# The Economic Impact of Metabolic Syndrome in Schizophrenia: A Claims-Based Analysis in the United States

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## Introduction

- Metabolic syndrome (MetS) is a cluster of metabolic abnormalities including central adiposity, insulin resistance, hypertension, and atherogenic dyslipidemia that affects about a third of people with schizophrenia[1,2]
- Although MetS-related disorders are known to contribute to increased morbidity and mortality in people with schizophrenia, there is limited evidence quantifying the economic burden

## Objective

- To assess the impact of one or more MetS-related disorders on medical costs in people with schizophrenia in the United States using claims data

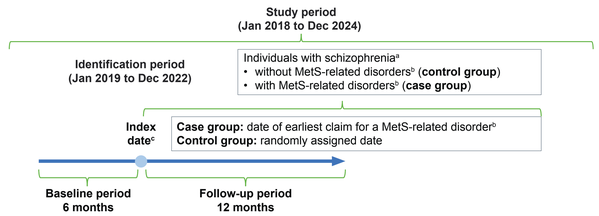
## Methods

- A retrospective cohort study was conducted using the STATinMED Real World Data Insights database covering the period from 2018 to 2024
- Patients included:
  - Adults ≥18 years of age with schizophrenia, ≥12 months of continuous enrollment before and after the index date, and either ≥2 outpatient claims on separate days or ≥1 inpatient claim for schizophrenia (based on ICD-10-CM codes) during the identification period were identified and grouped into cohorts with ≥1 MetS-related disorder (obesity, hyperlipidemia, hypercholesterolemia, diabetes, and/or hypertension) or controls (without these disorders) (**Figure 1**)
- Propensity score matching was applied to balance baseline characteristics
- The primary outcome was all-cause medical costs, during a 12-month follow-up, adjusted for insurance status and inflation and stratified by the number of MetS-related disorders (0 in controls; 1–5 in cases)
- Costs were adjusted for insurance status in the analysis and according to the consumer price index for 2024 and were rounded to the nearest US dollar
- A generalized linear model was employed to assess annualized healthcare cost per individual per year stratified by the number of MetS-related disorders with adjustment for insurance status

## Results

- Overall, 122,248 individuals were eligible before being matched; 71,570 had ≥1 MetS-related disorders (case group) and 50,678 had no MetS-related disorders (control group) (**Table 1**)
- 40,552 individuals in the case group were matched to the same number of individuals in the control group. The median age was 47 years in the case group and 44 years in the control group, and the majority of individuals in both groups were male (cases: 69%; controls: 72%) (**Table 2**)
- After matching, the numbers for MetS-related disorders and the people in each group were: 0, n=40,552; 1, n=15,840; 2, n=11,833; 3, n=8119; 4, n=4074; 5, n=686. The distribution of observed medical costs per person per year (PPPY) by number of MetS-related disorders (0 to 5) is shown in **Figure 2**.
- In individuals with schizophrenia, the mean all-cause total medical costs increased with the number of MetS-related disorders (0, $8396; 1, $14,069; 2, $16,999; 3, $18,637; 4, $22,451; 5, $34,441) with groups of individuals with ≥1 MetS-related disorders having significantly greater medical costs than the group with no MetS-related disorders ($P$<0.0001) (**Table 3**)
- Individuals with all five MetS-related disorders incurred estimated total medical costs of $34,441 PPPY, >4 times higher than costs of $8396 for individuals without any MetS-related disorders (**Table 3**)

### Figure 1. Study design, periods, and timelines




[a]Schizophrenia was defined based on ≥2 outpatient claims on separate days or ≥1 inpatient claim related to schizophrenia; at least one of these claims was required to occur in the 12 months before the index date. [b]MetS-related disorders comprise obesity, hyperlipidemia, hypercholesterolemia, diabetes, and hypertension. [c]All individuals (in case and control groups) must have ≥12 months of continuous enrollment leading up to and following the index date. MetS, metabolic syndrome.

### Table 1. Number of individuals by eligibility in the case and control groups

| Case group | N |
|---|---|
| Presence of ≥1 MetS-related disorder (obesity, hyperlipidemia, hypercholesterolemia, diabetes, and hypertension) | 24,191,864 |
| ≥12 months of continuous enrollment immediately before and after the index date | 21,793,372 |
| ≥2 outpatient claims on separate days or ≥1 inpatient claim for schizophrenia, with at least one claim in the year prior to the index date | 372,919 |
| ≥18 years of age at index date | 371,354 |
| No evidence of bipolar disorder, major depressive disorder, and schizoaffective disorder based on ICD-10-CM codes | **71,570** |
| **Control group** | **N** |
| ≥2 outpatient claims on separate days or ≥1 inpatient claim for schizophrenia, with at least one claim in the year prior to the index date | 821,454 |
| ≥12 months of continuous enrollment immediately before and after the index date | 750,346 |
| ≥18 years of age at index date | 741,543 |
| Without any MetS-related disorder (obesity, hyperlipidemia, hypercholesterolemia, diabetes, and hypertension) | 169,439 |
| No evidence of bipolar disorder, major depressive disorder, and schizoaffective disorder based on ICD-10-CM codes | **50,678** |

