Association of Antidepressant Medications With Incident Type ۲ Diabetes Among Medicaid-Insured Youths

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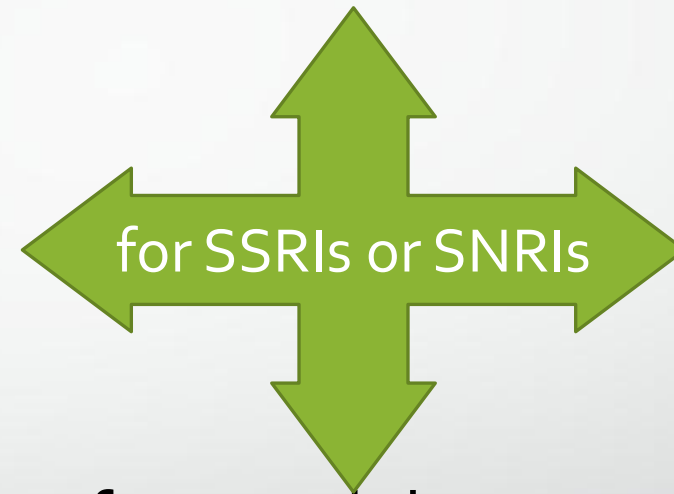
Introduction

- antidepressants are one of the most commonly prescribed psychotropic medication classes among US youths.

- increase in the percentage of US children and adolescents who use antidepressants

- antidepressants evidence-based indications:

✓ major depressive disorder

✓ obsessive-compulsive disorder

✓ childhood enuresis

Introduction

- Many published studies— in adults—report increased risk of type ٢ diabetes associated with antidepressant use.

- No population-based study has comprehensively examined the independent effect of antidepressants on the risk of incident type ٢ diabetes among youths.

- This study is a large, retrospective cohort study of youths insured by Medicaid who initiated treatment with antidepressants

Introduction

- assessment the risk of incident type ٢ diabetes by antidepressant subclass and according to :

✓ duration of use

✓ cumulative dose

✓ average daily dose

✓ interaction between the duration of use and the average daily dose

for SSRIs or SNRIs

Methods , Data Source

- The Medicaid Analytic eXtract (MAX) database
- from ۴ large, geographically diverse states of US
- January ۱, ۲۰۰۴, through December ۳۱, ۲۰۰۹
- Medicaid administrative claims data include:
- ✓ enrollment files
- ✓ claim files
- ✓ inpatient and outpatient services
- ✓ prescription drug dispensings

Methods , Study Design and Population

- retrospective cohort study

- youths insured by Medicaid between ۵ to ۲۰ years of age

- ۱۱۹ ۶۰۸ youths who initiated antidepressant treatment

- The antidepressant initiation date served as the index date for cohort entry.

Exclusion criteria

- Received antidepressant medication during the ۳۶۵ days preceding the index date

- Enrolled in a comprehensive or behavioral managed care plan

- Admitted to long-term care facility or life-threatening illness during the ۳۶۵ days preceding the index date

- gestational diabetes

- polycystic ovarian syndrome

- With diagnosis of diabetes (type ۱ or type ۲) or received insulin or oral antidiabetic medications during the ۳۶۵ days preceding the index date

Incident Type ٢ Diabetes

- The main study outcome was diagnosis of incident type ٢ diabetes, which was identified by the use of a validated, computerized database algorithm.

- This algorithm had a positive predictive value of ٨٣,٩%

- case definition of diabetes:

✓ an inpatient stay with a primary diagnosis of diabetes

✓ a combination of ٢ or more different diabetes-related medical care within a ١٢٠-day period

Incident Type ٢ Diabetes

- The incidence of type ٢ diabetes = the number of new cases of type ٢ diabetes per ١٠ ٠٠٠ person-months of follow-up

- Youths in the study were followed up until :

✓ The incident type ٢ diabetes

✓ their ٢١st birthday

✓ the end of the study (December ٣١, ٢٠٠٩)

Antidepressant Medication Use

- ۴ time-dependent measures:

✓ status of use (current vs former use)

✓ duration of use (in days)

✓ cumulative dose exposure

✓ average daily dose

- current use = medications were not discontinued for more than ۹۰ days

- former use = medications were discontinued for more than ۹۰ days.

- average daily dose (mg/d) = the cumulative dose (in fluoxetine equivalents) divided by the duration of use

Results

study cohort :

- Youths ۱۰-۱۷ years of age (۶۹,۵%)

- nonwhite (۵۳,۷%)

- eligible for Medicaid based on low family income (۶۷,۹%)

- Male = female

most common psychiatric diagnoses :

- depressive disorders (۳۷,۴%)

- attention-deficit/hyperactivity disorder (۲۵,۹%)

- anxiety disorders (۱۷,۷%)

Results

- mean follow-up = ۲۸٫۸ months

- SSRIs and SNRIs (۶۶٫۳%) were the most commonly used

- mean duration of ۱۷۹٫۷ days

- ۲۳۳ incident cases of type ۲ diabetes:

