods**: This is a longitudinal study with a 10 year follow up in Turkestan city 2012–2024. Information was collected through physical exams, blood tests, and anthropometric measurements. Logistic regression and ROC curve analysis were used to find which factors increase risk of MetS. **Results**: Among 434 participants analyzed, the incidence of MetS at follow-up was 40%. Key risk factors for newly diagnosed MetS included elevated blood pressure and increased waist circumference. Multivariate analyses highlighted these components as the strongest predictors of MetS, with significant associations observed for participants with two or more MetS components at baseline. **Discussion**: Elevated blood pressure and central obesity were identified as pivotal contributors to MetS progression. Given the raising prevalence of Mets and its implications, these results show the need to start treatment and check these risks early to prevent serious health problems.

Keywords: Adult, cohort studies, metabolic syndrome, epidemiology, risk factors.

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1. Introduction

Metabolic syndrome (MetS) is a combination of conditions, including central obesity, high blood pressure, elevated blood sugar, and abnormal cholesterol levels, that together raise the risk of cardiovascular diseases (CVD), type 2 diabetes (T2DM), and mortality from any cause [1]. The dynamics of MetS are driven by multiple factors, including genetic tendencies, lifestyle choices, and metabolic issues [2]. This syndrome has become a major global health concern due to its increasing prevalence [3] and connection to serious health problems [4].

The prevalence of MetS in most countries of the European World Health Organization (WHO) region varies between 20 and 30%, with relatively equal distribution across genders [5, 6]. Previous analyses in Kazakhstan have reported a prevalence of MetS among women of 21.8% and 23.9% for men, based on IDF criteria. Abdominal obesity was the most prevalent component of MetS, followed by hyperglycemia, systolic hypertension and diastolic hypertension [7]. One problem that complicates assessing the epidemiology of MetS and for comparison between countries and settings is the use of different definitions by different researchers.

MetS does not progress in a straight line but is dynamic, involving shifts between different levels of metabolic health, from mild to severe disorders. Knowing the factors associated with these changes is crucial for making effective treatments that can stop MetS from worsening and, ideally, reverse some of its effects [8]. Recent research has used multi-state models, such as the Markov model, to predict these changes and give insight into both the worsening and improvement of MetS components [9].

In this research, we look at the progression to MetS in a general adult population in Kazakhstan. Examining the main mechanisms and contributing factors, this study aims to improve our understanding of how MetS progresses, which in future can help to create more effective prevention and treatment strategies. Therefore, the objective of this study was to obtain the incidence of MetS and to evaluate the specific components associated with the emergence of new MetS cases in this population.

2. Materials and Methods

This is a longitudinal study that involved the collection of data from 938 participants initially recruited in 2012-14 residing in Turkestan city and who were invited for a second interview and blood tests in 2024. Patients were recruited from Khoja Akhmet Yassawi International Kazakh-Turkish University Outpatient Clinic in Turkestan.

Participants were thoroughly informed about the study's objectives, methodology, potential risks, and anticipated benefits. Detailed explanations were provided to ensure that participants fully understood each aspect of the study, including the procedures, their roles, and any associated commitments. Following this comprehensive briefing, informed consent was obtained from all participants, confirming their voluntary agreement to participate. This consent process adhered to ethical standards and was documented to confirm that each patient had the opportunity to ask questions and had received satisfactory answers before consenting.

After informed consent, participants underwent physical examination, blood draw and questionnaire. Anthropometric measurements: height, weight, neck, waist, and hip measurements are taken.

Glucose levels were measured with a glucometer (ATCare) using capillary blood from the fingertip, both fasting and two hours after a standardized breakfast. Complete blood count was conducted on a BS-6000 Mindray device, with 3 ml of blood collected in a purple-top EDTA tube.

For this study, we used the definition of MetS according to the 2006 International Diabetes Federation (IDF) criteria, MetS is diagnosed when three or more criteria are met: Triglycerides 150 mg/dl or greater; HDL-cholesterol < 40 mg/dl in men and < 50 mg/dl in women; BP 130/85 mmHg or greater; Fasting glucose 100 mg/dl or greater; Waist circumference > 90 cm in men and > 80 cm in women [10].

Cases meeting the criteria for MetS in 2014 were excluded to accurately estimate the incidence of MetS in 2024. Chi-square tests and mean comparisons were performed, followed by multivariable logistic regression. Models will be analyzed: 1) considering the values of the different parameters to estimate MetS; 2) considering the components that define MetS; and 3) the number of components to be considered to define MetS. To assess the predictive capacity of the logistic regression models, receiver operating characteristic (ROC) curve analysis was conducted.

