Efficacy of injectable extended-release naltrexone for severe and chronic relapsing alcohol use disorders

**Background:** According to the World Health Organization, alcohol use disorders are the third leading cause of disease burden in developing countries. Unfortunately, the percentage of patients receiving pharmacotherapy to treat this condition is still very small. Naltrexone is a mu opioid antagonist that is posited to reduce the neurobiological reward obtained from alcohol by causing reduced dopamine release, craving, and reduced alcohol intake. Naltrexone oral has better outcomes when taken consistently, but unfortunately people suffering the severe later stages of alcohol use disorders (AUD) have notoriously low medication adherence and high medical and behavioral crisis ED visits, complicated by costly hospitalizations in turn. One solution to this problem has been the development of a injectable extended-release naltrexone (XR-NTX) which provides a sustained release of medication for up to four weeks. This more aggressive sustained pharmacotherapy remains unappreciated and underused in the management of chronic AUD.

**Introduction:** This study subjects comprised 25 Minneapolis VA Medical Center patients with a diagnosis of severe alcohol dependence receiving injectable extended-release naltrexone (XR-NTX) at any time during their treatment course. They had been offered this medication option because of their demonstrated treatment resistance to conventional abstinence approaches. The efficacy of the medication was determined by how many alcohol related emergency room visits took place and whether the patient was on or off the XR-NTX at the time of the visit. During both the pre and post stages the ED was the best indicator of admit to both medical and psychiatric inpatient beds for costly acute care for AWS, Delirium and Suicide intent. In most cases the time on monthly ER-NTX administrations proved to be discontinuous rather than sustained. Nonetheless a comparison of effectiveness of the medical morbidity in the year prior to intervention with XR-NTX and afterward for more than 2 years of episodic treatment was reviewed.

**Methods:** This study entailed a detailed, retrospective chart review of 25 Minneapolis VA Medical Center patients ≥18 years with a diagnosis of alcohol dependence, documented treatment resistance to conventional abstinence approaches, and who then received extended-release naltrexone injection at any time during their treatment course. Subjects encompassed a broad age range, with 24/25 males. Subjects were identified by the VA pharmacy Prior Approval Requests for ER-NTX submitted by addiction physicians after its formulary inclusion in 2008. The patient had to meet the defined VA use criteria and give voluntary consent to the parenteral injection procedure. The efficacy of the medication was evaluated by the number of alcohol related ED visits before and after the first naltrexone injection and Blood Alcohol Level (BAL) and/or breathalyzer values at the time of the ED visit. Results here focus on the number of ED visits prior to- and following the first naltrexone injection.

**Data collection process:** Medical records of 25 subjects were abstracted. The study successfully extracted medical records for the 12 month interval immediately before the first naltrexone injection (reference date) for 21 of the 25 subjects (with 4, 7, 10, and 11 months of look-back available for the other 4 subjects), and medical records were extracted for at least 12 months following the reference date for all 25 subjects. Longitudinal data included naltrexone injection dates, blood alcohol level/Breathalyzer measurement dates and results, alcohol-related ED visits and their duration, shown in a time continuum before, during, and after receiving naltrexone.
Results: Alcohol-related ED visit results. The 25 subjects had an average of 1.68 alcohol-related ED visits in the 12 months immediately before the first naltrexone injection, compared with 0.96 visits per year in the first 12 months after treatment. The statistically significant rate ratio of 0.56 corresponds to a 44% reduction in the rate of alcohol-related ED visits.

Conclusions: The number and rate of alcohol-related ED visits was reduced in patients having a diagnosis of severe alcohol dependence following administration of injectable extended-release Naltrexone. Naltrexone extended release reduces the occurrence and frequency of alcohol-related emergency room visits during the approximately 4-week period it is actively released from its depot stores. Even discontinuous monthly ER-NTX administration for up to 3 years still resulted in a 51% reduction in the rate of ED visits compared to the year prior to first dose. The discontinuous treatment presentation may be reduced by an assertive case management model of intervention for improved adherence to care and reduced morbidity and costly ED visits.

Biography
Scott McNairy has 38 years’ experience in the delivery of clinical health care focused on treatment for chronic pain, addictive and combat stress disorders. He is Board Certified in the Addiction Psychiatry. His post-graduate training in psychiatric medicine began at the Mayo Clinic 1975-1979. He is most indebted to early Mayo consultants for pioneering novel addiction and pain medicine treatment practices which serve as a foundation for his practice at the VA medical center Minneapolis. He has had a lifelong interest in using evidence-based psychopharmacology, blended with alternative and complementary treatment approaches. Scott was an early board member for Minneapolis Pathways, one of the first health crisis resource centers for life-threatening medical illness in the country. Many of those practices are now well-integrated in to treatment for cancer and end of life care. He champions greater use of addiction pharmacotherapy in primary care and psychiatry and trains physicians for the DEA buprenorphine waivered licensure. Another current interest is the utilization of pharmacy data mining for monitoring treatment outcomes that will enhance patient safety and care. His clinical outcome studies have included 1) development of a medication management support group for opioid dependent patients treated with buprenorphine to promote treatment success and 2) the use of parenteral depot naltrexone for high medical risk, chronic and treatment refractory alcohol dependent veterans which dramatically reduces overall costs of care and disease progression. At the University of Minnesota - VA campus he directs the fellowship in addiction psychiatry and site directs the ABAM addiction medicine fellowship newly recognized by ABMS and the Board of Preventive Medicine. He is recognized for his excellence in teaching and modeling positive clinical encounters. He places primary emphasis on restoration of function and prevention of deterioration as outcomes for success. Scott is an integral part of a treatment team comprised of physicians, nurses, social workers and psychologists without whom he could not have achieved the success that he has had.

scottmd75@mac.com