Incidence of Total Hip and Knee Replacement in UK Patients with Ankylosing Spondylitis

To the 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 characterized by subchondral bone inflammation that can result in joint erosion and eventual destruction. There have been emerging data on the need for joint replacement surgery among patients with AS[1,2,3], although these data have mainly originated from cohorts of patients under hospital care or registry data and therefore may be more selective of severe disease. Our aim here was to better understand the need for joint replacement surgery in the overall AS population in the United Kingdom by using National Health Service (NHS) primary care electronic medical records to determine the incidence of total hip replacement (THR) and total 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 United Kingdom between January 1, 1995, and March 31, 2014. We excluded patients with a diagnosis of > 1 type of inflammatory arthritis. CPRD is a primary care database that includes computerized, anonymized general practitioner records for over 6 million current UK patients. 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 until the date of first recorded THR and/or TKR (analyzed separately) or censoring [death, transference out of CPRD, or end of study period (April 2014)]. Unadjusted incidence rates were calculated per 1000 person-years (PY) and stratified by sex, age category, indices of multiple deprivation (IMD), region, and availability of anti–tumor necrosis factor (TNF) therapy for patients with AS (i.e., before vs after publication of National Institute for Health and Care Excellence TA143, guidance that first recommended the use of TNF-α inhibitors in AS, in 2008). The CPRD independent scientific advisory committee reviewed and approved the study (protocol number: 14_126RAR). Further ethical approval was not required because this study used only pseudo-anonymized routinely collected health data.

We identified 9766 patients with incident AS. The mean age at diagnosis was 50.0 years (SD 16.8), and 62.1% were female. In total, 173 THR and 139 TKR occurred at an incidence rate of 2.65/1000 PY (95% CI 2.29–3.08) and 2.13/1000 PY (95% CI 1.80–2.51), respectively. Incidence rates stratified by demographic variables are shown in Table 1. Joint replacement rates rose with increasing age but did not change according to sex, geographic region, availability of TNF-α inhibitors, or 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 1 and Figure 2).

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

However, comparing our estimates to those of previous AS studies is difficult because of differences in study designs and data used. Interestingly, we identified more AS cases in women than in men. This finding is not without support from population and magnetic resonance imaging–based studies that show nearly comparable sex ratios and that suggest that male sex may be a marker for more severe radiographic disease rather than for the disease itself[6,7,8].

In contrast to the findings of Nystad, *et al*[2], we did not detect lower THR rates following the introduction of TNF-α inhibitors in AS. Our findings on TKR also contrast with UK studies on rheumatoid arthritis[4,9]. It may be that we had an inadequate followup period to detect a change following introduction of TNF-α inhibitors in 2008. Further, the relatively stable rates of arthroplasty 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 THR/TKR procedures as reported in CPRD has previously been demonstrated[4]. We also recognize that AS-specific clinical variables (e.g., AS severity or presence of entheseal 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 show here that the 10-year risks of THR and TKR are 2.6% and 1.8%, respectively, suggesting a greater need for THR and to a lesser extent, TKR in patients with AS compared to the general population. These findings will be helpful for healthcare economic planning for patients with AS.

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Table 1. Incidence rates (per 1000 person-yrs) of total hip replacement (THR) and total knee replacement (TKR).

