Incidence of Cardiometabolic Events Among Patients With Major Depressive Disorder Treated With Antidepressants and/or Adjunctive Antipsychotics: A Real-World Evidence Study

Nilanjana Dwibedi[1]; Zhiheng Zhang[2]; Hrishikesh Kale[1]; Kathryn Krupsky[3]; M. Janelle Cambron-Mellott[3]; Kyla Finlayson[3]; Manish Jha[4]; Joshua Hamilton[5]

AFFILIATIONS: [1]Johnson & Johnson, Raritan, NJ, USA [2] Janssen Global Affairs, Raritan, NJ, USA [3] Oracle Life Sciences, Austin, TX, USA [4] UT Southwestern Medical Center, Dallas, TX, USA [5] Washington State University, Spokane, WA, USA

Background

- Major depressive disorder (MDD) is a prevalent, burdensome condition associated with significant morbidity and reduced quality of life;[1] pharmacologic treatments, including antidepressants and adjunctive antipsychotics, are widely used[1]
- These treatments are associated with cardiometabolic adverse effects (e.g., weight gain, hypertension, dyslipidemia), which may reduce adherence, worsen quality of life, and increase healthcare utilization[2,3]
- Limited real-world evidence on the incidence and timing of cardiometabolic events hinders risk assessment in clinical practice and underscores the unmet need for safer, more effective treatment options

Objective

- 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

- Retrospective cohort study using Oracle Real-World Data (claims + EHR), 2016–2022 (**Figure 1**)

POPULATION

- Adults ≥18 years with MDD
- Initiated antidepressant or antipsychotic (index date)
- Continuous enrollment of ≥12 months in baseline and ≥36 months in follow-up

EXCLUSIONS

- Patients with pre-existing cardiometabolic events
- Patients diagnosed with schizophrenia, dementia, or other severe psychiatric disorders

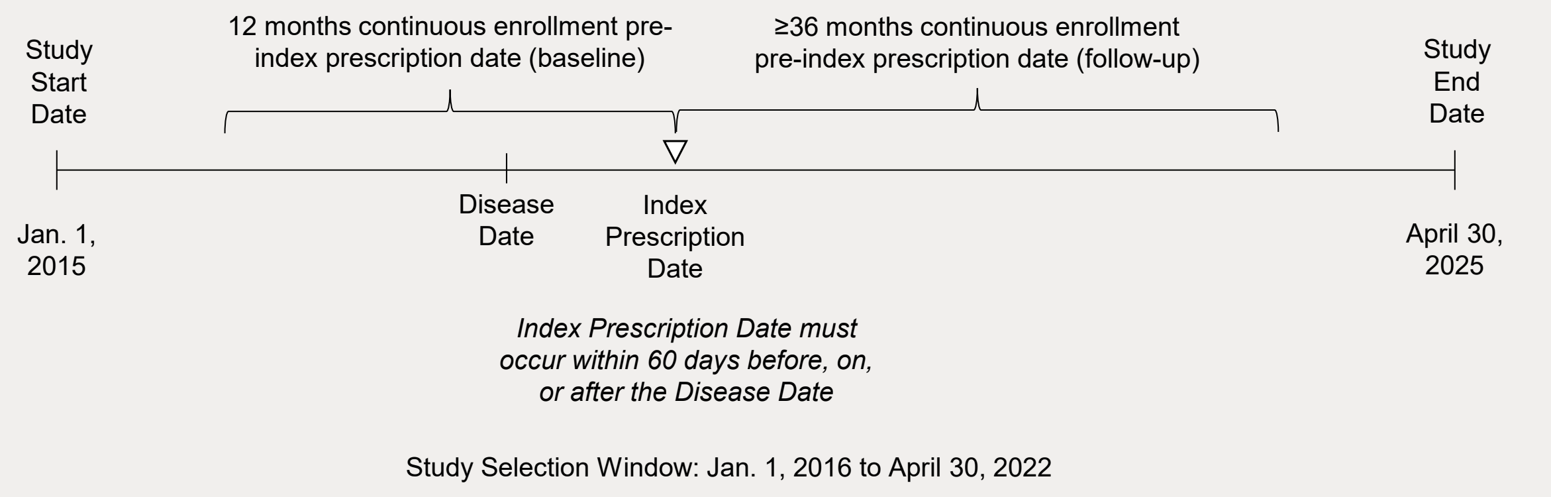
OUTCOMES

- Hypertension, prediabetes, type 2 diabetes, CVD, hyperlipidemia, obesity, and weight gain

