

Continued Statin Prescriptions after Adverse Reactions and Patient Outcomes

BACKGROUND:

- Twenty-five to fifty percent of patients that receive a statin prescription stop taking their prescription within 6 months
- Adverse effects are among the most common reason for discontinuation
- Discontinuation of statin therapy leads to an increased risk for cardiovascular events and death
- Permanent discontinuation of statins after an initial adverse event has not been well studied

OBJECTIVE:

- To determine if patients who continue statin therapy after a reported adverse reaction can do so safely and with a lower risk for future cardiovascular events and death

METHODS:

- **Design:** Retrospective cohort study. Duration: 11 years
- **Inclusion criteria:** 18 years or older, having a presumed adverse reaction to a statin documented in the electronic medical record, and being a patient of a primary care provider affiliated with Brigham and Women's Hospital or Massachusetts General Hospital
- **Exclusion criteria:** patients having a previous adverse reaction to a statin, missing demographic information, patients not followed before the first documentation, or patients that did not follow up with their PCP within a year
- **Primary outcome measure:** time to the first of a cardiovascular event (myocardial infarction or stroke) or death from any cause
- **Secondary outcome measure:** time to death from any cause and time to the first cardiovascular event
- 28,266 patients included in the study
- Baseline characteristics were compared using t tests, chi square tests, and Cox hazard ratio
 - Various multiplicity tests utilized
- Kaplan-Meier survival curve was calculated

RESULTS:

- 28,266 patients met inclusion criteria → 70.7% continued statin therapy after an initial adverse event and 29.3% discontinued therapy.
- **Primary outcome measure:** 13.9% of patients without continued statin prescriptions had reached the primary outcome, compared to 12.2% of those on statins (1.7% difference, 95% CI 0.8 to 2.7%; $p < 0.001$)
- **Secondary outcome measures:** 1.2% lower rate of death (95% CI 0.6 to 1.9; $p < 0.0001$) 0.9% lower rate of cardiovascular event (95% CI 0.1-1.7%; $p = 0.024$) in patients continuing to take a statin
- **Cox multivariable analysis:**
 - Hazard ratio of 0.87 (CI, 0.81 to 0.93; $p < 0.001$) for composite primary outcome
 - HR of 0.79 (CI 0.72 to 0.87; $p < 0.001$) for death

- HR of 0.92 (CI 0.84 to 1.00; p=0.054) for cardiovascular events; not statistically significant
- Author's conclusion: In patients that continue statins after an initial adverse reaction, incidence of cardiovascular events and death are lower. Continuation of a statin after an adverse event should be evaluated on a case by case basis between the physician and patient.

STRENGTHS

- Large number of patients included

LIMITATIONS

- Retrospective cohort study design
- Lack of determining if patients were adherent to statin therapy before or after (if continued) adverse event
- Any cause of death included in outcome measures
- Computer software accuracy: could have included or excluded patients based on inaccurate scanning of the EMR
- Impossible to determine if adverse event was actually cause by a statin or if patients were prescribed the appropriate statin based on their 10 year risk score
- Patients were a high-risk group on average
- Multiplicity of statistical analyses

CONCLUSION

- Although the study had an impressive number of patients, there were few clinically useful results provided that are not already used in practice
 - Clinical trials and countless clinical studies have emphasized the importance of statins in reducing cardiovascular events
 - The 2013 ACC/AHA Cholesterol Guidelines recommend evaluating continuation of a statin after an adverse event based on patient risk factors and severity of the reaction
- The most innovative data was outlined in the supplemental materials explaining patterns of statin therapy after an initial adverse reaction
- Future research could be performed comparing outcomes after an adverse event from a statin comparing statins to non-statin therapy

Reference:

Zhang H, Plutzky J, Shubina M, Turchin A. Continued statin prescriptions after adverse reactions and patient outcomes. *Ann Intern Med.* 2017; 167(4):221-227.

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