Variables	n (%)	THR (95% CI)	TKR (95% CI)
Age, yrs			
< 55	6129 (62.8)	1.05 (0.79–1.41)	0.56 (0.37–0.83)
55–69	2245 (23.0)	5.17 (4.15–6.45)	3.90 (3.03–5.02)
≥ 70	1392 (14.3)	6.91 (5.22–9.14)	7.79 (5.98–10.15)
Sex			
Female	6061 (62.1)	2.72 (2.25–3.27)	2.56 (2.12–3.10)
Male	3705 (37.9)	2.56 (2.00–3.29)	1.39 (1.00–1.95)
IMD			
1st quintile (least deprived)	1535 (15.7)	3.48 (2.50–4.85)	2.48 (1.67–3.67)
2nd quintile	1137 (11.6)	3.46 (2.34–5.12)	2.33 (1.45–3.74)
3rd quintile	991 (10.2)	3.53 (2.34–5.31)	2.58 (1.61–4.16)
4th quintile	957 (9.8)	2.05 (1.19–3.54)	2.21 (1.31–3.73)
5th quintile (most deprived)	831 (8.5)	1.39 (0.70–2.79)	1.74 (0.94–3.24)
Unknown	4315 (44.2)	2.36 (1.86–2.98)	1.91 (1.47–2.48)
Region			
North East	129 (1.3)	3.02 (0.98–9.38)	1.98 (0.49–7.90)
North West	1818 (18.6)	1.68 (1.09–2.61)	1.93 (1.28–2.91)
Yorkshire and Humber	470 (4.8)	2.57 (1.34–4.95)	3.69 (2.14–6.35)
East Midlands	260 (2.7)	0.62 (0.09–4.41)	1.87 (0.60–5.81)
West Midlands	835 (8.6)	2.18 (1.27–3.76)	2.85 (1.77–4.59)
East England	647 (6.6)	2.71 (1.50–4.89)	1.47 (0.66–3.26)
South West	1105 (11.3)	4.51 (3.16–6.46)	2.54 (1.58–4.09)
South Central	843 (8.6)	3.11 (1.93–4.99)	1.45 (0.72–2.90)
London	634 (6.5)	2.54 (1.37–4.73)	1.78 (0.85–3.74)
South East Coast	855 (8.8)	3.94 (2.57–6.05)	2.81 (1.70–4.67)
Northern Ireland	647 (6.6)	1.78 (0.89–3.56)	2.00 (1.04–3.83)
Scotland	742 (7.6)	2.75 (1.63–4.64)	0.98 (0.41–2.34)
Wales	781 (8.0)	2.59 (1.59–4.22)	2.26 (1.34–3.82)
NICE TA143*			
Pre-	6601 (67.6)	2.62 (2.23–3.09)	2.11 (1.76–2.53)
Post-	3165 (32.4)	2.82 (1.96–4.06)	2.23 (1.48–3.36)

*NICE TA143 refers to NICE guidance that first recommended the use of TNF-α inhibitors in ankylosing spondylitis in the UK (2008). IMD: indices of multiple deprivation; NICE: UK National Institute for Health and Care Excellence; TNF-α: tumor necrosis factor-α.

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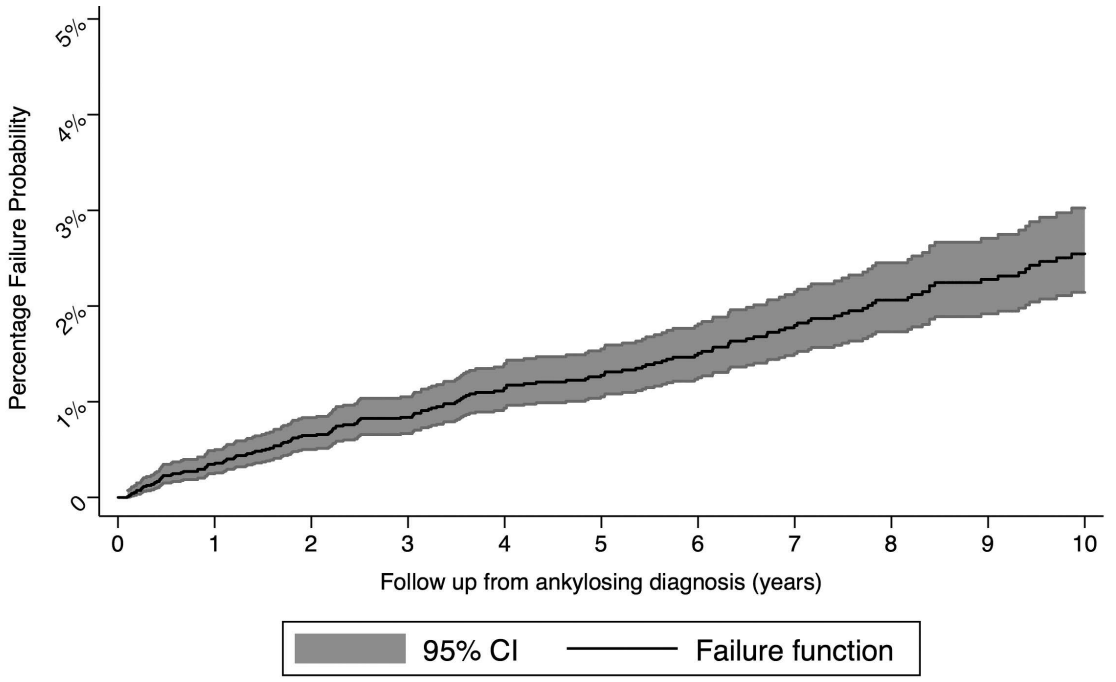