✓ ۱۵۶ current use

✓ ۷۷ former use

- current use of antidepressants = ۱٫۹۲-fold increased risk of type ۲ diabetes

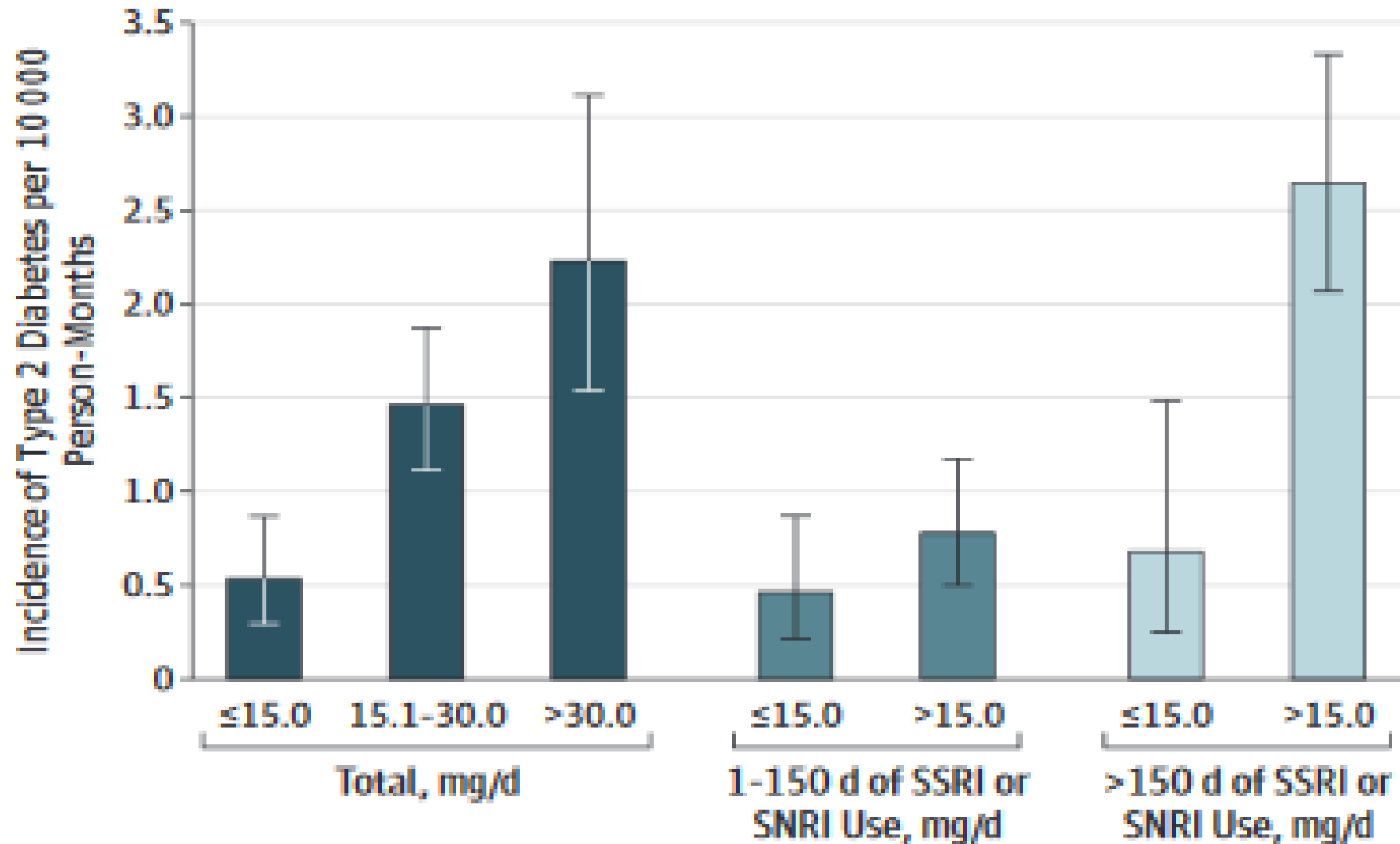# Results

- Current use of SSRIs or SNRIs or TCAs was associated with an increased risk of type ٢ diabetes.

- other antidepressants was not significantly associated with an increased risk of type ٢ diabetes

- the risk of type ٢ diabetes intensified with increasing duration of SSRI or SNRI use

- in users of other antidepressants, the duration of use was not significantly associated with an increased risk of type ٢ diabetes

Results

- **risk of type ٢ diabetes:**

✓ cumulative dose of SSRIs or SNRIs >٣٠٠٠ mg   **………**   > ٢-fold increased

✓ average daily dose of SSRIs or SNRIs > ١٥ mg/d **…...** significantly increased

✓ significant interaction between the duration of SSRI or SNRI use and the average daily dose of SSRI or SNRI on the risk of type ٢ diabetes.

Risk of Incident Type ٢ Diabetes By Average Daily Dose

Discussion

- There is a growing number of studies of adults that corroborate the increased risk observed in our study.

- Adult studies suggest that long-term use of antidepressants, particularly those with a high affinity for serotonin receptors, may be associated with increased weight gain

- Mechanisms incidence of Type ٢ diabetes in SSRI use:

  ✓ Weight gain

  ✓ Disturbances in glucose homeostasis

  ✓ decreased pancreatic insulin secretion

  ✓ increased cellular insulin resistance

- Nevertheless, much remains to be elucidated about the biological pathway for incident type ٢ diabetes following antidepressant use among youths

Conclusions

- use of SSRIs and SNRIs was associated with an increased risk of type ٢ diabetes

- intensified with increasing duration of use, cumulative dose, and average daily dose.

- The increased risk was particularly prominent for long-term use of SSRIs or SNRIs that occurred in greater daily doses.

- more than half of antidepressant prescriptions to US youths occur in outpatient visits

- impetus for policy development to improve monitoring for the benefits vs risks of antidepressant use in pediatric care models.

- specifically for serotonin reuptake inhibitors, the most commonly used antidepressant subclass