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The Risk of Mortality in Patients with Psoriatic Arthritis, Rheumatoid Arthritis, and Psoriasis: A Longitudinal Cohort Study

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Cegedim Strategic Data (CSD) Medical Research UK is an expert in UK anonymous patient data for the healthcare industry. CSD is a commercial organization that supplies data and trains and supports researchers in the use of primary care patient data. Data is available for use in medical research in the academic setting as well as in industry for a fee which varies depending on the type of data requested. Aside from undergoing ethical review by the Scientific Review Committee at Cegedim, independent academic groups who voluntarily act as an ethical review body, this protocol was not in any way discussed with Cegedim nor were any changes made by the company. We did not receive financial support or other forms of computational or analytical support from Cegedim/THIN. The data was collected by Cegedim and the general practitioners without knowledge of the study objectives and hypotheses.

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Abstract

Background—Conflicting reports of the mortality risk among patients with psoriatic arthritis (PsA) exist in the literature. The objective of this study was to examine the risk of mortality in patients with PsA compared to matched controls and to patients with psoriasis and those with rheumatoid arthritis (RA).

Methods—A longitudinal cohort study was performed in a large United Kingdom medical record database,The Health Improvement Network (THIN), among patients with PsA, RA, or psoriasis with data from 1994-2010. Unexposed controls were matched on practice and start date within the practice for each patient with PsA. Cox proportional hazards models were used to calculate the relative hazards for death.

Results—Patients with PsA (N=8,706), RA (N=41,752), psoriasis (N=138,424) and unexposed controls (N=82,258) were identified; 1,442,357 person-years were observed during which 21,825 deaths occurred. Compared with population controls, patients with PsA did not have an increased risk of mortality after adjusting for age and sex (DMARD users: HR 0.94, 95%CI: 0.80-1.10, DMARD non-users: HR 1.06, 95%CI: 0.94-1.19) whereas RA patients had increased mortality (DMARD users HR 1.59, 95%CI: 1.52-1.66, DMARD non-users HR 1.54, 95%CI: 1.47-1.60). Patients with psoriasis who had not been prescribed a DMARD had a small increased risk of mortality (HR 1.08, 95%CI: 1.04-1.12) while those who had been prescribed a DMARD, indicating severe psoriasis, were at increased risk (HR 1.75, 95%CI: 1.56-1.95).

Conclusion—Patients with RA and psoriasis had elevated mortality compared to the general population. However, patients with PsA did not have a significantly elevated risk of mortality.

Keywords

Mortality; Psoriatic Arthritis; Psoriasis; Rheumatoid Arthritis; Epidemiology

Introduction

Psoriatic arthritis (PsA) is a chronic progressive inflammatory disease that affects over 500,000 Americans and can cause permanent joint damage and severe disability.(1) However, it is unclear whether PsA confers an increased risk of mortality as, to date, observational studies have yielded conflicting evidence.(2) Such studies have been limited by small sample size with few events and the potential for selection bias in clinic-based studies. Furthermore, very little is known about the risk of mortality in PsA from a population based perspective.

Given that previous studies have demonstrated increased mortality among patients with psoriasis and RA,(3,4) we hypothesized that patients with psoriatic arthritis would similarly have increased rates of mortality compared to the general population. The objective of this study was to measure the risk of all-cause mortality among patients with psoriatic arthritis as compared to the general population and to patients with psoriasis only (without a diagnosis of psoriatic arthritis) and rheumatoid arthritis.

Methods

Study Design and Data Source

Acohort study was undertaken using data from The Health Improvement Network (THIN) in the United Kingdom (UK) between 1994 and 2010. The UK is an ideal health system for capturing medical record data as the general practitioner (GP) is the primary contact for all aspects of the patient's care.(5) In the United Kingdom, 95% of patients are registered with a general practitioner.(6) Participating GPs record data as a part of routine patient care (e.g., demographics, medical diagnoses, laboratory data, and prescriptions) in the electronic medical record including recommendations made by specialists in secondary and tertiary care. (However, some therapies may be initially prescribed by a specialist and often, the GP will thereafter assume prescribing the medication. Tumor necrosis factor alpha prescriptions are not generally recorded in THIN as these are exclusively prescribed by the specialist.) The data are anonymized and collected by THIN, assessed for quality, and made available for research use.(7) The Health Improvement Network draws patients from 514 general practices and is representative of the United Kingdom population in terms of age, sex, geography, and medical conditions.(8-11)

Study Population

All patients with PsA, psoriasis or RA between the ages of 18 and 89 at the start date were included if they had observation time in THIN after Vision software implementation. Patients were excluded if they died or transferred out of the practice prior to the implementation of Vision software. Up to 10 unexposed controls from the general population were randomly selected for each patient with PsA and were matched on practice and start date within the practice. Unexposed controls were assigned a “diagnosis” date within 6 months of the PsA patient's diagnosis date. This algorithm was designed to minimize bias by ensuring that PsA and unexposed controls are followed by similar doctors during similar time periods. Patients were not eligible to serve as unexposed controls if they had PsA, psoriasis, or RA, or were utilizing disease modifying anti-rheumatic drugs (DMARDs).

