diabetology

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Metabolic Syndrome and Risk of New-Onset Type 2 Diabetes Mellitus: An Eight-Year Follow-Up Study in Southern Israel

Tsafnat Test [1,2,*], Yan Press [1,3,4,5], Tamar Freud [1], Ruth Kannai [1,6] and Robert Satran [1,2]

1 Department of Family Medicine and Siaal Research Center for Family Practice and Primary Care, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva P.O. Box 653, Israel; yanp@bgu.ac.il (Y.P.); freudt@bgu.ac.il (T.F.); rkannai@gmail.com (R.K.); rsatran@gmail.com (R.S.)
2 Clalit Health Services, Beer-Sheva P.O. Box 616, Israel
3 Unit for Community Geriatrics, Division of Health in the Community, Ben-Gurion University of the Negev, Beer-Sheva P.O. Box 653, Israel
4 Department of Geriatrics, Soroka Medical Center, Beer-Sheva P.O. Box 151, Israel
5 Center for Multidisciplinary Research in Aging, Ben-Gurion University of the Negev, Beer-Sheva P.O. Box 653, Israel
6 Clalit Health Services, Jerusalem P.O. Box 27670, Israel
* Correspondence: tsafatest@gmail.com; Tel.: +972-8-6477432

Abstract

Background: Metabolic syndrome (MetS) comprises a cluster of metabolic abnormalities that increase the risk of type 2 diabetes mellitus (T2DM) and cardiometabolic morbidity. Although widely recognized, evidence on its documentation and follow-up in primary care is limited. This study aimed to evaluate the extent of MetS documentation in electronic medical records (EMRs), examine follow-up patterns and metabolic changes over time, and assess the incidence and predictors of new-onset T2DM according to baseline MetS severity. **Methods**: A retrospective cohort study was conducted on 8170 adults aged 30–50 years, insured by Clalit Health Services in Southern Israel, who met ATP III criteria for MetS in 2008 and were followed through 2015. MetS severity was classified as mild (three components), moderate (four), or severe (five). Changes in metabolic indices were assessed longitudinally, and predictors of T2DM were analyzed using Kaplan–Meier survival and multivariable Cox regression models. **Results**: Although all participants met the diagnostic criteria, only 1.6% had a recorded MetS diagnosis. Over the eight years of follow-up, 26% developed T2DM, with incidence increasing from 21% among those with mild MetS to 49% among those with severe MetS ($p < 0.0001$). Fasting plasma glucose rose significantly (median +13 mg/dL, $p < 0.001$), BMI remained stable, and modest improvements were observed in blood pressure and lipid levels. Elevated fasting glucose (HR 2.13, $p < 0.001$), higher BMI (HR 1.33, $p = 0.010$), and lower HDL (HR 1.26, $p = 0.045$) independently predicted diabetes onset. **Conclusions**: MetS remains markedly under-documented and insufficiently integrated into primary care follow-up. Despite regular clinical follow-up, improvements in metabolic indices were limited. These findings highlight the need for structured strategies to enhance MetS recognition and long-term management within routine practice.

Keywords: metabolic syndrome; Type 2 diabetes mellitus; obesity; fasting plasma glucose; hypertension

Received: 11 August 2025
Revised: 9 November 2025
Accepted: 24 November 2025
Published: 1 December 2025

Citation: Test, T.; Press, Y.; Freud, T.; Kannai, R.; Satran, R. Metabolic Syndrome and Risk of New-Onset Type 2 Diabetes Mellitus: An Eight-Year Follow-Up Study in Southern Israel. *Diabetology* **2025**, *6*, 150. https://doi.org/10.3390/diabetology6120150

1. Introduction

Metabolic syndrome (MetS) is a major public health challenge characterized by central obesity, hypertension, dyslipidemia, and hyperglycemia, many of which are linked to insulin resistance, which can lead to type 2 diabetes mellitus (T2DM) [1]. The global prevalence of MetS ranges from 22% to 34%—depending on diagnostic criteria—and continues to rise worldwide, underscoring the need for early identification and prevention [2–4]. MetS is increasingly observed among young and middle-aged adults, in whom timely intervention may alter disease trajectories [5].

MetS has been firmly established as a strong predictor of both T2DM and cardiovascular morbidity [1–12]. However, debate persists regarding whether MetS itself provides greater predictive value than its individual components, particularly impaired fasting glucose (IFG) [6,13,14]. For example, the Framingham Offspring Study found that participants with MetS, including IFG had a relative risk (RR) of 11.0 for T2DM, compared with 5.0 among those without IFG [6]. These findings highlight the heterogeneous contribution of individual components to overall metabolic risk.

Recent studies have emphasized the use of continuous MetS severity scores (cMetS-S) to quantify risk more precisely. Longitudinal cohorts demonstrate that higher cMetS-S trajectories and persistent MetS status strongly predict future T2DM [8–10]. Nevertheless, in EMR-based population studies, the component-count method (3–5 criteria) remains the most practical approach. Despite frequent monitoring, MetS is rarely documented in primary care, and prior cohorts revealed worsening fasting glucose and sharp increases in T2DM incidence with higher component counts [12]. Because individual traits vary in prognostic weight, refined scoring and follow-up strategies are needed.

Lifestyle modification remains the cornerstone of MetS management; this includes weight reduction, increased physical activity, and smoking cessation [13–17]. However, its long-term effectiveness in real-world primary care remains uncertain and warrants further study.

The southern region of Israel (the Negev) provides a relevant setting for studying MetS and its associated risk of diabetes. This region shows higher rates of obesity and diabetes than national averages, particularly among the Bedouin population [18,19]. Clalit Health Services' EMR data, covering most regional residents, enable robust population-based analyses to identify modifiable risk patterns and guide targeted prevention [18–20]. Understanding how MetS is documented and managed in a community with marked health disparities is essential for designing effective, equitable prevention strategies.

Focusing on adults aged 30–50 years offers a critical window for early risk modification before progression to overt disease. This life stage often marks the transition from subclinical metabolic abnormalities to overt diabetes, making it particularly suitable for preventive interventions within primary care. Despite extensive international literature, data from Israeli primary care remain limited. Gaps persist regarding MetS documentation, follow-up intensity, and the relative impact of individual components on diabetes onset.

