

Cardiometabolic Risk After Antidepressant and Antipsychotic Treatment in Major Depressive Disorder: Evidence from German Health Claims Data

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Background

Major depressive disorder (MDD) is a common and disabling mental health condition characterized by persistent depressed mood and/or anhedonia as core symptoms, along with variable levels of functional impairment. (1)

Pharmacological treatment is central to MDD management, most commonly with antidepressants such as selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressants. In treatment-resistant cases, antipsychotics are frequently prescribed as adjunctive therapy. (2)

While cardiometabolic effects of antidepressant and antipsychotic use have been described in clinical trials, evidence from real-world routine care, particularly from German claims data, remains comparatively limited.

Objective

This study aimed to estimate the incidence and timing of cardiometabolic events among adults with MDD initiating antidepressants and/or antipsychotics in a real-world setting.

Methods

STUDY DESIGN

This is a retrospective cohort study using German claims data from the WIG2 benchmark database between January 2014 and December 2024 (Figure 1).

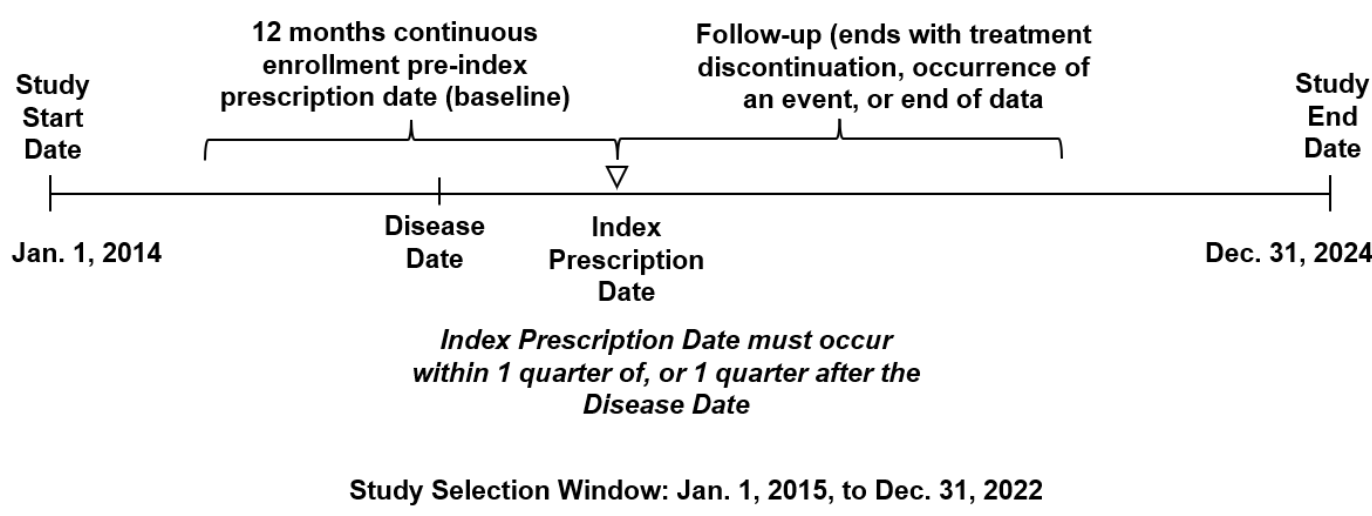


Figure 1. Study design

Demographics were assessed at index and baseline cardiometabolic events during the 365-day pre-index period. Incident outcomes were assessed until the earliest of a cardiometabolic event, treatment discontinuation (>60-day gap), last EHR/claims record, or study end.

