GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of April May 3 - 7, 2021

SPOTLIGHT: Are statins linked with neuropsychiatric disorders?

- Turns Out "Cutting Back" Does Not Quite Make the Cut

Are statins linked with neuropsychiatric disorders?

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SPOTLIGHT

Associations between statin use and suicidality, depression, anxiety, and seizures: a Swedish total-population cohort study

Molero Y, Cipriani A, Larsson H, Lichtenstein P, D'Onofrio BM, Fazel S. Associations between statin use and suicidality, depression, anxiety, and seizures: a Swedish total-population cohort study. *Lancet Psychiatry*. 2020; 7(11):982–990.

KEY TAKEAWAY: Statin use is not associated with suicidality, anxiety disorders or seizures in individuals 15 and older.

STUDY DESIGN: Retrospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Often patients' resistance to starting important statin therapy include concerns of alleged side effects of the medication such as possible decline in neurocognition. Statins as a cause of dementia and memory loss has largely been debunked, however there are reports of possible mood changes with statins.

PATIENTS: Swedish patients 15 years or older

INTERVENTION: Statin

CONTROL: No Statin

OUTCOME: Self-injurious or suicidal behavior, depressive disorders, anxiety disorders, and seizures

Secondary: Arrests for violent crime and arrests for non-violent crime

METHODS (BRIEF DESCRIPTION):

Participants were Swedish individuals aged 15 or older who were prescribed statins at any time. They were followed for a period of time (1/1/06–12/31/13) before and after starting statin therapy. Simvastatin, atorvastatin, rosuvastatin, pravastatin, fluvastatin were included. Dosages were not noted. Incidence of defined outcomes were measured through within-individual design analysis of data from the national registry by linking data of statin prescriptions and visits to ER or outpatient care for the defined outcomes. Of note, 88% of statins prescribed were simvastatin, however doses were not reported.

INTERVENTION (# IN THE GROUP): 1,149,384

COMPARISON (# IN THE GROUP): 1,149,384

FOLLOW UP PERIOD: 8 years, from 1/1/2006–12/31/2013

RESULTS:

- No clear associations found during statin treatment compared to no statin with:
  - Suicidal behavior or deaths from suicide (hazard ratio [HR] 0.99; 95% CI, 0.90–1.1)
  - Anxiety disorders (HR 0.99; 95% CI, 0.95–1.0)
  - Seizures (HR 1.0; 95% CI, 0.97–1.0)
- During period of statin treatment compared to no statin, they found:
  - Reduction in arrests for violent crimes (HR 0.81; 95% CI, 0.73–0.89)
  - Reduction in nonviolent crimes (HR 0.90; 95% CI, 0.88–0.93)

LIMITATIONS:

Within-individual design may not account for time-related issues including changes in diet and exercise that often go along with statin initiation. Because data was collected through the registry, details on medication adherence was not available to the researchers. Statin class-dependent variation in outcomes were observed; however, details were not reported, including lack of attention to medication dosages.

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Turns Out "Cutting Back" Does Not Quite Make the Cut

Dose-Response Association of Low Intensity and Nondaily Smoking with Mortality in the United States
Inoue-Choi M, Christensen CH, Rostron BL, et al. Dose-Response Association of Low-Intensity and Nondaily Smoking with Mortality in the United States. *JAMA Net Open*. 2020; 3(6).

KEY TAKEAWAY: Nondaily cigarette smoking is associated with an increase in mortality risks compared to those who have never smoked.
STUDY DESIGN: Prospective cohort study
LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Smoking tobacco has long plagued all of humanity, killing indiscriminately. While fortunately the number of daily smokers has decreased, there has been an increase in nondaily and low intensity (<10 per day) cigarette smokers. The ramifications of these changes, and their impact on health are historically poorly understood.

PATIENTS: Patients in the United States >18 and <103 years old
INTERVENTION: Never smoking
CONTROL: Those who have smoked at least 100 cigarettes in their lives; further defined by daily smoking, or former smokers (not smoking in the last 30 days)
OUTCOME: Mortality risk

METHODS (BRIEF DESCRIPTION):
- Data from the Tobacco Use Supplement to the Current Population Survey (TUS-CPS) questionnaires from 1992-2011 was collected regarding detailed smoking patterns
- Participants were followed for mortality after questionnaire administration
- Mortality risk was further delineated into risk specific to current daily smokers, current nondaily smokers, former daily smokers, and former nondaily smokers

INTERVENTION (# IN THE GROUP): 299,200
COMPARISON (# IN THE GROUP): 206,300

FOLLOW UP PERIOD: Mean of 9.8 years

RESULTS:
- Daily smokers had a higher mortality risk compared to never smokers (HR 2.3; 95% CI, 2.3–2.4)
- Nondaily smokers to have a higher mortality risk compared to never smokers (HR 1.82; 95% CI, 1.7–2.0)
- There is no statistically significant difference between former smokers who have not smoked in at least 10 years compared to never smokers (HR 1.2; 95% CI, 0.79–1.8)

LIMITATIONS:
- The smoking status of patients reported on questionnaire may have changed during follow up
- There was an opportunity for recall bias as some questionnaires were filled out by proxies
- Confounders (diet, physical activity, medical history) were not considered

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