Accordingly, this study aimed to assess MetS documentation in routine care, examine longitudinal changes in metabolic indices, and determine the incidence of T2DM by baseline MetS severity while exploring the relative contribution of each component to future diabetes risk.

2. Methods

2.1. Study Design and Population

This retrospective cohort study included patients aged 30–50 years in 2008 who met criteria for metabolic syndrome (MetS) within Clalit Health Services (CHS) in Southern Israel. This age range was selected to target younger adults, in whom early manifestations

of MetS are more amenable to the prevention of T2DM, and to minimize confounding from comorbidities and age-related metabolic changes.

2.2. Definition of Metabolic Syndrome

MetS is defined using multiple criteria. For this study, we adopted the Adult Treatment Panel (ATP) III definition, which requires the presence of at least three out of the following five criteria:

1. Central abdominal obesity, defined as a waist circumference > 102 cm in males or >88 cm in females.
2. Blood pressure $\geq$130/$\geq$85 mmHg or ongoing antihypertensive treatment.
3. Fasting plasma glucose (FPG) $\geq$ 100 mg/dL or treatment for diabetes mellitus.
4. Triglyceride levels $\geq$ 150 mg/dL.
5. Low high-density lipoprotein cholesterol (HDL-c), defined as <40 mg/dL in males or <50 mg/dL in females.

An alternative definition by the World Health Organization (WHO, 1999) includes body mass index (BMI) > 30 kg/m^2 instead of abdominal obesity. Given that waist circumference (WC) is not routinely measured in Israel, we employed the ATP III definition with BMI $\geq$ 30 kg/m^2 in lieu of WC, consistent with the alternative WHO definition [21]. BMI is routinely available in the EMR and is widely used as a pragmatic surrogate when WC data are not available.

2.3. Inclusion and Exclusion Criteria

Eligible participants were individuals aged 30–50 years in 2008 who met at least three of the five MetS criteria and did not have T2DM at baseline. Absence of T2DM was determined based on their electronic medical records (EMRs), defined as no recorded diagnosis and no documented FPG measurement > 125 mg/dL.

The dataset provided for analysis included only individuals who remained alive and continuously enrolled in Clalit Health Services throughout the study period. The process of participant selection, including inclusion and exclusion criteria, is illustrated in Figure 1.

2.4. Data Collection

Longitudinal data were extracted from CHS EMRs for the years 2008 to 2015. Variables included demographic characteristics, plasma lipid levels (triglycerides, HDL-c, and low-density lipoprotein cholesterol [LDL-c]), BMI, glycated hemoglobin (HbA1c), smoking status, frequency of primary care physician (PCP) visits ($\geq$3 min), referrals to a dietitian, and consultations with diabetes and cardiology specialists.

Laboratory test results were standardized and automatically uploaded into the EMR, with LDL-c levels measured directly. BMI was automatically calculated based on weight and height measurements obtained in clinical settings by physicians or nurses. The study outcomes included changes in MetS indices and HbA1c over time and incidence of new-onset T2DM.

2.5. Ethical Considerations

This study was approved by the CHS Institutional Ethics Committee (approval number 0227-15-COM1) and was exempt from requiring informed consent. Patients or the public were not involved in the design, conduct, reporting, or dissemination of this research.

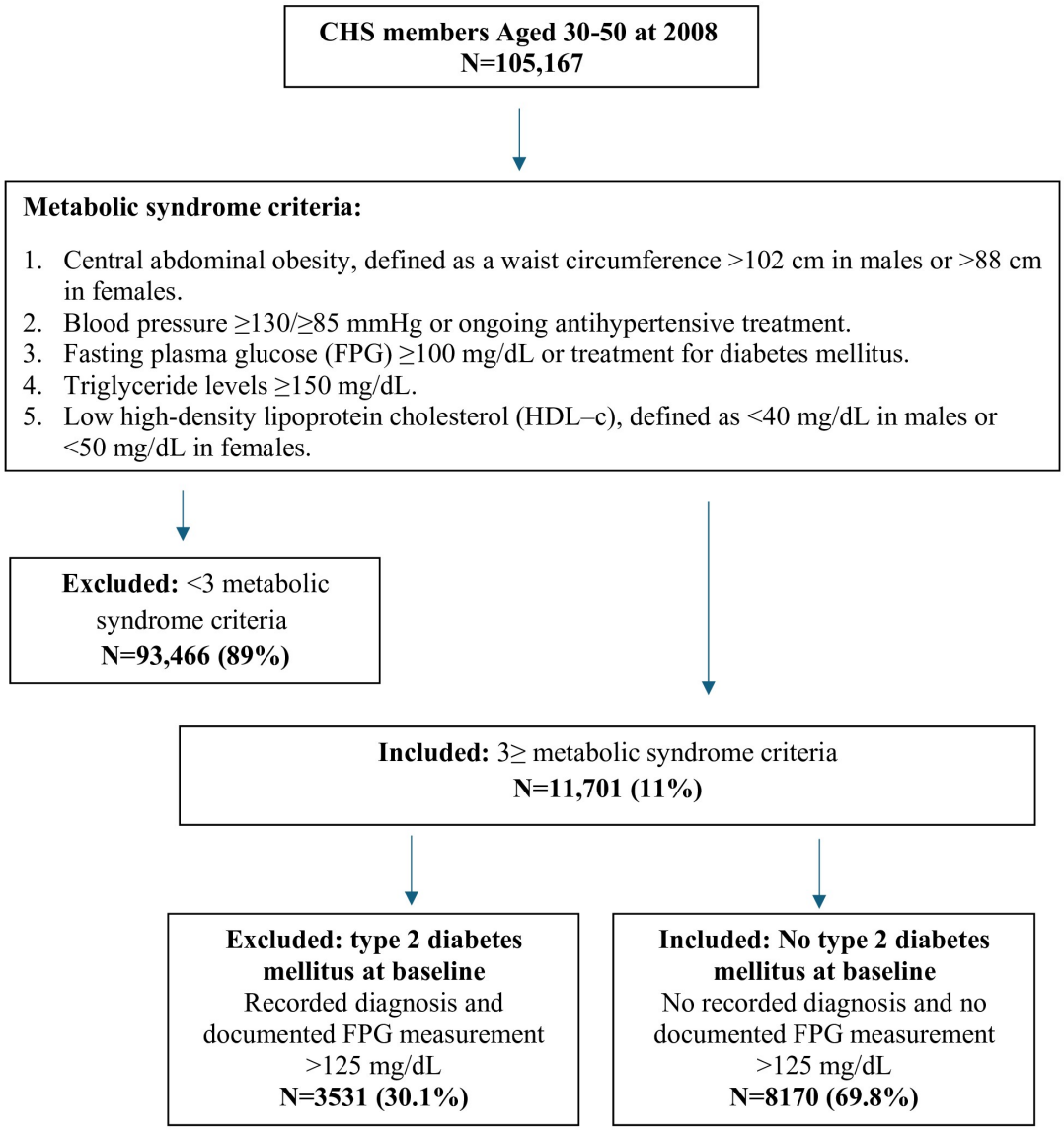

Figure 1. Study flow chart.