POPULATION

- Adults ≥18 years with MDD
- Initiation of antidepressant or antipsychotic (index date)
- At least 12 months of continuous enrolment prior to and 24 months following the index date

EXCLUSION CRITERIA

- Patients with pre-existing cardiometabolic events
- Patients diagnosed with schizophrenia, cognitive impairment, psychotic disorders, dementia, or personality disorders during the available backward period

OUTCOMES

- Hypertension, prediabetes, type 2 diabetes, cardiovascular disease (CVD), hyperlipidemia, obesity, and weight gain

ANALYSIS

- Incidence rates (IRs) with 95% confidence intervals (CIs) were estimated per 1,000 person-months at risk
- Median time-to-event (TTE) with interquartile range (IQR) were also reported
- Kaplan-Meier estimates of 3-, 6-, and 12-month cumulative incidence
- Observation time was defined as the earlier of medication discontinuation, occurrence of an event, or the end of available data

Results

Patient selection

- Of all individuals within the database (n = 4,562,822), 7.1% (n = 322,621) had initiated treatment for MDD as defined (Figure 2).
- After applying the exclusion criteria, the overall study population comprised 91,892 patients, of whom 40.4% (n = 37,112) had no cardiometabolic event at baseline.

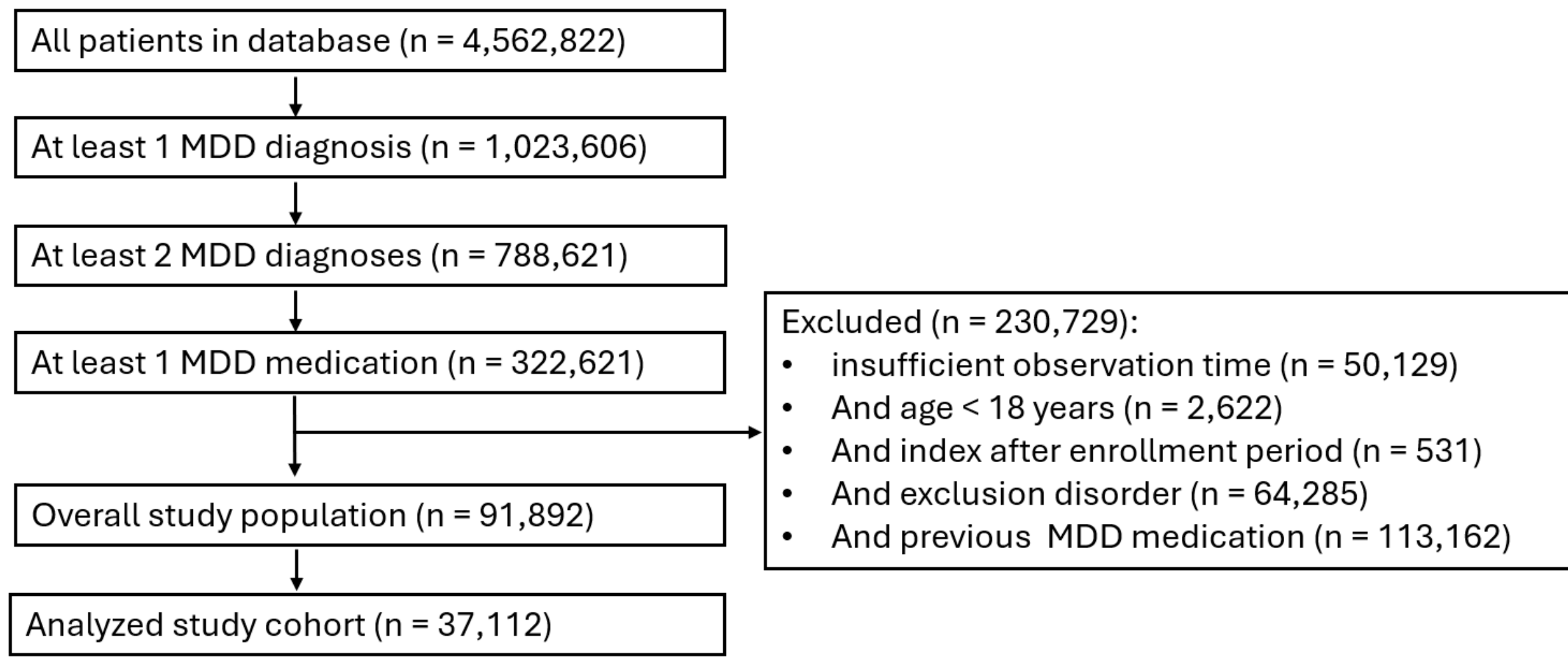


Figure 2. Patient selection

Overview

- 37,112 patients were included in our cohort (Table 1)
- The mean age was 38.7 (12.8) years; 54.2% of the patients were between 18-39 years
- Most of the patients were female (55.3%)
- A moderate MDD episode was most common (51.4%)
- The median observation time was 168 days.