Person Time Calculation

Cohort entry was defined as the latest of diagnosis , six months after initial registration with the practice, DMARD initiation, implementation of Vision software in the patient's practice, or a practice acceptable mortality reporting.(7,12) (The first three are patient level factors and last two are practice level factors). The rationale for choosing these elements is further described in the online supplementary methods section. Censoring occurred when the patient died, left the practice, the practice stopped participating in THIN, or study ended in September 2010.

Exposure Definitions

PsA, psoriasis, and RA were defined by the presence of at least one READ code consistent with these diseases. READ codes are a comprehensive hierarchical alphanumeric clinical language developed in the UK to record diagnoses, symptoms, and tests, similar to International Classification of Diseases (ICD) codes.(14) READ codes for psoriasis and rheumatoid arthritis have been previously validated within the same or analogous large medical record databases.(15-17) READ codes for psoriatic arthritis have a positive predictive value of 85% as determined by survey of 100 randomly selected general practitioners caring for patients with PsA.(18) We have also used this definition of PsA in other studies.(19)

Outcome Definition

The primary outcome, death, was defined by specific codes noting death and/or codes indicating the patient was transferred out of the practice because of that person's death.(13) An algorithm recommended by Cegedim, the administrators of THIN, was used and identifies death codes from within the patient, medical, and administration files. This algorithm has been used in other studies and has a sensitivity of 99.7%.(13)

Covariates of Interest

All covariates of interest were measured prior to cohort entry. The following potential confounders were measured: Charlson comorbidity score,(20) smoking, body mass index, blood pressure at baseline, depression, prior hospitalization in the baseline follow up period, year of cohort entry, socioeconomic status (via Townsend deprivation score), urban versus rural living environment, chronic kidney disease, heart disease, atrial fibrillation, diabetes, hypertension, history of cancer, asthma, chronic obstructive pulmonary disease, and liver disease. Furthermore, a priori we hypothesized a statistical interaction between disease status and DMARD use. DMARDs included methotrexate, sulfasalazine, azathioprine, leflunamide, cyclosporine, mycophenolate, hydroxychloroquine, and biologic disease modifying agents including adalimumab, etanercept and infliximab. In the United Kingdom, these medications can be prescribed by consultants (specialists) but should be captured by general practitioner records with the exception of the biologic medications which are rarely recorded.(18)

Statistical Analysis

Power calculations prior to the start of the study revealed that with 7,000 patients with PsA and 35,000 unexposed patients, we would have 96% power to detect a hazard ratio as small as 1.05 for patients with PsA with an average of 5 years of follow-up per patient. Descriptive statistics were used to examine age, sex, person-time and covariate distribution between the four groups. We fit Cox proportional hazards regression model, adjusting for age and sex, to determine the overall hazard ratio (HR) for each group compared to the unexposed. We then tested the hypothesized statistical interaction and fit models with the hypothesized confounders using a purposeful selection modeling approach.(21) More detail with regard to the modeling approach can be found in the online supplementary methods. Log-log survival plots were generated to assess the assumption of proportionality. All statistical analysis was performed using STATA 11.0 (College Station, TX).

Sensitivity analyses

The following sensitivity analyses were conducted: 1) Multiple imputation was performed for body mass index and smoking status where missing and models containing these variables were retested. 2) DMARDs were included as a time-varying covariate rather than a stratification variable. 3) We restricted patients to only those followed for at least one year prior to start date to ensure capture of comorbidities. 4) To examine whether missed DMARD prescriptions would have an impact on the results, we imputed additional DMARD users by first creating a propensity score for DMARD use and then assigning 25% of the non-DMARD users with the highest propensity scores to DMARD use. 5) We restricted the cohort to only those with incident disease defined as patients with at least one year of follow up prior to the first diagnosis code. 6) Finally, we conducted an unmeasured confounder analysis to test the assumption that there is a confounder that we are unable to measure that may skew the results had we been able to measure this confounder. More detail with regard to the methods used in the sensitivity analyses can be found in the online supplementary methods.

Ethics Board Approval

All data in this study was anonymous to the investigators. This study was approved by the University of Pennsylvania Institutional Review Board and Cegedim's Scientific Review Committee.

Results

Between 1994 and 2010, 8,706 patients with PsA, 41,752 with RA, and 138,424 patients with psoriasis met inclusion criteria and 82,258 unexposed patients were randomly selected using the described criteria. Baseline characteristics are displayed in Table 1. Age was significantly greater among patients with RA. RA patients were predominantly female while the male: female ratio was closer to 1:1 in the other three groups. Mean person time contributed was 5.3 years. Median year of cohort entry was one year earlier for patients with RA compared to the other three groups. DMARDs were prescribed to 48%, 52% and 3% of patients with PsA, RA and psoriasis respectively. Prevalence of comorbidities was highest among patients with RA in nearly all categories.