2.6. Data Analysis

Participants were categorized into three groups based on the number of MetS criteria met: mild (3/5 criteria), moderate (4/5 criteria), and severe (5/5 criteria) MetS. This classification has been previously applied in prior epidemiological studies as a simple and reproducible framework to examine the dose–response relationship between the number of MetS components and cardiometabolic outcomes [8–10].

2.7. Outcome Measures

1. Changes in Metabolic Indices: A comparative analysis was conducted to evaluate changes in metabolic parameters between 2008 and 2015. The first recorded measurement in 2008 was compared to the last recorded value in 2015. It is important to note that the initial 2008 measurement was not necessarily the highest recorded value that year or the one that met inclusion criteria.

2. New-Onset T2DM: Additional analyses were performed to examine the incidence of newly diagnosed T2DM over the study period. Incident T2DM was defined as a physician-recorded diagnosis of type 2 diabetes in the electronic medical records (EMRs) among individuals without diabetes at baseline. This definition was selected to ensure

high diagnostic specificity and to minimize potential misclassification related to transient laboratory findings.

2.8. Statistical Methods

Continuous variables were reported as mean ± standard deviation (SD) for normally distributed data and as median with interquartile range (IQR) for non-normally distributed data. Normality was assessed using the Shapiro–Wilk test. Categorical variables were presented as counts and percentages.

Comparisons of normally distributed continuous variables were conducted using paired t-tests, while non-normally distributed variables were analyzed using the Wilcoxon Signed-Rank Test. Categorical variables were compared using the chi-square test.

Missing values were assessed using descriptive statistics. The proportion of missing data was minimal (<2% across all variables). Analyses were conducted using listwise deletion, such that participants with missing values for a given variable were excluded from analyses involving that variable.

Time-to-diagnosis of type 2 diabetes mellitus (T2DM) was analyzed using Cox proportional hazards regression models, with results expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). Covariates included individual components of the metabolic syndrome—blood pressure, fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-c), triglycerides, and body mass index (BMI)—as well as gender and age. The proportional hazards assumption was verified using Schoenfeld residuals and by visual inspection of log-minus-log survival plots. No significant violations of the proportionality assumption were detected. Kaplan–Meier survival curves were generated to illustrate cumulative incidence, and log-rank tests were used to compare survival distributions between groups. A p-value < 0.05 was considered statistically significant for all analyses.

3. Results

In 2008, the electronic medical records (EMRs) of 105,167 patients enrolled in Clalit Health Services (CHS) in the Southern District of Israel, aged 30–50 years, were reviewed. Among them, 11,701 patients (11%) met at least three criteria for metabolic syndrome (MetS), and 8170 of these patients did not have T2DM at baseline, forming the study cohort. The prevalence of MetS was found to be 34.7% among individuals aged 30–39 years and 65.3% among those aged 40–50 years. The mean age at study entry was 41.9 ± 6.2 years, with 53.5% of the cohort being female (Table 1).

Table 1. Metabolic syndrome criteria of the study population in 2008.

	Total Population (N = 8170)		
	N	**%**	**Mean ± std (Median)**
Age (yrs)			41.9 ± 6.2
Gender (Female)	4370	53.5%	
Metabolic Syndrome Criteria			
BMI ≥ 30	4441	54.4%	35.1 ± 4.5
Fasting Plasma Glucose ≥ 100	3746	45.9%	121.0 ± 29.9
150 ≤ Triglicerides ≤ 500 *	6325	77.4%	234.8 ± 74.3
HDL Cholesterol: male < 40, female < 50	5880	72.0%	37.3 ± 6.2
Blood Pressure			
Systolic ≥ 130	6442	78.8%	150.2 ± 16.5
Diastolic ≥ 85	5126	62.7%	96.1 ± 9.1

Table 1. *Cont.*

	Total Population (N = 8170)		
	N	**%**	**Mean ± std (Median)**
Risk Stratification			
Low Risk (3/5 criteria)	5724	70.1%	
Mod Risk (4/5 criteria)	2047	25.1%	
High Risk (5/5 criteria)	399	4.9%	

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein cholesterol. * Triglyceride levels > 500 mg/dL were retained in the dataset but were not classified as meeting the '150 ≤ Triglycerides ≤ 500' criterion for metabolic syndrome, given their potential to represent rare inherited conditions and disproportionally affect group definitions.

Men had significantly higher levels of triglycerides (224.98 ± 110.63 vs. 181.59 ± 87.58 mg/dL), fasting plasma glucose (92.68 ± 15.19 vs. 91.82 ± 14.47 mg/dL), systolic blood pressure (129.42 ± 15.77 vs. 125.92 ± 16.58 mmHg), and diastolic blood pressure (80.96 ± 21.18 vs. 78.36 ± 13.95 mmHg), while women had higher BMI (33.24 ± 6.07 vs. 30.92 ± 5.21 kg/m^2) and HDL cholesterol (45.03 ± 10.04 vs. 41.49 ± 9.78 mg/dL) (Table 2). Among the patients who met the diagnostic criteria for MetS, only 128 (1.6%) had a MetS diagnosis in their medical records.

Table 2. Change in metabolic syndrome criteria from 2008 to 2015 in the total study cohort.