3. Results

Of the 938 participants in the baseline data collection in 2012 to 2014, 56 participants have since passed away. It was not possible to contact 130 of them, probably due to changes of residence to other locations, and 200 declined further participation. The remaining 552 participants were reviewed through the national medical database and contacted by phone with the help of their general practitioners. Figure 1 depicts the flow chart of the data.

Figure 1. Flow chart.

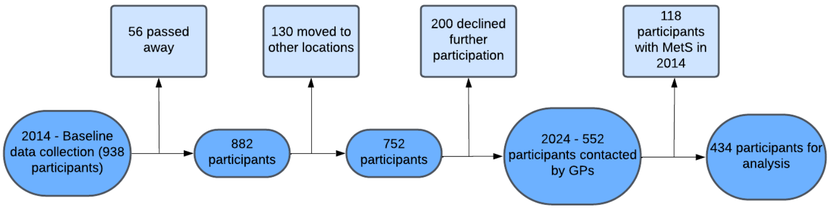


Table 1 represents the main characteristics of the population in the 2 periods of time analyzed, baseline and follow up. The prevalence of the 2 more frequent components of MetS (blood pressure and waist circumference) increased from 20.5% and 65.9%, to 33.9% and 74.4%.

Table 1. Main characteristics of the sample

Categories		**BASELINE**	**FOLLOW UP**
Sex	Male	21.2%	
	Female	78.8%	
Age		40.87 (10.9)	52.9 (10.7)
	< 36 years	34.3%	5.7%
	36-45 years	29.7%	22.5%
	> 45 years	35.9%	71.8%
Systolic Blood Pressure	Mean (SD)	113.29 (17.19)	120.37 (18.56)
Diastolic Blood Pressure	Mean (SD)	75.42 (11.28)	78.25 (11.17)
Waist circumference	Mean (SD)	90.169 (14.17)	93.90 (14.20)
Triglycerides	Mean (SD)	1.28 (0.35)	1.55 (0.71)
HDL	Mean (SD)	1.52 (0.27)	1.34 (0.61)
Glucose	Mean (SD)	4.98 (0.84)	5.29 (1.22)
Met S Components			

MS Blood Pressure		20.5%	33.9%
MS Glucose		10.8%	26.5%
MS Triglycerides		6.5%	36.9%
MS WC		65.9%	74.4%
MS HDL		4.6%	50.9%
NUMBER MS	Mean (SD)	1.08 (0.76)	2.23 (1.30)
	Median	1	2
Metabolic Syndrome		–	40.3%
Total		434	

The values of all the MetS components analyzed, showed a worsening in the follow up. To highlight that, at baseline 66% had < 2 MetS component, while at follow-up only 31%. The number of cases that at follow-up 40% met the criteria for MetS (Figure 2) was 40.3%. Almost 15% had 4 or more components at follow-up. In Supplementary Table 1 we can see the frequency of aggregation of the different MetS components at baseline.

Figure 2. Distribution of participants at baseline and follow up by number of metabolic syndrome components.

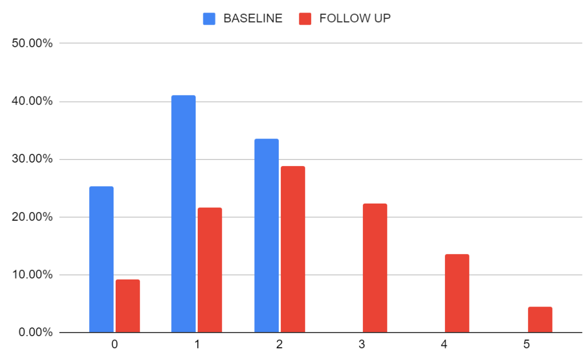


Table 2 reports the risk associated with the incidence of MetS, by age and sex, by the number of components and by the presence of specific components at baseline. The results reflect the significant association with 2 MetS components: elevated blood pressure and higher values of waist circumference. Age was also associated with a higher incidence.

Table 2. Incidence of Metabolic Syndrome in Follow Up by age, sex and metabolic syndrome components at baseline

	NO	YES%	p-value
< 36 years		26.8%	<0.001
36-45 years		43.4%	
> 45 years		50.6%	
Men		44.6%	0.350
Women		39.2%	
0 MS Component		13.6%	<0.001
1 MS Component		37.6%	
2 MS Components		63.7%	
MS Blood Pressure	34.2	64.0	<0.001
MS Glucose	39.0	51.1	0.112
MS Waist circumference	15.5	53.1	<0.001
MS Triglycerides	39.7	50.0	0.280
MS HDL	30.0	40.8	0.335

In figure 3 we can see how most participants showed a deterioration of their MetS components between baseline and follow up. The increase in the number of components was especially relevant for those with 2 MetS components at baseline. Most cases deteriorated the number of MetS components from baseline to follow-up (68.4%). Only 26.5% maintained the number of MetS components and 5.1% had a lower number of components.