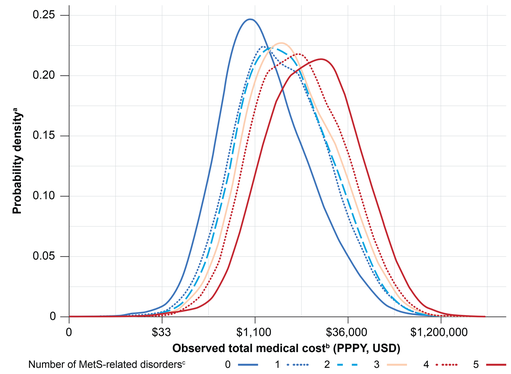
Note: For patients with >1 MetS disorder, the index date represents the earliest claim(s) of the latest occurrence of MetS disorders. MetS, metabolic syndrome.

### Table 2. Demographic and clinical characteristics for the matched case and control groups, with SMDs of matched covariates after propensity score matching

| Characteristics (matched groups) | Cases (N = 40,552) | Controls (N = 40,552) | SMD for matched covariates |
|---|---|---|---|
| **Age at index date,** median (IQR), years | 47 (37–60) | 44 (35–57) | 0.148[a] |
| **Sex**, n (%) | | | |
| Female | 12,727 (31) | 11,335 (28) | – |
| Male | 27,825 (69) | 29,217 (72) | 0.075 |
| **US region**, n (%) | | | |
| Midwest | 7540 (19) | 7735 (19) | 0.012 |
| Northeast | 8951 (22) | 7941 (20) | 0.061 |
| South | 14,087 (3) | 12,932 (32) | 0.06 |
| West | 9974 (25) | 11,944 (29) | 0.11 |
| **Insurance status**, n (%) | | | |
| Commercial only | 5874 (14) | 7417 (18) | – |
| Medicaid only | 13,604 (34) | 15,967 (39) | – |
| Medicare only | 8842 (22) | 8888 (22) | – |
| Dual type | 11,176 (28) | 7115 (18) | – |
| Other | 1056 (3) | 1165 (3) | – |
| **Metabolic disorders**, n (%) | | | |
| Hyperlipidemia | 22,034 (54) | – | – |
| Diabetes | 15,140 (37) | – | – |
| Hypercholesterolemia | 4893 (12) | – | – |
| Obesity | 16,360 (40) | – | – |
| Hypertension | 25,162 (62) | – | – |
| **Mental health disorders**, n (%) | | | |
| Anxiety disorder | 6377 (16) | 4518 (11) | 0.135 |
| Substance use disorder | 6355 (16) | 5550 (14) | 0.056 |
| PTSD | 802 (2) | 713 (2) | 0.016 |
| Personality disorder | 868 (2) | 598 (2) | 0.05 |
| **Psychotropic medication**, n (%) | | | |
| Antipsychotics | 12,779 (32) | 12,183 (30) | – |
| Antidepressants | 4845 (12) | 4478 (11) | – |
| Antianxiety | 2649 (7) | 2520 (6) | – |
| Hypnotics | 1028 (3) | 780 (2) | – |
| Mood stabilizers | 1994 (5) | 1678 (4) | – |
| **Nonpsychotropic medication**, n (%) | | | |
| Antihypertensive | 7362 (18) | 1961 (5) | – |
| Lipid-lowering agents | 5313 (13) | 1261 (3) | – |
| Antidiabetics | 3849 (10) | 536 (1) | – |
| GLP-1RAs | 354 (1) | 39 (<1) | – |

[a]Mean (SD) age in cases and controls were 48.1 (14.7) and 46.0 (13.8) years, respectively. GLP-1RA, glucagon-like peptide-1 receptor agonist; ICD-10, International Classification of Disease Tenth Revision Clinical Modification; IQR, interquartile range; PTSD, post-traumatic stress disorder; SMD, standardized mean difference; US, United States.

### Figure 2. Probability density[a] plot showing the distribution of observed PPPY all-cause medical cost[b] by the number of MetS-related disorders[c]




[a]Probability density is scaled such that the total area under each curve in the plot equals to 1. [b]All-cause medical cost comprised outpatient, inpatient, emergency room, and stay-related costs. [c]MetS-related disorders comprised obesity, hyperlipidemia, hypercholesterolemia, diabetes, and hypertension. MetS, metabolic syndrome; PPPY, per person per year.