Incidence of cardiometabolic events

- 10.1% of patients (n = 3,748; Table 2) experienced a cardiometabolic event within their observation time, with an incidence rate of 10.2 per 1,000 person-months (95% CI: 9.70, 10.60; Figure 3).
- The most common events experienced were hypertension, hyperlipidemia and any obesity (Table 2), with incidence rates of 3.86, 2.77, and 2.46, respectively (Figure 4).

Table 1. Baseline characteristics (N = 37,112)

Age in years (continuous)	Mean (SD)	38.7 (12.8)	
	Median	38	
	IQR (Q1 - Q3)	28 - 48	
	Min - Max	18 - 96	
Age (groups)	18-39 years	20,117	54.2%
	40-64 years	16,181	43.6%
	65+ years	814	2.2%
Sex	Male	16,566	44.6%
	Female	20,538	55.3%
	Unknown	8	0.0%
MDD severity	Mild	8,635	23.3%
	Moderate	19,061	51.4%
	Severe	3,095	8.3%
	Unspecified	6,321	17.0%
Deceased	Yes	189	0.5%
	No	36,923	99.5%
Observation time (days)	Mean (SD)	351.6 (473.2)	
	Median	168	
	IQR (Q1 - Q3)	110 - 360	
	Min - Max	1 - 3,648	