Figure 3. Dynamic transition of participants by the number of metabolic syndrome components at baseline and follow up.

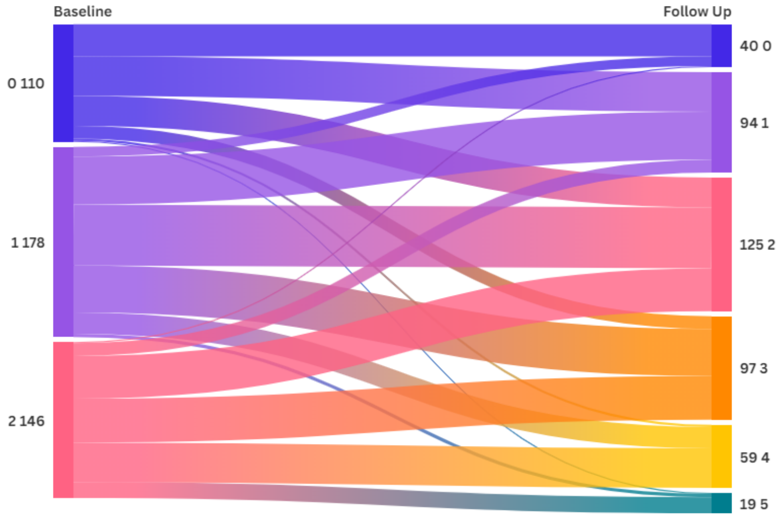


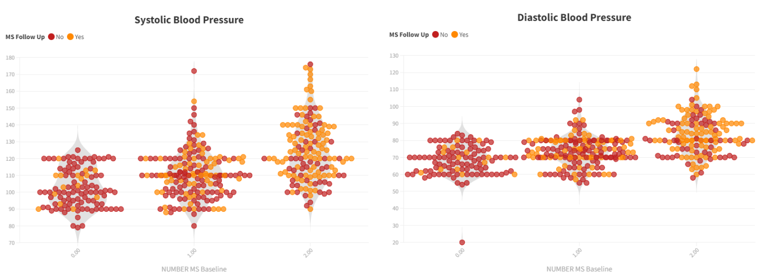
Table 3 indicates that all parameters were higher at baseline for participants that developed MetS at follow-up, including age, except for HDL, and that worsening of all, except for HDL and Glucose, were associated with a higher risk of developing MetS at follow-up.

Table 3. Means values of Metabolic syndrome components in 2014 and Incidence of Metabolic Syndrome in 2024.

	Age	SBP	DBP	WC	TG	HDL	Glucose
No MetS at follow up	38.69	108.36	72.39	85.710	1.21	1.51	4.83
MetS at follow up	44.09	118.66	79.06	96.769	1.37	1.52	5.05
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	0.631	0.015
OR Incidence of MetS IC95%	1.05 1.0-1.07	1.04 1.02 - 1.05	1.06 1.04 - 1.08	1.08 1.06 - 1.10	4.29 2.24 - 8.23	1.20 0.58 - 2.47	1.35 0.99 - 1.84

In figure 4 it could be observed that elevated blood pressure and waist circumference were highly prevalent in cases with 2 MetS components, and that those factors were strongly associated with new cases of MetS at follow-up.

Figure 4. Violin graphs representing the incidence of metabolic syndrome at follow up based on metabolic syndrome components and number of affected metabolic components at baseline.



Tables 4, 5 and 6 show the results of multivariate analysis with different exposure variables and the AUC results of the models. The model including MetS components Blood pressure and Waist Circumference is the model with the highest predictive value as estimated by AUC (Figure 5). This model includes MetS Blood Pressure and MetS WC, which are the 2 characteristics that were independently associated with a higher risk of newly diagnosed MetS. Although age showed an association in univariate analysis, its effect did not remain significant in multivariate analyses.