Criteria	N	No. of Tests Median (IQR) (2008–2015)	Beginning of Study Median (IQR)	End of Study Median (IQR)	Change Median (IQR)	* *p* Value
BMI	8045	7.0 (4.0, 11.0)	31.6 (28.4, 35.3)	31.6 (28.2, 35.4)	0.15 (−1.21, 1.88)	<0.001
Triglycerides	8163	9.0 (6.0, 12.0)	184.0 (144.0, 240.0)	165.0 (122.0, 223.0)	−13.0 (−64.0, 31)	<0.001
Fasting Plasma Glucose	8146	10.0 (6.0, 15.0)	92.0 (81.0, 103.0)	101.0 (92.0, 116.0)	13.0 (0, 26.0)	<0.001
HDL-c	8164	8.0 (5.0, 12.0)	40.0 (35.0, 46.0)	41.0 (36.0, 48.0)	1.0 (−3.0, 6.0)	<0.001
Systolic blood pressure	8131	11.0 (6.0, 18.0)	126.0 (119.0, 136.0)	126.0 (120.0, 134.0)	0.0 (−11.0, 10)	<0.001
Diastolic blood pressure	8132	11.0 (6.0, 18.0)	80.0 (72.0, 85.0)	78.0 (70.0, 83.0)	−1.0 (−10.0, 5.0)	<0.001

Abbreviations: BMI, body mass index; HDL-c, high-density lipoprotein cholesterol. * *p*-values < 0.05 were considered statistically significant.

3.1. Changes in MetS Indices over Eight Years

Changes in MetS indices over the eight-year follow-up period (2008–2015) are presented in Table 2 (with changes by gender and MetS severity shown in Table A1). Fasting plasma glucose increased significantly (median +13 mg/dL, IQR: 0–26; $p < 0.001$), progressing from normal to prediabetic ranges in the mild and moderate MetS groups, and from prediabetic to diabetic levels in the severe group. Each patient underwent a median of 10 tests (IQR: 6–15) during follow-up. BMI increased modestly in the low-risk group (+0.33 kg/m^2 IQR: −9.59–1.95, $p < 0.001$), remained stable in the moderate-risk group, and decreased significantly in the high-risk group (−0.38 kg/m^2, IQR: −3.08–1.28, $p < 0.001$). Significant improvements were also observed in blood pressure, triglyceride

levels, and HDL cholesterol, while HbA1c levels remained stable with no statistically significant changes. Sex-stratified analyses further showed that women experienced a modest increase in BMI, whereas men demonstrated greater declines in triglyceride and LDL cholesterol levels. In addition, men had higher baseline fasting glucose and blood pressure, while women consistently exhibited higher HDL-c levels throughout the follow-up. These observations underscore distinct metabolic patterns between sexes during the study period. Additional metabolic parameters, including sex-stratified data, are presented in Table A1.

3.2. Healthcare Utilization

During the eight-year follow-up, patients had a median of 96 general practitioner (GP) visits (IQR 59–144). Women visited more frequently than men (median 111, IQR 73–162 compared with 80, IQR 47–123; $p < 0.001$). The frequency of visits also increased with MetS severity: 92 (IQR 57–139) in the low-risk group, 104 (IQR 63–156) in the moderate-risk group, and 104 (IQR 63–156) in the high-risk group ($p < 0.001$) (Table A2). Only 14.3% of patients were referred for dietitian consultations, with referrals more common among women than men (16.5% vs. 11.9%, $p < 0.0001$) and among patients with severe MetS compared to those with moderate or mild MetS (19% vs. 17.2% and 13%, $p < 0.0001$). A total of 4.2% of patients consulted a diabetes specialist, with no significant gender difference. However, the proportion of patients consulting a diabetes specialist increased with MetS severity (3.4%, 5.6%, and 8.8% for mild, moderate, and severe MetS, respectively, $p < 0.001$). These measures were included to describe healthcare utilization patterns and were not analyzed as direct predictors of diabetes outcomes.

3.3. Incidence of New-Onset T2DM

A total of 2093 patients (26%) developed new-onset T2DM during the study period (Table 3). Among patients with severe MetS at baseline, 49% developed T2DM by the end of the study, compared to 21% and 34% among patients with mild and moderate MetS, respectively. The time-to-T2DM diagnosis is presented in Figure 2. Kaplan–Meier survival analysis revealed significant differences in the cumulative incidence of T2DM across risk strata (log-rank $\chi^2 = 16.64$, df = 2, $p < 0.001$). Mean diabetes-free survival time was longest in the low-risk group (7.74 years, 95% CI 7.59–7.89) and shortest in the high-risk group (6.77 years, 95% CI 6.24–7.29), with the moderate-risk group showing intermediate survival (7.52 years, 95% CI 7.30–7.74).

Table 3. Incidence of Type 2 Diabetes Mellitus among the study population.

	Total Population			
	Total	**Patients with New T2DM Diagnosis**		
Group		**N**	**%**	***p* Value**
All Study Population	8170	2093	26%	-
By Gender				
Female	4370	1135	26%	0.431
Male	3800	958	25%	
By Risk Group				
Low Risk (3/5 criteria)	5724	1197	21%	<0.0001
Moderate Risk (4/5 criteria)	2047	700	34%	
High Risk (5/5 criteria)	399	196	49%	

Abbreviations: T2DM, type 2 diabetes mellitus, *p*-values < 0.05 were considered statistically significant. *p* value for comparison of T2DM incidence between men and women, and across MetS risk groups.

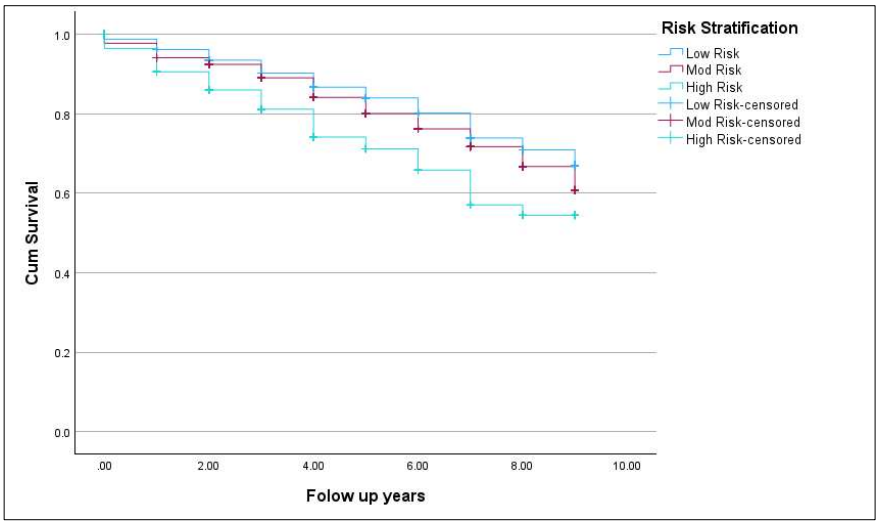

Figure 2. Kaplan–Meier curves for cumulative incidence of type 2 diabetes mellitus (T2DM) by metabolic syndrome (MetS) severity; Abbreviations: MetS, metabolic syndrome; T2DM, type 2 diabetes mellitus.