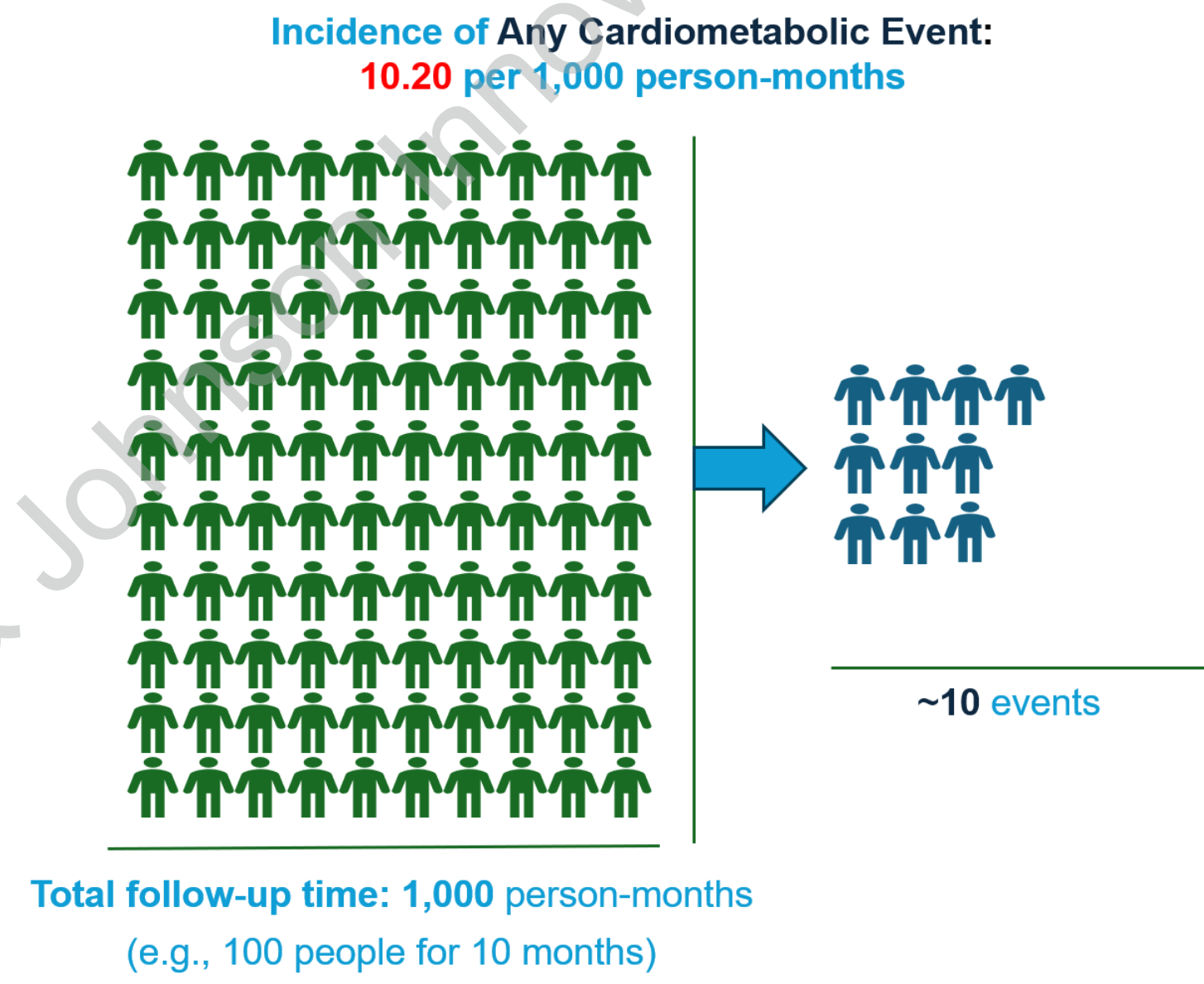


Figure 3. Incidence of any cardiometabolic event

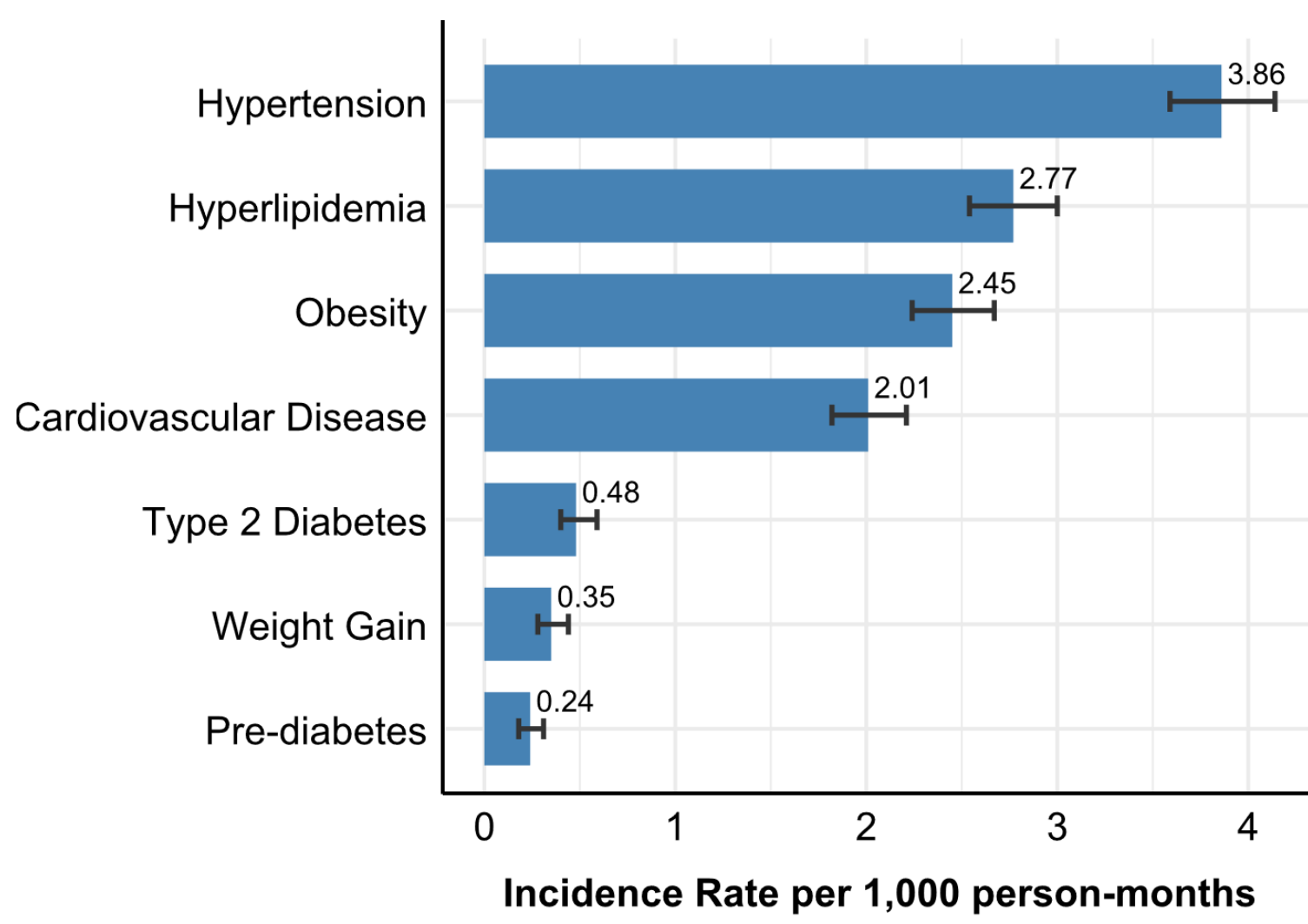


Figure 4. Incidence rates of specific cardiometabolic events (per 1,000 person months)

Table 2. Number of Cardiometabolic Events & Time-to-event

Event Type	n (%)	Median TTE (months)*	IQR (Q1-Q3)
Any Cardiometabolic Event	3,748 (10.1%)	3.9	1.1 – 12.1
Any Hypertension	1,552 (4.2%)	4.4	1.1 – 13.6
Any Pre-diabetes	101 (0.3%)	13.1	3.3 – 36
Any Type 2 Diabetes	206 (0.6%)	7.3	1.7 – 24.3
Any Cardiovascular Disease	833 (2.2%)	6.9	2 – 19.8
Any Hyperlipidemia	1,133 (3.1%)	5.6	1.3 – 19.8
Any Weight Gain ²	150 (0.4%)	8.8	4.1 – 20.6
Any Obesity	1,010 (2.7%)	5.6	1.8 – 16.4

Time-to-event

- The median time-to-any-cardiometabolic event among those who experienced an event (n = 3,748) was 3.9 months (Table 2).
- The estimated 12-month cumulative incidence for any cardiometabolic event was 11.4% (95% CI: 10.9, 11.8%; Figure 5)
- The median time-to-event for hypertension, hyperlipidemia, and any obesity was 4.4, 5.6, and 5.6 months, respectively (Table 2)
- The estimated 12-month cumulative incidence for the 3 most common conditions was:
 - Hyperlipidemia: 3.0% (95% CI: 2.8, 3.3%)
 - Obesity: 3.0% (95% CI: 2.7, 3.2%)
 - Hypertension: 4.6% (95% CI: 4.3, 4.9%)