Table 4. Multivariable Logistic Regression of incidence of Metabolic Syndrome by values of components of Metabolic Syndrome at baseline

	OR	IC95%
DBP_2014	1.04	1.02 - 1.07
WC_2014	1.06	1.04 - 1.08

Table 5. Multivariable Logistic Regression of incidence of Metabolic Syndrome by components of Metabolic Syndrome at baseline

	OR	IC95%
MS_BP_2014	2.97	1.77 - 4.99
MS_WC_2014	5.71	3.43 - 9.51

Table 6. Logistic Regression Model of the incidence of metabolic syndrome by the number of of metabolic syndrome components at baseline

	OR	IC95%
0 MetS components	REF	
1 MS	3.82	2.05-7.13
2 MS	11.11	5.86-21.09

No differences between men and women were identified in these analyses.

In Supplementary Table 2 we can see the lack of association between IFG, IGT, insulin resistance, beta cell deficit with the incidence of MetS.

4. Discussion

The main finding of this longitudinal analysis that explored the dynamic progression of MetS and its components in a general adult population is an incidence of 40% of MetS after 10 years of follow-up. The second is that the most relevant factors that increased the risk of newly diagnosed MetS in the follow-up period are elevated blood pressure and waist circumference. Both factors, blood pressure and waist circumference, were independently associated in multivariable models that indicated a reasonable capacity to predict the 10-year incidence of MetS in this population. Another finding of this study is that, although blood pressure and waist circumference are strongly associated, the higher number of MetS components affected also increases the risk of incidence of MetS. The incidence of new cases of MetS was found to be higher in those with already 2 MetS components at baseline but also was found in cases with 1 or even 0 components. A relevant finding of this study is the lack of association between glucose levels or glucose metabolism indexes, including insulin resistance, and the incidence of MetS in this population.

MetS is a complex disorder with multiple factors that can interchange with time. Although numerous studies have aimed to determine pathogenesis of this condition, the exact pathways linked with the development of MetS are still unclear due to the complexity of disease and many factors contribute to it. Factors that have been described as pivotal in the incidence and progression of MetS as are low-grade inflammation driven by excess visceral fat, which disrupts glucose metabolism and increases CVD and T2DM risks [11], as well insulin resistance [12], lipid metabolism dysregulation [13]. The influence of genetic predisposition is also being increasingly recognized [14, 15].

Elevated blood pressure (BP) is a significant component of MetS and one of the criteria for this diagnosis. Elevated BP levels are associated typically with the incidence of MetS and are considered a strong precursor of MetS, highlighting the importance of early BP management to prevent the syndrome's onset. A five-year retrospective cohort study examined the relationship between BP levels and the incidence of MetS. The study found that individuals with higher baseline BP were more likely to develop MetS over time [16], while people with optimal and normal BP levels were less susceptible to developing MetS over time, suggesting that abnormal BP could be considered as a pre-existing phase of MetS and the relevance for maintaining high-normal BP for MetS prevention [17, 18].

The pathophysiology that connects high BP to MetS is explained by several interconnected mechanisms. Central obesity and abnormal levels of lipids may cause endothelial dysfunction, reducing the availability of nitric oxide and affecting proper vasodilation, which is an important factor in how MetS develops. Inflammation, which is at a low level but constant in both conditions, makes this worse by triggering more inflammatory reactions that encourage the progression of MetS. Understanding how BP contributes to MetS shows how important it is to check CVD risks properly and take timely actions. If high BP is managed early, it might help stop or delay MetS and its complications [19].

Waist circumference (WC) is a crucial marker for central obesity and a significant contributor to MetS. Central obesity is strongly associated with insulin resistance, dyslipidemia, and hypertension—key components of MetS. The rising prevalence of obesity is identified as a primary driver of MetS, emphasizing prevention and management strategies. A comprehensive review of the connection between obesity, MetS, and T2DM has stressed that these conditions have similar mechanisms and often happen one after another, increasing the risk of CVD events. The rising number of obesity cases is pointed out as a main cause of MetS, showing the importance of good prevention and management plans [20]. Dysfunctional adipose tissue in obesity contributes to insulin resistance and lipid metabolism disorders, both central to MetS development [21].

WC has also been identified as a valid estimate for predicting changes in body composition related to MetS. In the dynamic behavior of MetS progression, central obesity, as indicated by increased WC, often precedes other MetS components. Regularly measuring WC is an effective way to identify individuals at risk for MetS [22]. Targeted lifestyle interventions focused on weight reduction are essential to prevent or delay the onset of MetS. In clinical practice, WC measurement is a simple and cost-effective method for assessing central obesity and evaluating MetS risk [23]. Current guidelines provide population-specific

WC thresholds to identify those at higher risk, ensuring tailored preventive strategies [24].

