The Robert Wood Johnson Foundation
Generalist Physician Faculty Scholar Program

Project Abstract

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Project Title: **Enhancing Drug Adverse Event Surveillance: The Case of Statins**

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Hypothesis: Post-marketing adverse event (AE) surveillance is inherently a passive process with a low fraction of AEs reported. We hypothesize that increased outreach through media and internet, targeted to patients, may improve the yield; and that use of an expanded set of inquiries can advance information obtained about AEs over current reporting systems. This information may include identification of hitherto unrecognized AEs; and information on timecourse of onset and recovery, quality of life impact, completeness of recovery, and interrelationship among AEs (for potential common or related mechanisms). Statin drugs are used as a demonstration case.

Methodology: 1. Develop, refine, pilot, and assess reliability of a suite of several surveys, general AE survey and surveys targeted to specific more-commonly reported AEs that address issues above. 2. "Recruit" subjects through media and internet outreach/ education efforts. 3. Assess yield of different recruitment approaches. 4. Analyze survey data to enhance understanding of drug AEs.

Status: Three AE surveys have been generated and undergone several revisions. A draft web based version was completed months ago; however release has been hindered by repeated IRB delays. Anticipating the web launch, we have worked with UCSD Health Science Communications to prepare a press release. To date, a case series related to severe irritability was published; an analysis of muscle adverse effects was completed (AHA abstract); an analysis of cognitive adverse effects has been conducted (published as student abstract); an analysis of subjects' perception of their physician's response when adverse effects were reported has been conducted (AHA abstract, recently revised with larger numbers for submission). Recently inaugurated efforts include modification of the survey to enable reporting by those without AEs to permit comparison of subject characteristics; inception of a case series of reported ALS-like cases; partnering with the new UCSD School of Pharmacy, for a residency project involving our statin neuropathy survey; an assessment of patient reported effects of coenzyme Q10 on the most commonly reported symptoms; an evaluation of the frequency distribution of spontaneous vs elicited symptom reporting; and of the relation between frequency of patient reporting and literature reports of different symptoms. Hypothesis generating information obtained from this effort led has led to a suite of submitted NIH grants with one funded.

Preliminary results: Approximately 850 participants have completed general surveys, with smaller numbers additionally completing muscle, cognition, and neuropathy surveys. Among 844 general survey subjects whose records were analyzed, X (n = X) reported muscle weakness, X% reported fatigue (n = X), and X% (n =X) reported cognitive problems. The approach was successful in identifying potential AEs that were previously unreported including transient global amnesia (~30 cases); irritability (case series published); and glucose elevation (which has now been verified in a randomized trial, the PROVE-IT/TIMI trial). An analysis of subjects who reported cognitive effects showed that over 60% also reported muscle effects, which motivated our hypothesis of a common mitochondrial mechanism. We procured supportive pilot 31P-MRS data on one subject and continue to seek funding to examine this in more detail. A series of ALS-like cases and cases of Parkinson's disease have come to our attention, and we are addressing use of other databases to examine a possible connection.

Future Direction: 1. Piloting of the internet version of surveys and trouble-shooting will be followed by securing test-retest reliability information; and information on convergent validity. 2. At that point more active recruitment efforts will begin through internet and media.