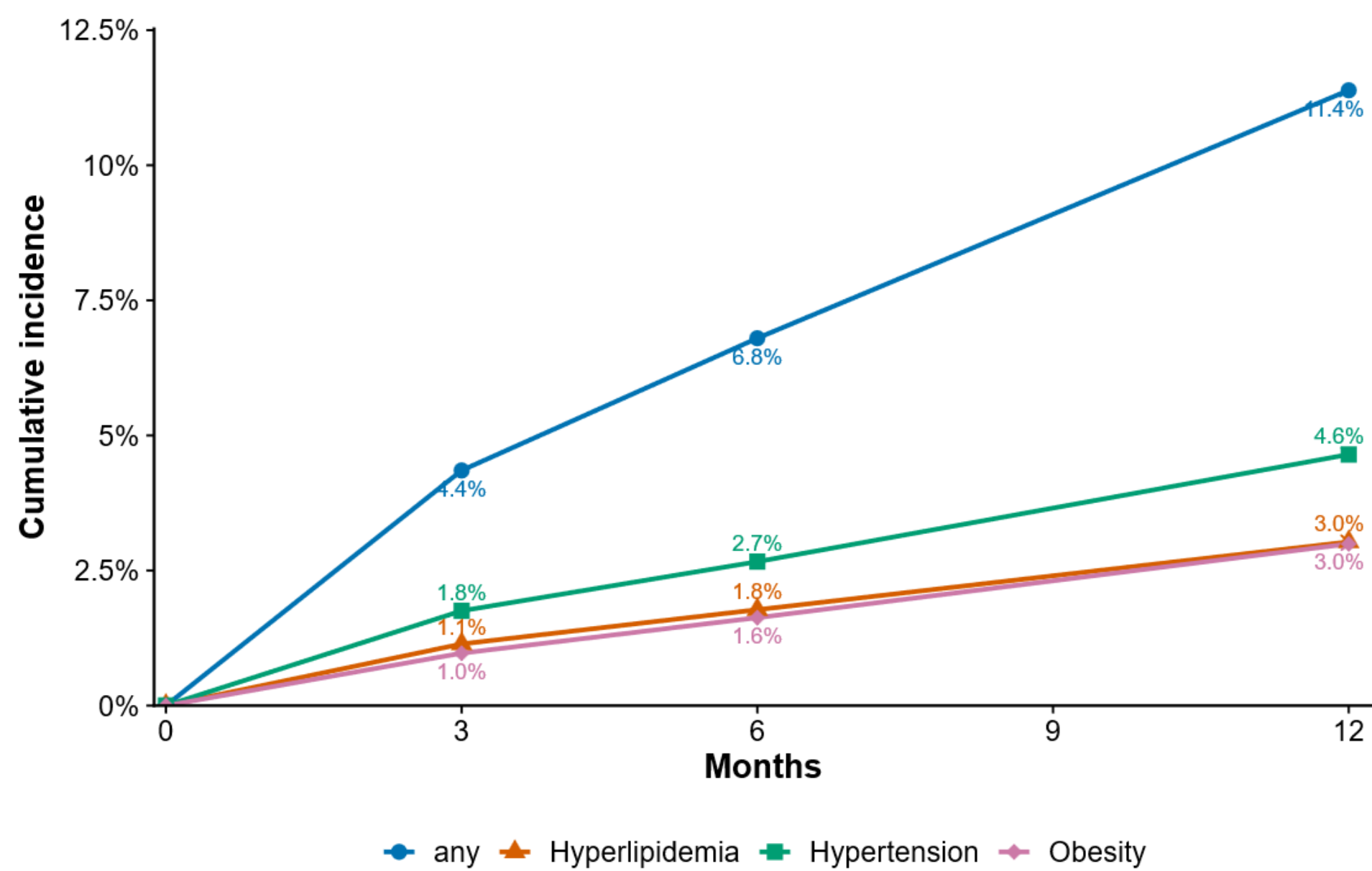


Figure 5. Time to first cardiometabolic event

Key takeaway



Following MDD treatment initiation:

- One in ten patients experienced at least one cardiometabolic event.
- Hypertension, hyperlipidemia, and obesity were the most frequently observed outcomes.
- Cardiometabolic events occurred relatively early, with a median time-to-event of approximately 3.9 months among affected patients.

Conclusions



Patients with MDD face a considerable burden of cardiometabolic events, with many outcomes arising during the initial months of follow-up.



These findings highlight the importance of considering cardiometabolic risk during MDD treatment, particularly during the early stages of care.



There is still a need for effective treatments with favorable cardiometabolic profiles to reduce the overall burden of comorbidity among patients with MDD.



Further research is needed to assess the effects of different treatment strategies on cardiometabolic outcomes and support informed clinical decision-making.

References

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Disclosures

N. Dwivedi is an employee of Johnson & Johnson and owns stock in Johnson & Johnson. J. Zhao was an employee of Johnson & Johnson. M. J. Cambron-Mellott, is an employee of Oracle Life Sciences, Oracle Corporation, who received funding from Johnson & Johnson to conduct and report on the study. M. J. Cambron-Mellott also holds stocks in Oracle Corporation. M. Dagher and M. Pignot are employees of ZEG Berlin, who received funding from Johnson & Johnson to conduct and report on the study. R. Kliemt and N. Kossack are employees of WIG2 GmbH, who received funding from Johnson & Johnson to conduct and report on the study.

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Major depressive disorder – Psychiatry



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