3.4. Risk Factors for New-Onset T2DM

In the multivariate Cox regression analysis (Figure 3), higher BMI (HR = 1.33, 95% CI 1.07–1.66, p = 0.010), lower HDL (HR = 1.26, 95% CI 1.01–1.59, p = 0.045), and elevated fasting plasma glucose (HR = 2.13, 95% CI 1.69–2.69, $p < 0.001$) were independently associated with an increased risk of developing T2DM. Triglycerides, blood pressure, age, and gender were not significantly associated with incident T2DM.

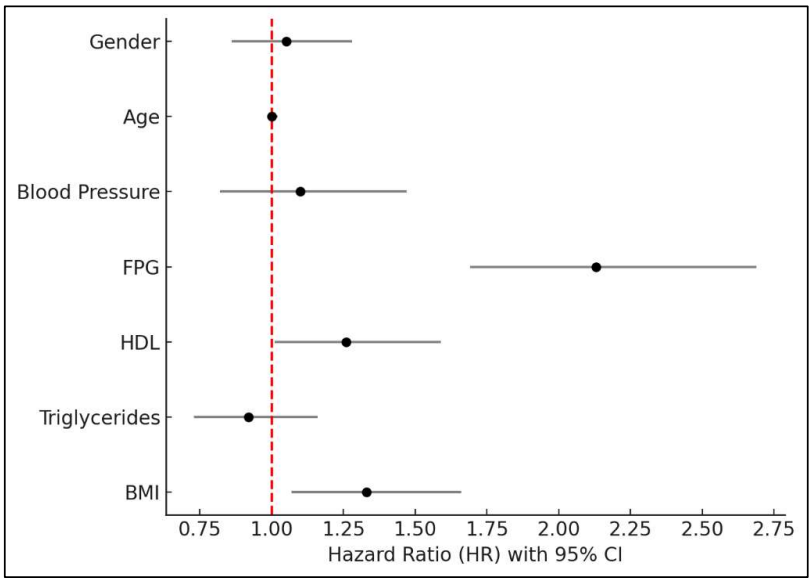

Figure 3. Forest plot of hazard ratios (HRs) for new-onset T2DM according to MetS components gender and age. Abbreviations: HR, Hazard ratio; CI, confidence interval 95%; BMI, body mass index; FPG, Fasting Plasma Glucose; HDL, high-density lipoprotein cholesterol; p-values < 0.05 were considered statistically significant.

4. Discussion

Our findings confirm that MetS is highly prevalent among young and middle-aged adults in Southern Israel, yet its documentation in EMRs was exceedingly rare (1.6%). This gap likely reflects under-coding and limited clinical attention to MetS as a unified diagnosis, suggesting potential gaps in preventive identification and management. Strengthening

physician awareness, incorporating automated EMR prompts, and integrating MetS indicators into routine dashboards may improve recognition and follow-up at the primary care level. Over the eight-year follow-up period, fasting plasma glucose levels increased significantly in individuals with MetS, whereas other metabolic indices exhibited modest improvements, such as a decline in LDL cholesterol likely reflecting statin use. The large cohort size and repeated measurements likely explain why small effect sizes nonetheless yielded highly significant *p*-values, underscoring the need to interpret clinical rather than purely statistical significance. These changes may represent treatment effects, regression to the mean, or measurement variability, and their overall clinical significance appears limited.

A key finding of this study is the substantial progression from MetS to T2DM, with over a quarter (26%) of the cohort developing diabetes, and the highest incidence observed among those classified as severe MetS at baseline. These results highlight the persistence of high diabetes incidence despite ongoing medical care, emphasizing the need to strengthen preventive approaches. Kaplan–Meier analysis demonstrated distinct trajectories of diabetes onset by MetS severity, reinforcing the role of MetS as a progressive condition with significant long-term implications.

Moreover, our study provides insights into the differential contributions of MetS components to diabetes risk. FPG and BMI emerged as the most influential predictors of new-onset T2DM, suggesting that a weighted scoring system may improve risk stratification [22].

HbA1c levels remained stable over the follow-up period, with no statistically significant change. This apparent stability, despite rising fasting plasma glucose levels, may reflect selective testing, sample size limitations, or differences in the temporal sensitivity and measurement frequency of the two glycemic markers. Future research should therefore explore modified MetS scoring models incorporating differential weighting of risk factors. Despite frequent primary care encounters, referrals to dietitians were rare, indicating possible underutilization of early lifestyle interventions. This finding likely reflects both patient- and system-level barriers, including limited access to allied health services and competing clinical demands. Embedding structured nutritional counseling within chronic care programs and incentivizing preventive referrals may help promote earlier intervention in routine practice. Pharmacological interventions, such as GLP-1 receptor agonists, may have a role in selected high-risk patients [23–25], but these should remain adjuncts to lifestyle modification rather than the main strategy for MetS management.

A public health approach is therefore essential to address the growing burden of MetS, with greater attention to upstream determinants such as socioeconomic disparities, food environments, and opportunities for physical activity. MetS disproportionately affects disadvantaged populations, particularly in Southern Israel, where high rates of obesity and diabetes have been documented. Sex-specific patterns further emphasize the need for tailored approaches: men exhibited higher fasting glucose, triglycerides, and blood pressure, whereas women had higher BMI and HDL cholesterol. During follow-up, women showed a modest increase in BMI, while men experienced greater declines in triglycerides and LDL cholesterol. These sex-specific patterns likely reflect differences in adiposity distribution, hormonal milieu, and regional cultural or behavioral factors, such as dietary habits and healthcare-seeking patterns. Addressing these differences through sex-responsive prevention and culturally adapted lifestyle programs could enhance the effectiveness of interventions in Southern Israel. While this study focused on the Southern Israeli population, its findings are consistent with international evidence showing rising MetS prevalence and suboptimal documentation in primary care settings. Broader comparisons across national cohorts may further clarify the generalizability of these trends. Primary prevention and

health promotion strategies including education, early identification of at-risk individuals, dietary interventions, and community-based programs remain key priorities for reducing the prevalence and the long-term impact of MetS.