ANALYSIS

- Incidence rates (per 1,000 person-months) with 95% confidence intervals (CI)
- Kaplan-Meier 3-, 6-, and 12-month cumulative incidence estimates with 95% CI
- Median time-to-event (TTE) with interquartile range (IQR)

Figure 1. Time to first cardiometabolic event



Index Prescription Date must occur within 60 days before, on, or after the Disease Date

Study Selection Window: Jan. 1, 2016 to April 30, 2022

Note. Patient demographics were evaluated at index. Baseline cardiometabolic events were evaluated 365 pre-index date, excluding the index date. Incident cardiometabolic outcomes were evaluated from index date to their last follow-up. It was anticipated that follow-up would end with the occurrence of a cardiometabolic event, the earliest date of treatment discontinuation (defined as a >60-day gap in medication supply), the last EHR or claims record in the study period, or the end of the study period

Results

Table 1. Baseline characteristics (N=31,190)

Characteristic	Level	Mean / N	SD / %
Age (years; continuous)		36.29	13.59
Age (n; %)	<50 years	25,173	80.7%
	50+ years	6,017	19.3%
Sex (n; %)	Male	8,959	28.7%
	Female	22,228	71.3%
	Unknown	3	0.01%
Race / ethnicity (n; %)	White	14,237	45.7%
	Black	2,119	6.8%
	Asian or Pacific Islander	671	2.2%
	Hispanic or Latino	5,023	16.1%
	Other	1,385	4.4%
	Unknown	7,755	24.9%
Insurance type (n; %)	Commercial	15,565	49.9%
	Medicaid	14,605	46.8%
	Medicare Advantage	864	2.8%
	Unknown/Other	636	2.0%
US Census Region (n; %)	Midwest	6,735	21.6%
	Northeast	6,719	21.5%
	South	7,158	23.0%
	West	10,443	33.5%
	Unknown	135	0.4%

OVERVIEW (Table 1)

- **N=31,190** patients were included in our cohort
- Mean (SD) age was 36.3 (13.6) years; 62.3% were between 18-39 years of age
- Most identified as female (71.3%) and the largest proportion were non-Hispanic White (45.7%)
- Roughly half (49.9%) of the sample were commercial insured and patients varied relative to geographic region

Table 2. Number of Cardiometabolic Events & TTE Among Those who Experienced an

Event Type	N (%) Events	Median TTE (months)[3]	IQR (Q1-Q3)
Any Cardiometabolic Event[1]	5,897 (18.91%)	1.87	0.66 - 7.50
Any Hypertension	2,156 (6.91%)	1.78	0.62 - 7.27
Any Pre-diabetes	1,090 (3.49%)	5.29	1.18- 17.83
Any Type 2 Diabetes	652 (2.09%)	1.35	0.49 - 6.42
Any Cardiovascular Disease	831 (2.66%)	3.91	0.92 - 14.79
Any Hyperlipidemia	2,880 (9.23%)	2.50	0.76 - 10.99
Any Clinically Meaningful Weight Gain[2]	190 (0.61%)	6.31	0.85 - 15.38
Any Obesity	2,254 (7.23%)	3.76	1.02 - 12.43

