

# THE EFFECTS OF DISEASE-MODIFYING ANTIRHEUMATIC DRUGS ON DEMENTIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: A POPULATION-BASED PROPENSITY-MATCHED COHORT STUDY OVER 15 YEARS

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## Background

Classical disease-modifying anti-rheumatic drugs (cDMARDs) have proven efficacy and can control disease activity, reduce joint erosions and improve quality of life. Rheumatoid arthritis (RA) is a systemic inflammatory disease and cDMARD therapy has also been shown to improve extra-articular inflammation-driven features such as accelerated cardiovascular disease. The aim of this study is to describe the association of cDMARD use on dementia.

## Methods

Incident diagnoses of RA in persons aged over 18 years from 1995 to 2011 were identified from the UK CPRD. The time-varying exposure of interest was whether or not a patient had been prescribed a cDMARD following RA diagnosis. Confounding variables included age, sex, body mass index, drinking, smoking, year of RA diagnosis, disease duration, UK region, co-morbidities, first presenting symptoms for early RA, medication use, steroid use and severity of RA. The outcome was time from RA diagnosis to dementia diagnosis. Propensity score matching was used to minimize confounding by indication. Kaplan–Meier plots estimated the probability of free-of-dementia up to fifteen years after RA diagnosis. Fine and Grey competing risks survival regression (with robust standard errors to allow for clustering on matched sets) described the association of cDMARD use on time to dementia.

## Results

Data were available on 11,772 patients with incident RA, of whom 8,312 (70.6%) became cDMARD users. These were followed for a median (interquartile range) of 6.5 (3.4–9.9) years (cDMARD users) and 5.1 (2.2–8.6) (non-users). cDMARD users were younger (mean age 58.3) compared to non-users (mean age 65.9) and a similar proportion were female (70%) in both groups. cDMARD users were more likely to drink and smoke, but less likely to have co-morbidities (e.g. cardiovascular related), be taking medications (e.g. antihypertensive) or steroids (prednisolone). To address the issue of confounding by indication 3,876 cDMARD users were propensity score matched to 1,938 non-users. Of the cDMARD users, 2,355 (60.8%) received Methotrexate, and 1,521 (39.2%) other cDMARDs. We observed a reduced risk of dementia in cDMARD users versus non-users, these being 0.5% versus 1.6% at 5-years and 1.5% versus 3.0% at 15- years.

Kaplan–Meier survival curves demonstrated that matched cDMARD users had a significantly lower probability of dementia. Regression models confirmed a lower risk of dementia in cDMARD users

versus non-users [Hazard Ratio 0.60 (95% CI (0.42, 0.85))]. The effect was strongest in Methotrexate users (Hazard Ratio 0.53 (95% CI 0.34, 0.82)).

### **Conclusion**

Although dementia was uncommon, the large sample size afforded by the study allowed us to identify a highly significant reduction in risk of dementia in cDMARD users. As a model of systemic inflammation, the strong effect of cDMARD use on a halving of dementia risk requires replication in a trial and may provide an important therapeutic pharmacological treatment.

### **Disclosure statement**

A.J.: Consultancies: Servier, UK Renal Registry, Oxford Craniofacial Unit, IDIAP Jordi Gol, Freshfields Bruckhaus Deringer. Honoraria: Anthera Pharmaceuticals. Grants/ research support: Roche. D.P-A.: Honoraria: Amgen Spain. N.K. Arden: Honoraria: Merck, Merck Sharp and Dohme, Roche, Novartis, Smith and Nep. C.C.: Honoraria: Servier, Amgen, Eli Lilly, Merck, Medtronic, Novartis. C.J.E.: Honoraria: Roche, UCB, Abbott, GlaxoSmithKline, Pfizer.