4.1. Strengths and Limitations

The primary strengths of this study include its large cohort (n = 8170), the use of comprehensive, longitudinal EMR data over an extended eight-year follow-up period, and the availability of detailed metabolic measurements. This robust dataset allowed for an in-depth analysis of MetS progression, healthcare utilization, and the impact of individual MetS components on diabetes risk.

The study was conducted using the database of the largest health maintenance organization (HMO) in Israel, specifically in the southern region—a population with higher rates of diabetes and obesity compared to the national average. Preventing the progression of diabetes in this population could potentially reduce cardiovascular morbidity and mortality.

However, several limitations should be acknowledged. First, restricting the cohort to adults aged 30–50 years improves internal validity but limits generalizability to older populations. Second, conducting the study in Southern Israel, with its unique demographic and cultural characteristics, may reduce applicability to other populations and healthcare systems. Third, reliance on computerized EMR data introduces potential misclassification due to incomplete or inconsistent data entry, and BMI $\geq$ 30 was used as a surrogate for waist circumference. While this approach was necessary given the lack of WC data, it may not accurately capture central adiposity and could lead to the misclassification of metabolic risk. Fourth, behavioral and sociodemographic factors—such as diet, physical activity, smoking intensity, socioeconomic status, and ethnicity—were unavailable, leaving possible residual confounding. Fifth, treatment-related data were incomplete: patients receiving antihypertensive or antihyperglycemic medications were classified as meeting the respective criteria, but information on other pharmacological treatments was lacking, limiting the ability to adjust for treatment effects. Sixth, referral data for dietary consultations were available only from 2010 onward, limiting assessment of earlier interventions. Seventh, individuals without continuous follow-up or who died before baseline were excluded rather than right-censored, which may have introduced selection bias and influenced incidence estimates. Eighth, changes in metabolic indices were assessed only between the first and last recorded measurements. The absence of intermediate values may not fully reflect longitudinal dynamics. Finally, the unusually high number of GP visits likely reflects the partial inclusion of administrative encounters. Restricting the analysis to visits lasting at least three minutes helped to mitigate this issue; however, some longer non-clinical encounters may still have been included. A discrepancy was also noted between initial blood pressure measurements and subsequent averages, likely reflecting a single abnormal value at baseline; however, other metabolic indices did not demonstrate similar inconsistencies, lending credibility to the overall findings.

4.2. Conclusions

This large retrospective cohort study shows that MetS represents an early stage of disease progression, with metabolic abnormalities often preceding overt T2DM by several years. Over eight years of follow-up, fasting plasma glucose levels worsened despite modest improvements in other metabolic indices, suggesting limited effectiveness of current primary care approaches in mitigating glycemic deterioration. Sex-specific patterns—higher fasting glucose and blood pressure in men, and higher BMI and HDL cholesterol in women—indicate that prevention strategies should be tailored by sex and context. Despite frequent

healthcare encounters, MetS was rarely documented, and referrals for lifestyle counseling were infrequent, pointing to possible missed opportunities for earlier preventive action. Strengthening physician awareness, integrating EMR-based prompts, and embedding team-based nutritional and lifestyle programs may help address these gaps. Overall, these findings underscore the importance of systematic identification, documentation, and proactive management of MetS in everyday clinical practice.

Author Contributions: Conceptualization, T.T. and R.S.; Data curation, T.T. and T.F.; Formal analysis, T.T., Y.P., T.F. and R.S.; Investigation, T.T., R.K. and R.S.; Methodology, T.T., Y.P., T.F. and R.S.; Resources, T.T.; Software, T.F.; Supervision, T.F.; Validation, T.T. and T.F.; Visualization, T.F.; Writing—original draft, T.T. and T.F.; Writing—review and editing, T.T., Y.P., T.F., R.K. and R.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and was approved by the Clalit Health Services Institutional Ethics Committee (Approval #0227-15-COM1 on 8 September 2016). It was exempt from requiring informed consent.

Informed Consent Statement: Patient consent was waived due to the study being a retrospective study using computerized records.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

Acknowledgments: Simon Vulfsons, Director of the Institute for Pain, Rambam Medical Center, Haifa, Israel. Gil Marcus, Department of Cardiology, Assaf Harofeh Medical Center, Zerifin, Israel.

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

Abbreviations

MetS	Metabolic Syndrome
FPG	Fasting plasma glucose
T2DM	Type 2 Diabetes Mellitus
CHS	Clalit Health Services
IFG	Impaired fasting glucose
RR	Relative risk
cMetS-S	Continuous MetS severity scores
ATP	Adult Treatment Panel
HDL-c	High-density lipoprotein cholesterol
WHO	World Health Organization
BMI	Body mass index
EMR	Electronic medical records
LDL-c	Low-density lipoprotein cholesterol
HbA1c	Glycated hemoglobin
PCP	Primary care physician
SD	Standard deviation
IQR	Interquartile range
ANOVA	Analysis of variance
GP	General practitioner
GLP-1	Glucagon-like Peptide-1
HMO	Health maintenance organization

Appendix A

Table A1. Changes in metabolic indices, from 2008 to 2015, stratified by gender and metabolic syndrome (MetS) severity.