### Table 3. Adjusted estimated medical costs[a] in individuals with schizophrenia by the number of MetS-related disorders[b]

| All-cause medical costs | Number of MetS-related disorders[b] | Estimated mean[a] (95% CI) | $P$ value[d] |
|---|---|---|---|
| **Outpatient** | 0 | 3912 (3838–3987) | Reference |
| | 1 | 5077 (4951–5206) | <0.001 |
| | 2 | 6050 (5883–6220) | <0.001 |
| | 3 | 6943 (6721–7172) | <0.001 |
| | 4 | 8242 (7888–8613) | <0.001 |
| | 5 | 13,825 (12,469–15,327) | <0.001 |
| **Inpatient (hospital)** | 0 | 21,939 (20,940–22,983) | Reference |
| | 1 | 29,437 (27,993–30,955) | <0.001 |
| | 2 | 38,105 (35,900–40,441) | <0.001 |
| | 3 | 38,052 (35,515–40,774) | <0.001 |
| | 4 | 42,907 (39,148–47,033) | <0.001 |
| | 5 | 51,062 (41,835–62,324) | <0.001 |
| **Emergency room** | 0 | 1093 (1050–1137) | Reference |
| | 1 | 1171 (1109–1236) | 0.02 |
| | 2 | 1303 (1220–1392) | <0.001 |
| | 3 | 1070 (989–1158) | 0.6 |
| | 4 | 1026 (923–1139) | 0.2 |
| | 5 | 911 (715–1161) | 0.1 |
| **Stay-related (nursing home, group home, and/or hospice)** | 0 | 5757 (5205–6369) | Reference |
| | 1 | 5664 (5100–6291) | 0.8 |
| | 2 | 5694 (5150–6296) | 0.8 |
| | 3 | 5604 (5022–6254) | 0.6 |
| | 4 | 7150 (6128–8342) | 0.01 |
| | 5 | 9685 (7007–13,386) | 0.002 |
| **Total medical cost[c]** | 0 | 8396 (8228–8568) | Reference |
| | 1 | 14,069 (13,701–14,445) | <0.001 |
| | 2 | 16,999 (16,495–17,517) | <0.001 |
| | 3 | 18,637 (17,987–19,310) | <0.001 |
| | 4 | 22,451 (21,388–23,565) | <0.001 |
| | 5 | 34,441 (30,709–38,631) | <0.001 |

[a]Mean costs were estimated from GLMs for matched cohort adjusted for individual insurance status. In the GLMs, for each medical cost type and total medical cost, the model-based estimates reflect mean cost among patients who incurred any medical cost (nonzero cost observations) stratified by number of MetS-related disorders, rather than the overall mean observed costs; [b]MetS-related disorders comprised diagnoses of obesity, hyperlipidemia, hypercholesterolemia, diabetes, and hypertension, based on ICD-10-CM codes; [c]Total medical costs comprised outpatients, inpatients, emergency visits, stay-related, and other unspecified costs. The estimated total medical costs were lower than estimated inpatient costs because data on inpatient costs were largely missing and the total medical cost reflected the costs in the other categories, which were typically smaller; [d]$P$ values were estimated using patients with 0 metabolic disorders (control) as the reference group and were considered statistically significant at $P$ <0.008 based on Bonferroni correction. CI, confidence interval; GLM, generalized linear model; ICD-10, International Classification of Diseases Tenth Revision-Clinical Modification, MetS, metabolic syndrome.

## CONCLUSIONS

- There is a substantial economic burden associated with MetS-related disorders in people with schizophrenia, primarily driven by outpatient and inpatient care
- The findings underscore the importance of managing MetS in this population, which includes early risk assessments, lifestyle modification, and the selection of antipsychotic medications with fewer metabolic adverse effects

## LIMITATIONS

- Reliance on administrative claims data (ICD-10 codes) rather than clinical measurements may fail to identify metabolic syndrome and underestimate true metabolic burden
- Incomplete cost data and limited healthcare utilization detail may lead to underestimation of the full economic impact, with findings generalizable mainly to insured U.S. populations

### References

1. Grundy SM, et al. *Circulation*. 2005;112(17):2735–52.
2. Saklayen MG. *Curr Hypertens Rep*. 2018;20(2):12.

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At Otsuka, we hold a deep respect for the value of every mind. We will not rest until mental illnesses and brain diseases are approached with the same priority and urgency as our physical health and recognized as chronic diseases that warrant early, equitable, and accessible intervention for patients and caregivers everywhere.

### Disclosures

**XH** and **ZZ** are full-time employees of Otsuka Pharmaceutical Development & Commercialization, Inc. **SCH** and **SA** are previous employees of Otsuka Pharmaceutical Development & Commercialization, Inc.