Dr. Khurana replies

To the Editor:

We appreciate the comments from Dr. Ranganathan and colleagues. We agree that in a large database there are bound to be some inconsistencies, but we believe the large patient population in our database and use of the computerized diagnosis database (with ICD coding methods) decreases the misclassification and recall bias to a large extent.

To answer specific questions raised by Dr. Ranganathan, *et al*: 1. "Use of ICD-9 code for RA accuracy": The report cited by Dr. Ranganathan (Singh, *et al*[2] [above]) suggests the administrative data definition of RA by ICD code 714.0 alone as 100% sensitive but with only 55% specificity. The addition of rheumatoid factor (RF) titer to ICD code 714.0 increased the specificity to 88% with a sensitivity of 91%. Further addition of DMARD prescription changed the sensitivity to only 76% and increased the specificity to 97%. Further in the results, the authors, Singh, *et al*, mention the area under the receiver-operation characteristic (ROC) curve was greatest (0.9) for the definition using ICD 714.0 and a positive RF titer. Other approaches, including ICD 714.0 plus DMARD prescription, DMARD prescription plus positive RF, and ICD 714.0 plus DMARD prescription and positive RF, had intermediate ROC curve areas in the range of 0.84–0.87. In our report, we described the cases of RA on the basis of ICD code 714.0 and those with a positive RF, which does describe the highest accuracy in regard to both sensitivity and specificity in classifying patients with RA. It is also described in Singh, *et al* that addition of DMARD therapy to further enhance the accuracy of the diagnosis of RA led to an unrepresentative sample of RA patients who were not yet started on DMARD therapy. There is also a possibility that some patients may receive drug prescriptions from an outside pharmacy, in addition to or instead of the VA pharmacy, and in those cases the data to include DMARD prescriptions as a more accurate way to diagnose patients with RA would not be valid.

2. "Use of a TNF antagonist was not included": Again as cited in Singh, *et al* [above], some patients may receive drug prescriptions from an outside pharmacy, in addition to or instead of the VA pharmacy, and in those cases the data to include prescriptions as a more accurate way to diagnose patients with RA would not be valid. Further in the reference there are data from clinic visits between January 2001 and July 2002. The data in our report are from 1998 to 2004. Use of anti-TNF data started mainly after 2000, so in our opinion the time was not long enough to influence the malignancy rates in the patients with RA secondary to anti-TNF use. Anti-TNF use causing malignancy by itself is very controversial. Though there are data that RA can increase the risk of malignancy, there are no data to date that anti-TNF therapy by itself increases the risk of malignancy in these patients.

3. "Unknown race making interpretation of the effect of race on outcome unreliable": The next report cited by Dr. Ranganathan (Kressin, *et al*[3] [above]) suggests that after exclusion of patients with missing race/ethnicity, agreement improved except for Native Americans, Asians, Pacific Islanders, and Hispanics. Their data[3] are from 1996-1998, as compared to our data from October 1998 to 2004, when the VA database was being perfected. Even though there was a large number of patients of unknown race (48.2%) for whom there was no observed significant association between lung cancer risk and RA ($p = 0.24$), a majority of the patients (50.3%) were either Caucasian or African American and for either race, risk for lung cancer was significantly increased among those with RA ($p < 0.05$). It can be surmised that most of those with unknown race are of mixed race. Among those known to belong to races other than Caucasian or African American, there was no observed significant association between lung cancer risk and RA ($p = 0.65$); hence, it can be concluded that among patients known to be either Caucasian or African American, risk for lung cancer was significantly higher among those with RA.

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