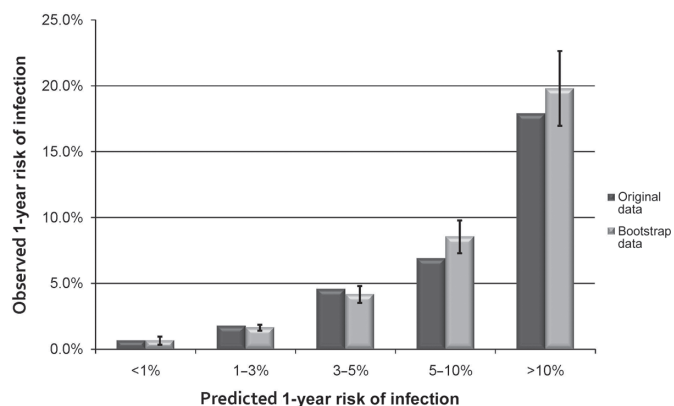


APPENDIX

Derivation and performance of infection risk score in original and bootstrap datasets

To derive and validate the infection risk score, we identified rheumatoid arthritis (RA) patients who were new users of methotrexate (MTX), leflunomide (LEF), sulfasalazine (SSZ) or hydroxychloroquine (HCQ) that were not exposed to any biologic in a subsequent 1-year period. The SSZ and HCQ patients must also have been on MTX in the preceding year so as to identify patients with greater RA severity. The outcome was hospitalised infection in the first year of follow-up (n=202 hospitalised infections used to develop the infection risk score). Logistic regression was used to derive the infection risk score equation by estimating the coefficients for each of the factors included in the score. Factors in the model were selected based upon clinical interest and review of the literature.^{13 26} These factors included age and sex; extra-articular RA (Felty's syndrome or other systemic involvement); comorbidity including prior outpatient infection, prior hospitalised infection, COPD, dementia, peptic ulcer disease, diabetes, obesity, alcoholism, liver disease, ischemic cardiovascular disease, CIRAS,²⁷ the Charlson Comorbidity Index; health services utilisation including number of outpatient physician visits, number of hospitalisations for conditions other than infections, number of liver function lab tests, any rheumatoid factor lab test, mammography; and medications including steroid use/dose (none, 0 to <5 mg/day, 5 to <10 mg/day, ≥10 mg/day) and narcotics.

Because any prediction model is subject to overfitting, we used bootstrapping to assess performance of the infection risk score, randomly selecting 200 bootstrap samples of equal size to the original dataset. Discrimination and calibration were averaged across the bootstrap samples (figure).



The c statistic (area under the receiver operator curve) was 0.74 for the original data; the median c statistic was 0.74 in the bootstrap data. Error bars indicate the SD of the infection risk score. Note: All factors were measured in the 1-year baseline period before starting MTX/LEF/SSZ/HCQ.