Criteria	Group	N **	No. of Tests Median (Q1–Q3) (2008–2015)	Beginning of Study Median (Q1–Q3)	End of Study Median (Q1–Q3)	Change Median (Q1–Q3)	*p* Value
BMI	**All Study Population**	8045	7.0 (4.0, 11.0)	31.6 (28.4, 35.3)	31.6 (28.2, 35.4)	0.15 (−1.21, 1.88)	<0.001
	By Gender						
	Female	4321	8.0 (5.0, 12.0)	32.8 (29.6, 36.5)	32.9 (29.1, 36.7)	0.35 (−1.39, 2.11)	<0.001
	Male	3724	6.0 (3.0, 10.0)	30.5 (27.5, 33.7)	30.5 (27.4, 33.8)	0.0 (−1.05, 1.63)	<0.001
	By Risk						
	Low Risk (3/5 criteria)	5617	6.0 (4.0, 10.0)	30.8 (27.5, 34.2)	30.9 (27.5, 34.6)	0.33 (−9.59, 1.95)	<0.001
	Moderate Risk (4/5 criteria)	2032	8.0 (5.0, 12.0)	33.2 (30.5, 36.9)	33.0 (29.7, 36.8)	0.0 (−1.68, 1.73)	0.771
	High Risk (5/5 criteria)	396	10.0 (7.0, 16.0)	35.1 (32.3, 38.3)	34.3 (30.7, 37.4)	−0.38 (−3.08, 1.28)	<0.001
Triglycerides	**All Study Population**	8163	9.0 (6.0, 12.0)	184.0 (144.0, 240.0)	165.0 (122.0, 223.0)	−13.0 (−64.0, 31)	<0.001
	By Gender						
	Female	4366	9.0 (6.0, 12.0)	169.0 (81.0, 217.0)	155.0 (114.0, 206.0)	−7.0 (−54.0, 33.25)	<0.001
	Male	3797	8.0 (5.0, 12.0)	203.0 (161.0, 264.0)	179.0 (132.0, 243.0)	−22.0 (−74.0, 26.0)	<0.001

Table A1. *Cont.*

Criteria	Group	N **	No. of Tests Median (Q1–Q3) (2008–2015)	Beginning of Study Median (Q1–Q3)	End of Study Median (Q1–Q3)	Change Median (Q1–Q3)	*p* Value
	By Risk						
	Low Risk (3/5 criteria)	5717	8.0 (5.0, 12.0)	176.0 (131.0, 231.0)	160.0 (117.0, 215.0)	−10.0 (−61.0, 32.0)	<0.001
	Moderate Risk (4/5 criteria)	2047	9.0 (7.0, 16.0)	197.0 (161.0, 254.0)	177.0 (135.0, 238.0)	−17.0 (−70.0, 30.0)	<0.001
	High Risk (5/5 criteria)	399	10.0 (7.0, 14.0)	201.0 (171.0, 259.0)	177.0 (137.0, 233.0)	−30.0 (−74.0, 12.0)	<0.001
Fasting Plasma Glucose	**All Study Population**	8146	10.0 (6.0, 15.0)	92.0 (81.0, 103.0)	101.0 (92.0, 116.0)	13.0 (0, 26.0)	<0.001
	By Gender						
	Female	4361	11.0 (7.0, 16.0)	91.0 (81.0, 102.5)	101.0 (92.0, 115.0)	13.0 (0.0, 27.0)	<0.001
	Male	3785	9.0 (6.0, 14.0)	93.0 (82.0, 104.0)	102.0 (93.0, 117.0)	13.0 (1.0, 25.0)	<0.001
	By Risk						
	Low Risk (3/5 criteria)	5707	10.0 (6.0, 14.0)	89.0 (80.0, 101.0)	100.0 (92.0, 112.0)	13.0 (1.0, 25.0)	<0.001
	Moderate Risk (4/5 criteria)	2040	11.0 (7.0, 16.0)	96.0 (84.0, 107.0)	104.0 (94.0, 122.0)	13.0 (0.0, 28.0)	<0.001
	High Risk (5/5 criteria)	399	13.0 (8.0, 18.0)	106.0 (101.0, 114.0)	111.0 (99.0, 138.0)	9.0 (−6.0, 30.0)	<0.001
HDL-c	**All Study Population**	8164	8.0 (5.0, 12.0)	40.0 (35.0, 46.0)	41.0 (36.0, 48.0)	1.0 (−3.0, 6.0)	<0.001
	By Gender						
	Female	4361	9.0 (6.0, 12.0)	44.0 (39.0, 49.0)	45.0 (39.0, 51.0)	1.0 (−4.0, 6.0)	<0.001
	Male	3794	8.0 (5.0, 12.0)	37.0 (33.0, 40.0)	38.0 (33.0, 43.0)	1.0 (−3.0, 5.0)	<0.001
	By Risk						
	Low Risk (3/5 criteria)	5710	8.0 (5.0, 12.0)	41.0 (36.0, 47.0)	42.0 (36.0, 49.0)	1.0 (−4.0, 5.0)	<0.001
	Moderate Risk (4/5 criteria)	2046	9.0 (6.0, 13.0)	39.0 (34.0, 44.2)	41.0 (35.2, 47.0)	1.0 (−2.0, 6.0)	<0.001
	High Risk (5/5 criteria)	399	10.0 (7.0, 14.0)	37.0 (34.0, 42.0)	39.0 (35.0, 45.0)	1.0 (−2.0, 6.0)	<0.001

Table A1. *Cont.*

Criteria	Group	N **	No. of Tests Median (Q1–Q3) (2008–2015)	Beginning of Study Median (Q1–Q3)	End of Study Median (Q1–Q3)	Change Median (Q1–Q3)	*p* Value
Systolic blood pressure	**All Study Population**	8131	11.0 (6.0, 18.0)	126.0 (119.0, 136.0)	126.0 (120.0, 134.0)	0.0 (−11.0, 10)	<0.001
	By Gender						
	Female	4358	12.0 (7.0, 20.0)	125.0 (115.0, 135.0)	125.0 (118.0, 132.0)	0.0 (−10.0, 10.0)	<0.001
	Male	3774	9.0 (5.0, 15.0)	130.0 (120.0, 139.0)	127.0 (120.0, 135.0)	0.0 (0.0, 9.0)	<0.001
	By Risk						
	Low Risk (3/5 criteria)	5690	10.0 (6.0, 16.0)	125.0 (117.0, 135.0)	125.0 (119.0, 133.0)	0.0 (−10.0, 10.0)	0.142
	Moderate Risk (4/5 criteria)	2044	13.0 (7.0, 21.0)	130.0 (120.0, 140.0)	127.0 (120.0, 135.0)	−1.0 (−13.0, 10.0)	<0.001
	High Risk (5/5 criteria)	397	15.0 (10.0, 24.0)	130.0 (120.0, 140.0)	129.0 (120.0, 135.0)	−3.0 (−15.0, 9.0)	<0.001
Diastolic blood pressure	**All Study Population**	8132	11.0 (6.0, 18.0)	80.0 (72.0, 85.0)	78.0 (70.0, 83.0)	−1.0 (−10.0, 5.0)	<0.001
	By Gender						
	Female	4357	12.0 (7.0, 20.0)	80.0 (70.0, 84.0)	77.0 (70.0, 82.0)	−1.0 (−10.0, 6.0)	<0.001
	Male	3774	9.0 (5.0, 15.0)	80.0 (74.0, 86.0)	79.0 (72.0, 84.0)	−1.0 (−10.0, 5.0)	<0.001
	By Risk						
	Low Risk (3/5 criteria)	5690	10.0 (6.0, 16.0)	80.0 (70.0, 85.0)	78.0 (70.0, 83.0)	0.0 (−9.0, 5.0)	<0.001
	Moderate Risk (4/5 criteria)	2044	13.0 (7.0, 21.0)	80.0 (74.0, 87.0)	78.0 (71.0, 83.0)	−2.0 (−10.0, 5.0)	<0.001
	High Risk (5/5 criteria)	397	15.0 (10.0, 24.0)	80.0 (75.0, 86.5)	80.0 (74.0, 83.5)	−3.0 (−10.0, 4.0)	<0.001