Although insulin resistance is considered a major pathogenic factor playing a crucial role in the development of MetS and has been proposed as a hallmark and one of its critical underlying causes [25, 26], in our study, glucose metabolism indexes—including both insulin resistance and pancreatic dysfunction—did not show a significant association with an increased risk of MetS incidence. During the early stages of insulin resistance, elevated insulin secretion may temporarily compensate to maintain metabolic balance, potentially masking its relationship with MetS. Other factors, such as inflammation, oxidative stress, or genetic predispositions, may independently drive MetS, diminishing the apparent role of insulin resistance. Since MetS is a cluster of risk factors—including obesity, dyslipidemia, hypertension, and hyperglycemia—individuals may meet its diagnostic criteria through combinations less dependent on insulin resistance, such as hypertension influenced by non-metabolic factors. In this population, waist circumference may reflect a predominance of subcutaneous fat rather than visceral fat, which is more metabolically active. As insulin resistance is more strongly linked to visceral fat, variations in fat distribution could obscure this relationship. Additionally, variability in metabolic factors, fat distribution, and population-specific characteristics, such as the unique ethnic traits of the Kazakh population, may further explain the lack of association observed in our study.

MetS is a significant public health concern in Kazakhstan, contributing to the high burden associated with the high incidence and mortality of CVD diseases in the country [27]. Several studies have explored the prevalence, pathogenesis, and clinical features of MetS within the Kazakh population. A 2018 study reported a prevalence of MetS among civil servants aged 35-70 of 40.3%, compared to 32.8% in the general population of the same age group. Both men and women across different age categories showed a higher incidence of individual symptoms and the syndrome compared to population averages. Specifically, rates of arterial hypertension, hypercholesterolemia, and carbohydrate metabolism disorders were significantly higher [28]. A study conducted among the Kazakh population in the Xinjiang region of China examined the relationship between MetS and the development of CVD [29]. The cohort study lasted for about 5.49 years and included 2644 participants. The results showed that elevated blood pressure, increased waist circumference, and high triglyceride levels were independent risk factors for CVD. Participants with multiple components of MetS had an increased risk of developing CVD, indicating the cumulative effect of these risk factors. Another study assessing the prevalence of MetS in southern Kazakhstan found that abdominal obesity was the most prevalent component of MetS in women (74.3%), followed by hyperglycemia (26.5%) and diastolic hypertension (25.5%), while the most common components for men were abdominal obesity (70.7%), systolic hypertension (44.4%), and diastolic hypertension (40.0%) [3].

This study has several limitations that warrant consideration. First, the relatively small sample size reduced the statistical power of the analysis. Additionally, imbalances in gender and age distribution posed challenges for conducting robust subgroup analyses and may have introduced bias into the results. Variations in definition of MetS may be associated with differences with results identified in other studies [30]. This study is not addressing the interrelationships between the different MetS components and how these interactions may increase the risk of their progression [31]. This study has not analyzed either the possible effects of socioeconomic variables on MetS dynamics [32] or lifestyles factors, physical activity, diet, smoking, or alcohol consumption [33]. Inflammatory markers were not included in these analyses [34]. Turkestan population characteristics, mostly composed by ethnic Kazakhs and Uzbeks, and their genetic characteristics may also potentially limit the generalizability of the findings [35].

This study has also relevant strengths. This is a prospective with a more than 10-year follow-up study conducted in the general population in Kazakhstan. There is limited data about MetS profiles and development in the Central Asian population, so this study provides important insights into its dynamic progression and the specific risk associated with their components.

5. Conclusions

This longitudinal study conducted in the Kazakh adult population has provided valid estimates of the incidence of MetS and its components suggesting targets that public health and clinical interventions would have to focus to curb the MetS pandemic in Kazakhstan. Logistic regression models and ROC analysis determined that the strongest predictors of MetS development are high blood pressure and increased waist circumference. Models including these parameters showed high prediction accuracy. Despite the association of age with an increased risk of MetS, this dependence was insignificant in multivariate analysis. No effect was found related to insulin resistance. This study highlights the variable nature of MS and emphasizes the importance of timely diagnosis and preventive measures to reduce its prevalence both in Kazakhstan and in other regions.

Supplementary Materials: Table S1. Supplementary Table 1. Frequency of the combination of metabolic syndrome components at baseline (in %). Table S2. Incidence of Metabolic Syndrome at follow up based on Glucose Metabolic indexes at baseline

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Data Availability Statement: Data can be obtained from the corresponding author upon request.

Conflicts of Interest: The authors declare no conflicts of interest.

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