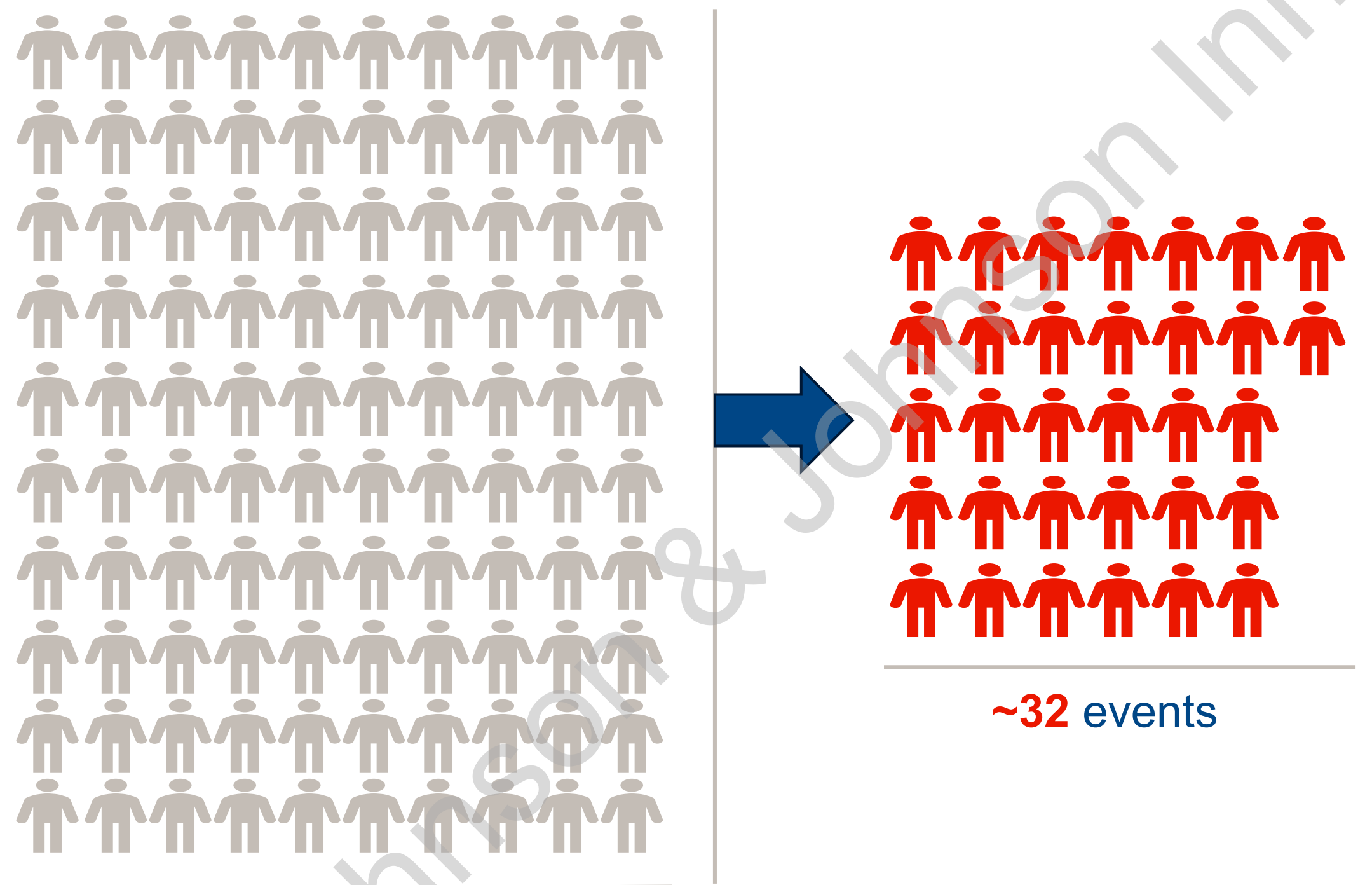
[1]Breakdown by first event: Hyperlipidemia (N=2,211), Obesity (N=1,708), Hypertension (N=1,658), Prediabetes (N=648), Cardiovascular Disease (N=470), Type 2 Diabetes (N=454), Clinically-Meaningful Weight Gain (N=143). It is possible for patients to have more than one event as their first cardiometabolic event if multiple occur on the same date, therefore these counts will not sum to the total N for any event

[2]Defined as those who experienced either weight gain of ≥3% within 30 days from index date OR weight gain of ≥7% at any point during the study period; weight gain was only assessment among patients with a weight measurement recorded in the follow-up period

[3]Time to event is calculated only among those who experienced an event; those who did not experience an event do not contribute to this measure.