Table A1. *Cont.*

Criteria	Group	N **	No. of Tests Median (Q1–Q3) (2008–2015)	Beginning of Study Median (Q1–Q3)	End of Study Median (Q1–Q3)	Change Median (Q1–Q3)	*p* Value
LDL	**All Study Population**	8066	8.0 (5.0, 11.0)	118.0 (96.0, 141.0)	109.0 (87.0, 133.0)	−3.55 (−28.0, 13.0)	<0.001
	By Gender						
	Female	4346	8.0 (5.0, 11.0)	117.0 (96.0, 139.4)	111.0 (90.0, 133.0)	−2.0 (−25.0, 15.0)	<0.001
	Male	3720	7.0 (4.0, 10.0)	120.0 (96.0, 143.0)	107.0 (85.0, 133.0)	−6.0 (−31.0, 11.0)	<0.001
	By Risk						
	Low Risk (3/5 criteria)	5655	7.0 (4.0, 11.0)	118.0 (96.0, 141.0)	110.0 (89.0, 133.0)	−3.0 (−26.0, 14.0)	<0.001
	Moderate Risk (4/5 criteria)	2018	8.0 (5.0, 11.0)	118.0 (96.0, 142.0)	107.0 (84.0, 132.2)	−6.0 (−32.7, 12.0)	<0.001
	High Risk (5/5 criteria)	393	9.0 (6.0, 12.0)	116.4 (97.0, 139.0)	104.0 (80.0, 129.5)	−11.9 (−35.0, 12.0)	<0.001
HbA1c	**All Study Population**	5109	3.0 (1.0, 6.0)	5.8 (5.5, 6.2)	5.8 (5.4, 6.3)	0.0 (−0.2, 0.2)	0.137
	By Gender						
	Female	2751	3.0 (1.0, 7.0)	5.8 (5.5, 6.2)	5.8 (5.5, 6.3)	0.0 (−0.2, 0.2)	0.21
	Male	2358	3.0 (1.0, 6.0)	5.8 (5.5, 6.2)	5.8 (5.4, 6.3)	0.0 (−0.2, 0.2)	0.407
	By Risk						
	Low Risk (3/5 criteria)	3349	3.0 (1.0, 6.0)	5.8 (5.4, 6.2)	5.8 (5.4, 6.2)	0.0 (−0.2, 0.15)	0.528
	Moderate Risk (4/5 criteria)	1435	4.0 (2.0, 7.0)	5.9 (5.5, 6.4)	5.9 (5.5, 6.5)	0.0 (−0.2, 0.3)	0.404
	High Risk (5/5 criteria)	325	5.0 (2.0, 10.0)	6.0 (5.6, 6.5)	6.0 (5.6, 6.8)	0.0 (−0.3, 0.4)	0.073

Abbreviations: BMI, body mass index; HDL-c, high-density lipoprotein cholesterol; LDL, Low-density lipoprotein; HbA1c, glycated hemoglobin; MetS, metabolic syndrome. *p*-values < 0.05 were considered statistically significant. ** individuals who have at least two tests

Table A2. Healthcare utilization by gender and metabolic syndrome (MetS) severity.

		Total	N	%	Median (IQR)	*p* Value *	*p* Value **
Visit to Family doctor	**All Study Population**	8170	8167	100.0%	96.0 (59.0, 144.0)	-	-
	By Gender						
	Female	4370	4370	100.0%	111.0 (73.0, 162.0)	0.101	<0.001
	Male	3800	3797	99.9%	80.0 (47.0, 123.0)		
	By Risk						
	Low Risk (3/5 criteria)	5724	5721	99.9%	92.0 (57.0, 139.0)	0.527	<0.001
	Mod Risk (4/5 criteria)	2047	2047	100.0%	104.0 (63.0, 156.0)		
	High Risk (5/5 criteria)	399	399	100.0%	104.0 (63.0, 155.5)		
Dietician Referrals	**All Study Population**	8170	1171	14.3%	1.0 (1.0, 1.0)	-	-
	By Gender						
	Female	4370	720	16.5%	1.0 (1.0, 1.0)	<0.001	0.030
	Male	3800	451	11.9%	1.0 (1.0, 1.0)		
	By Risk						
	Low Risk (3/5 criteria)	5724	742	13.0%	1.0 (1.0, 1.0)	<0.001	0.387
	Mod Risk (4/5 criteria)	2047	353	17.2%	1.0 (1.0, 1.0)		
	High Risk (5/5 criteria)	399	76	19.0%	1.0 (1.0, 1.0)		
Visit to diabetes specialist	**All Study Population**	8170	342	4.2%	2.0 (1.0, 3.0)	-	-
	By Gender						
	Female	4370	197	4.5%	2.0 (1.0, 3.0)	0.121	0.176
	Male	3800	145	3.8%	1.0 (1.0, 3.0)		
	By Risk						
	Low Risk (3/5 criteria)	5724	192	3.4%	1.0 (1.0, 2.0)	<0.001	0.038
	Mod Risk (4/5 criteria)	2047	115	5.6%	2.0 (1.0, 3.0)		
	High Risk (5/5 criteria)	399	35	8.8%	2.0 (1.0, 4.5)		

Abbreviations: MetS, metabolic syndrome. Mod Risk, Moderate Risk. IQR, Interquartile Range, *p*-values < 0.05 were considered statistically significant. * *p* value for comparison of proportions (e.g., whether a referral or visit occurred). ** *p* value for comparison of counts (number of referrals or visits).

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