

# **Incidence of total hip and knee replacement in Ankylosing Spondylitis patients within the UK**

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Dear Editor,

Ankylosing spondylitis (AS) is a chronic inflammatory disease of the axial skeleton manifested by back pain and progressive stiffness. However, It is not uncommon for peripheral joints to be involved, the underlying histopathology of which is characterised by subchondral bone inflammation that can result in joint erosion and eventual destruction. There has been emerging data on the need for joint replacement surgery among AS patients (1-3), although these data have mainly originated from cohorts of AS patients under hospital care or registry data and as such maybe more selective of severe disease. Our aim here was to better understand the need for joint replacement surgery in the overall AS population in UK actual-practice by using NHS primary care electronic medical records to determine the incidence of total hip (THR) and knee replacement (TKR) following diagnosis of AS.

We identified patients in the Clinical Practice Research Datalink (CPRD) with a first diagnosis of AS within the UK between 01/01/1995 and 31/03/2014. We excluded patients with a diagnosis of >1 type of inflammatory arthritis. CPRD is a primary care database that includes computerised anonymised general practitioner records for over six million current patients within the UK. First occurrence of THR or TKR after AS diagnosis was identified using previously published/validated Read code lists (4). Patients were followed from AS diagnosis up until date of first recorded THR and/or TKR (analysed separately) or censoring (death, transference out of CPRD or end of study period (April 2014)). Unadjusted incidence rates were calculated per 1,000 person-years (PYs) and stratified by sex, age category, indices of multiple deprivation (IMD), region and availability of anti-TNF therapy for AS patients (i.e. before vs. after publication of NICE TA143 in 2008).

We identified 9,766 incident AS patients, for which mean age at diagnosis was 50.0 years (S.D. 16.8) and of whom 62.1% were female. In total, 173 THRs and 139 TKRs occurred at an incidence rate of 2.65/1,000 PYs (95% CI 2.29-3.08) and 2.13/1,000 PYs (95% CI 1.80-2.51), respectively. Incidence rates stratified by demographic variables are shown in table 1. In summary, joint replacement rates rose with increasing age but did not change according to gender, geographic region, availability of TNF- $\alpha$  inhibitors or index of multiple deprivation (IMD), although there was a trend toward lower rates among those most deprived. Overall 5-year cumulative percentage probability (using the Kaplan-Meier method) of THR and TKR were 1.28% (95% CI 1.05-1.55) and 1.04% (0.83-1.30), respectively. At 10 years these rates were 2.55% (2.14-3.02) and 1.79% (1.47-2.19) (figure 1a & figure 1b).

For the general UK population (CPRD), previously reported estimates of 10-year risk (aged 50) of undergoing THR were 1.1% (95% C.I. 0.8-1.4) and 0.8% (95% C.I. 0.5-1.0) for females and males, respectively (5). Estimates for TKR were 1.1% (95% C.I. 0.8-1.4) and 0.6% (95% C.I. 0.4-0.9) for females and males, respectively. Our data, in conjunction with these previous estimates, tend to suggest a greater need for both THR and TKR in AS patients compared to the general population, especially so for THR.

Comparing our estimates to those of previous AS studies is however difficult due to differences in study designs and data used. Interestingly, we identified more AS cases in females than males. This finding is not without support from recent population and MRI-based studies that show approximately comparable sex ratios and that possibly suggest that male sex is a marker for more severe radiographic disease rather than the disease itself. (6-8)

In contrast to the findings of Nystad et al (2) we did not detect lower THR rates following the introduction of TNF- $\alpha$  inhibitors in AS. Our findings on TKR also contrast with UK studies on rheumatoid arthritis (4, 9). It maybe that we had an inadequate follow up period here following introduction of TNF- $\alpha$  inhibitors in 2008 in order to detect a change. Furthermore, the relatively stable rates of arthroplasty as found here should be interpreted in conjunction with other reports of a general increase in such surgeries for the general population (10).

We acknowledge our lack of individual validation of each patient diagnosis (AS) and surgery (THR/TKR), although the accuracy of TKR/TKR procedures as reported in CPRD has previously been demonstrated (4). We also recognise AS specific clinical variables (e.g. AS severity or presence of enthesal disease) and certain data on demographic characteristics were unknown/incomplete.

A key strength however is the use of a large primary care cohort using “real-world” UK data that includes potentially anyone seen in the NHS with a diagnosis of AS. We here show that 10-year risk of THR and TKR is 2.6% and 1.8%, respectively, which suggests a greater need for THR and, to a lesser extent, TKR in AS patients as compared to the general population. These findings will be helpful for informing health care economic planning for AS patients.

## Figure Legends

Figure 1: Kaplan-Meier estimate: percentage probability of (A) total hip and (B) total knee replacement following Ankylosing Spondylitis diagnosis (first 10 years).

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