No. 74	**Antipsychotic Use And Subsequent Major Depressive Disorder In Patients With Generalized Anxiety Disorder: A Retrospective Cohort Study**
Theme	A. Non-communicable diseases

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Purpose / Background:

- **Generalized anxiety disorder (GAD)**
  - One of the most prevalent types of mental disorders
  - Major risk factor for subsequent **major depressive disorder (MDD)**
- **Antipsychotic medications**
  - Primarily used to treat schizophrenia
  - Increasingly prescribed for GAD patients who are unresponsive to first-line treatment due to their efficacies in relieving anxiety symptoms
- **Mechanism**
  - GAD patients are likely to develop subsequent MDD because the constant fear and worry significantly impair their role functioning which might lead to self-isolation or constant depressed mood. Eventually, the distress caused by anxiety may develop into depression.
  - Given that antipsychotics can relieve GAD symptoms, which will restore functioning among patients, we hypothesize that antipsychotic use is a protective factor for subsequent MDD.
- **Study objective**
  - Examine whether antipsychotic use is associated with the reduction of subsequent MDD symptoms among patients with GAD in the U.K.

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Methods:

Design	Population-based retrospective cohort design
Data source	The Health Improvement Network (THIN) database: contains electronic medical records from over 700 general practitioners (GPs) across the United Kingdom (UK), with good representativeness of the UK population regarding demographic structure and chronic disease prevalence
Cohort selection	The study cohort consists of all patients who received a GAD diagnosis in the database between 2009 to 2012. Patients with history of MDD will be excluded from the cohort.
Exposure	Antipsychotic use: any antipsychotic medicine prescriptions listed by the U.K. government in 2005, within 12 months after GAD diagnosis. The date of the earliest antipsychotic prescription within the designated period was considered as baseline
Outcome	Time to the first observed MDD diagnosis, death, or end of the observation period, whichever the earliest
Potential confounders	Age, sex, schizophrenia, bipolar disorder, and dementia
Statistical analysis	Propensity score matching: based on birth year, sex, schizophrenia, bipolar disorder, and dementia, with standardized mean differences of > 0.1 considered an indication of imbalance Cox proportional-hazards model: examine the hazard ratios of newly developed MDD within the follow-up period between patients who were prescribed with antipsychotics and patients who were not Sensitivity analysis: leave-one-out approach to replicate the main analysis multiple times in each of which removing one type of the antipsychotic medication in the definition of antipsychotic use.

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Clinical Implications

- ➤ GAD is a strong predictor of the subsequent development of MDD morbidity.

- ➤ By adopting a retrospective cohort design using population representative primary care data, this study may

  - ▪ Provide new insights in understanding the function of antipsychotic drugs

  - ▪ Provide new direction for their usage in the management of MDD symptoms among GAD patients