Figure 2. Incidence of any cardiometabolic event

Incidence of Any Cardiometabolic Event: 31.60 per 1,000 person-months



~32 events

Total follow-up time: 1,000 person-months

(e.g., 100 people for 10 months)

INCIDENCE OF CARDIOMETABOLIC EVENTS

- 18.9% (n=5,897; **Table 2**) patients experience a cardiometabolic event, with an incidence rate of 31.60 per 1,000 person-months (95% CI: 30.80, 32.42; **Figure 2**)
- The most common events experienced were hyperlipidemia, any obesity, and hypertension (**Table 2**), with incidence rates of 13.08, 9.70, and 9.26, respectively (**Figure 3**)

Figure 3. Incidence rates of specific cardiometabolic events (per 1,000 person months)

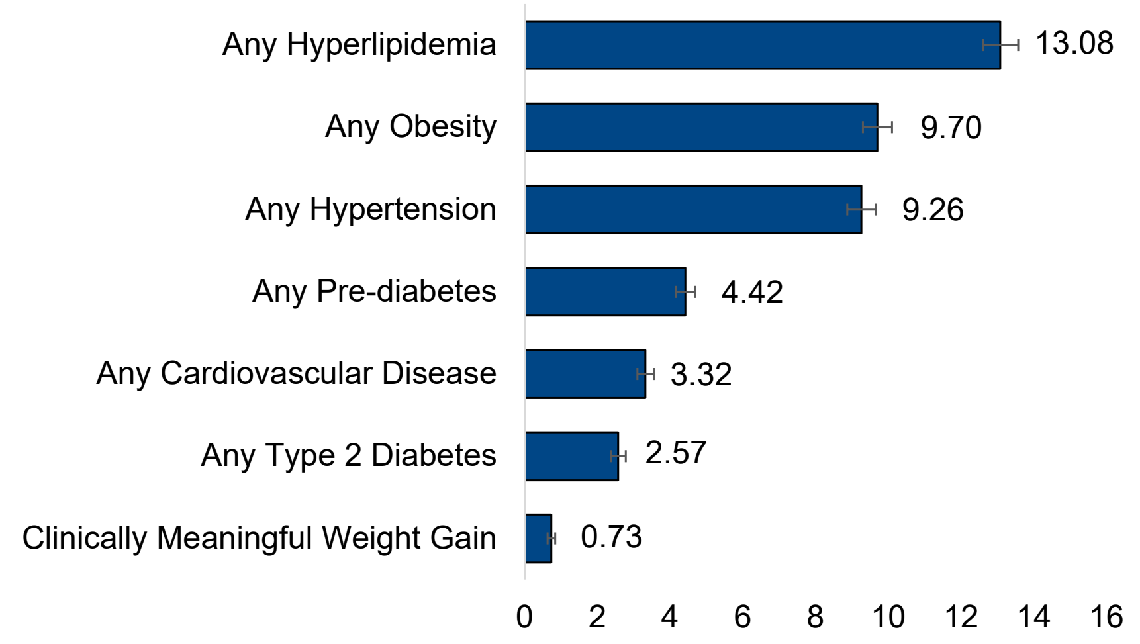
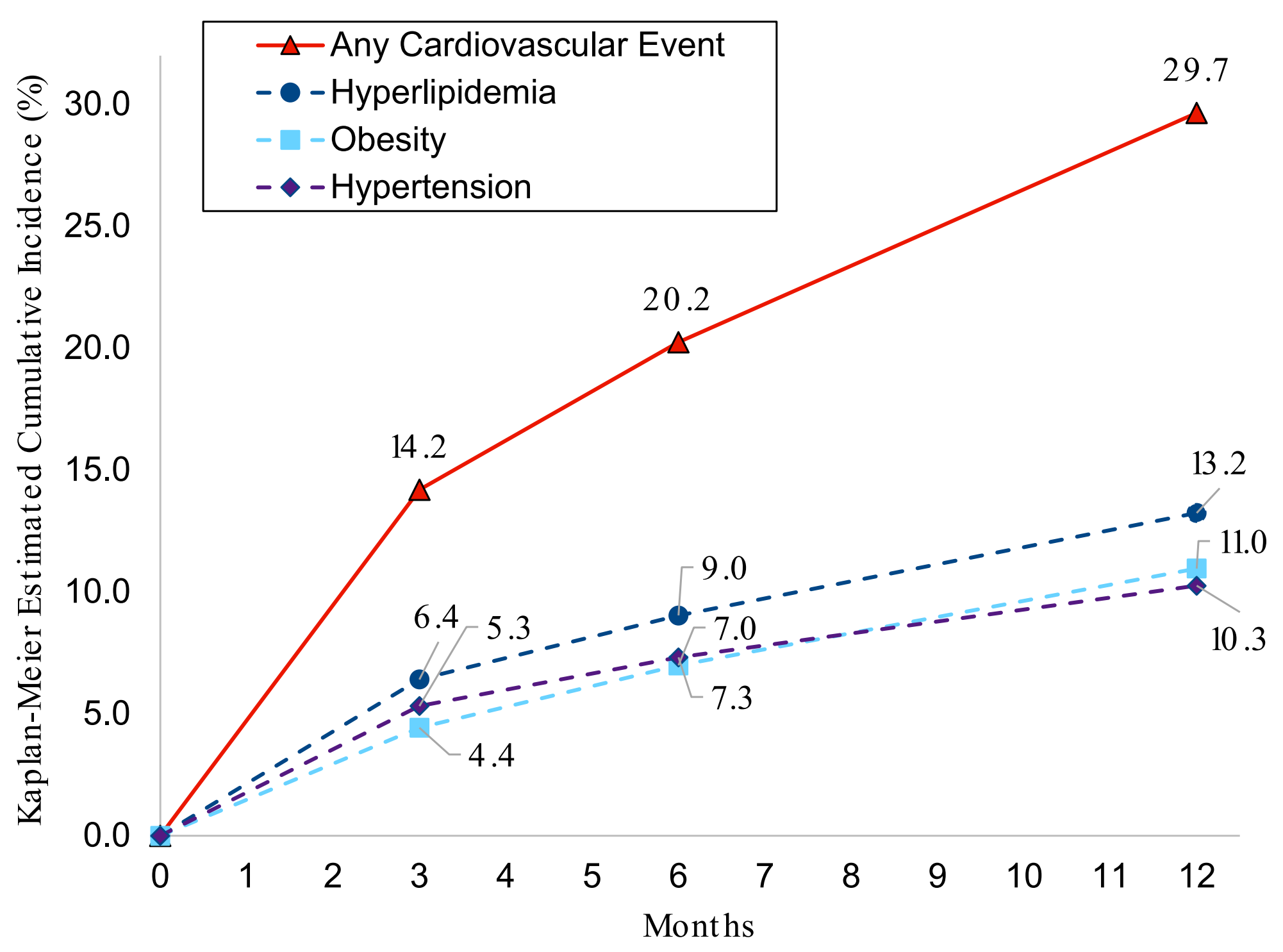


Figure 4. Time to first cardiometabolic event



Note. This graph illustrates the Kaplan-Meier estimated percentage of patients with any cardiometabolic event and the 3 most common events, hyperlipidemia, obesity, and hypertension, at 3, 6, and 12-months.