Figure 1. Kaplan-Meier failure function: percentage probability of total hip replacement following ankylosing spondylitis diagnosis (first 10 years).

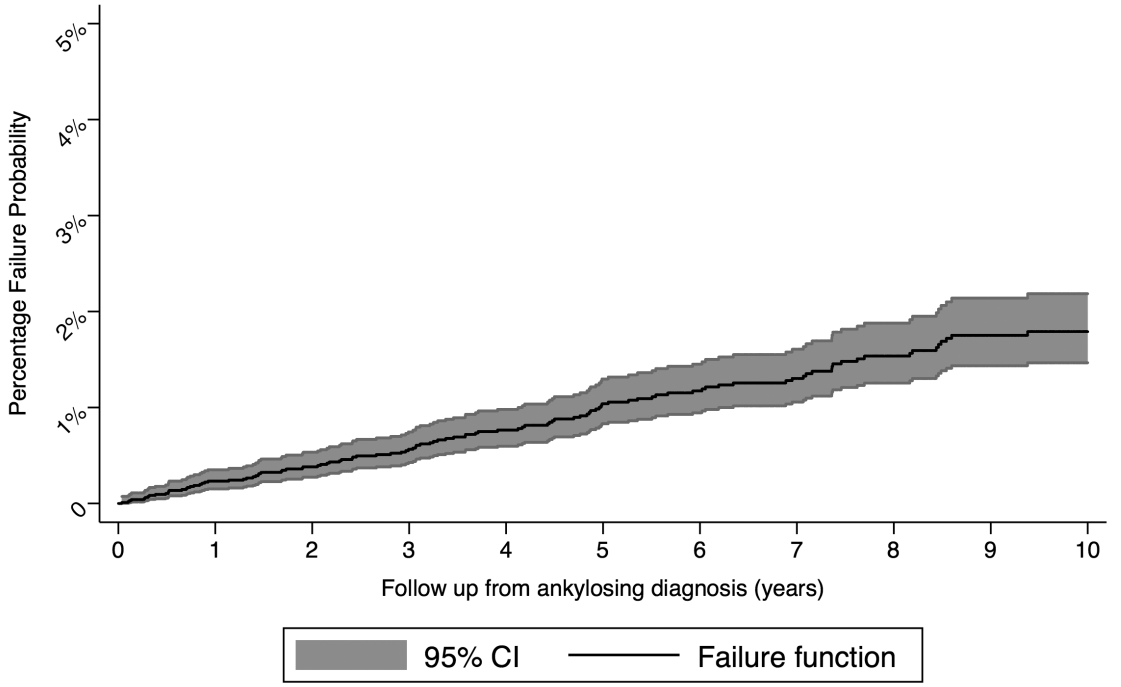

Figure 2. Kaplan-Meier estimate: percentage probability of total knee replacement following ankylosing spondylitis diagnosis (first 10 years).