TIME-TO-EVENT

- **The median time-to-any-cardiovascular event, among those who experienced an event (n=5,897) was 1.87 months (Table 2)**
  - The estimated **12-month cumulative incidence for any cardiometabolic event was 28.65%** (95% CI: 27.84, 29.45%; **Figure 4**)
- The median time-to-event for hyperlipidemia, obesity, and hypertension was 2.50, 3.76, and 1.78 months, respectively (**Table 2**)
  - The estimated 12-month cumulative incidence for the 3 most common conditions was:
    - ✓ **Hyperlipidemia**: 13.24% (95% CI: 12.64, 13.83%)
    - ✓ **Obesity**: 10.96% (95% CI: 10.39, 11.52%)
    - ✓ **Hypertension**: 10.26% (95% CI: 9.74, 10.78%)

Key takeaway

- Cardiometabolic events are common and occur early, with an incidence rate of 31.6 per 1,000 person-months
- ~29% estimated cumulative incidence of any cardiometabolic event by 12 months
- Risk varies by condition, with the highest incidence observed for hyperlipidemia, obesity, and hypertension
- Time to event is short for many outcomes, often within the first 1–4 months, highlighting a critical early risk window

Conclusions

✓ Patients with MDD experience a **substantial burden of cardiometabolic events**, with many outcomes occurring within the first few months of follow-up

✓ These findings underscore the importance of **considering cardiometabolic risk in treatment selection**, particularly during the early phase of care

✓ There remains a need for **effective treatments with favorable cardiometabolic profiles** to help mitigate the overall burden of comorbidity in patients with MDD

✓ Further research is warranted to **quantify the impact of different treatment strategies on cardiometabolic outcomes** and inform clinical decision-making

Acknowledgments

The authors acknowledge James Geary, Danny Myers, Vicky Li, and Stacey Purinton of Oracle Life Sciences, for their assistance with the study design, data extraction, and analysis

Disclosures

N. Dwibedi, Z. Zhang, and H. Kale are employees of Johnson & Johnson and own stock in Johnson & Johnson. K. Krupsky, M. J. Cambron-Mellott, and K. Finlayson are employees of Oracle Life Sciences, Oracle Corporation, which received funding from Johnson & Johnson to conduct and report on the study. K. Krupsky and M. J. Cambron-Mellott also hold stocks in Oracle Corporation. M. Jha: In the past 36 months, Dr. Jha has received contract research grants from Neurocrine Bioscience, Navitor/Supernus and Janssen Research & Development; honorarium to serve as Section Editor of the Psychiatry & Behavioral Health Learning Network and as Guest Editor for Psychiatric Clinics of North America from Elsevier; consultant fees from Janssen Scientific Affairs, Sanofi, Neurocrine, Abbvie, MindMed and Boehringer Ingelheim; fees to serve on Data Safety and Monitoring Board for Worldwide Clinical Trials (Eliem, Skye and Inversargo), Vicore Pharma and IQVIA (Click); and honoraria for educational presentations from North American Center for Continuing Medical Education, Medscape/WebMD, Clinical Care Options, Soterix Medical Inc., Physicians' Education Resource, Efficient CME, and H.C. Wainwright & Co.

J. Hamilton: Josh Hamilton is a consultant and key opinion leader for Johnson & Johnson; a paid ambassador for the Point of Care Network; and a Senior Medical Science Liaison for Tempus AI. All conflicts of interest have been mitigated as Dr. Hamilton is an uncompensated author/content contributor for this project.

Funding

This study was funded by Johnson & Johnson.

Novel Pathways In Depression

Scan the QR code

References:

1. Simon GE, et al. Population-based study of depression burden and treatment patterns. JAMA. 2024;332(2):141–152
2. Gafoor R, et al. Antidepressant utilisation and incidence of weight gain during 10 years' follow-up: population-based cohort study. BMJ. 2018;361:k1951.
3. McIntyre RS, et al. The effects of antidepressants and antipsychotics on cardiometabolic risk in patients with major depressive disorder. Am J Psychiatry. 2024;181(1):26–38.

Presented at: Psych Congress Elevate; June 3-6, 2026, Las Vegas, Nevada, USA