Among the 271,140 patients, 21,825 deaths were observed over 1,442,238 person years (Table 2). The unadjusted incidence of mortality was highest in patients with RA (Table 3). The interaction between disease status and history of DMARD use was statistically significant and therefore results stratified by DMARD use are presented. The addition of hypothesized confounders to the model did not change the model substantially. (All of the covariates listed in the methods section were tested but individual p-values and hazard ratios are not provided due to space restrictions). Therefore, the final model is the age- and sex-adjusted model demonstrating increased mortality risk among patients with RA (DMARD users HR 1.59, 95%CI: 1.52-1.66, DMARD non-users HR 1.54, 95%CI: 1.47-1.60)and psoriasis (DMARD users HR 1.75, 95%CI: 1.56-1.95, DMARD non-users HR 1.08, 95%CI: 1.04-1.12) but no increased mortality risk among patients with psoriatic arthritis (DMARD users HR 0.94, 95%CI: 0.80-1.10, DMARD non-users HR 1.06, 95%CI: 0.94-1.19).

Reasons for censoring (patient leaving the practice, practice stopped contributing to THIN, and end of study in September 2010) were not significantly different among the groups (see online supplementary Table S1). The five sensitivity analyses conducted did not change the results of the final model (Table S2). An unmeasured confounder analysis revealed that the even if the unmeasured confounder has a hazard ratio of 10.0 and a prevalence of 60% among patients with PsA, the mortality risk for patients with PsA would not significantly change (Table S3).

Conclusion

In this large population-based study, we found that patients with psoriatic arthritis did not have a statistically significant elevation in mortality compared to the general population. Furthermore, patients with rheumatoid arthritis and those with severe psoriasis (DMARD users) had significantly higher mortality than the general population. The elevated all-cause mortality risk in patients with psoriasis not utilizing DMARDs (8% increase over the general population) is small and statistically similar to the PsA groups based on the 95% CIs. These results are consistent with the findings of other population-based studies (3,4,22-29) and were robust to multiple sensitivity analyses. This is the first study to directly compare the risk of all-cause mortality in PsA to an unexposed population rather than using standardized mortality ratios to compare to census statistics. Internal controls are generally felt to provide a better approximation of the true effect than standardized mortality ratios.(30)

Most previous studies of mortality in PsA have been performed within specialty clinics. These studies have had mixed results ranging from no difference in mortality when compared to local census statistics to a standardized mortality ratio (SMR) of 1.62 (95% CI: 1.21-2.12).(31) (Of note, the SMR was 1.36, 95%CI: 1.12-1.64, in the same cohort 10 years later).(32) Clinic and hospital-based studies demonstrating higher mortality could be capturing a larger proportion of patients with severe disease reflecting selection bias. In the general population, a larger proportion of patients are likely to have mild disease. It is possible that severity of disease is a driver of mortality risk. We were unable to test this hypothesis in THIN, however, a sensitivity analysis demonstrated that the effect size of this unmeasured confounder must be substantial (HR=10) in order to change the results. Finally, it is possible that mortality has declined over time in the PsA population.(32) However, adjusting the regression model for start year in the cohort did not change the results of the final model.

Population-based studies using large medical record databases have tremendous advantages in examining mortality. Consideration must be given to the choice of the unexposed or control population in such studies as control patients may not have regular contact with their physicians and new diagnoses or events may not be captured. It was for this reason that we chose to include only patients who had contact with their GP around the time the matched patient with PsA was diagnosed. Selecting patients in this way may increase the “illness level” of patients in the unexposed group and reduce the hazard ratio for mortality in patients in the exposed groups. Therefore, it is possible that there is a minimally increased risk of mortality in patients with PsA. On the other hand, we included patients with prevalent diagnoses in this study. Studies including patients with prevalent diagnoses are generally thought to have higher mortality rates than those with incident disease.(33) However, a sensitivity analysis including only cases with at least one year prior to the first diagnosis code (a commonly used definition of incident disease) did not substantially change the results.

Potential limitations of this study include misclassification of diagnoses and missing information regarding DMARD use. Our previous validation study showed limited misclassification of patients with a psoriatic arthritis diagnosis (i.e., a high positive predictive value for the diagnostic code).(18) In fact, there was an even higher PPV (93%) for patients with a diagnostic code for PsA patients with a DMARD prescription, further decreasing the likelihood that misclassification could be the reason for the null result (unpublished data). While we are confident in the diagnostic code for PsA, there may be patients with PsA categorized as psoriasis only (e.g., undiagnosed cases of PsA among patients with psoriasis).(34) It is not possible to identify the frequency of this phenomenon in this population-based study. Population based studies such as those performed in THIN often lack information on disease activity measures and disease characteristics. However, the goal of this study was to examine patients with already diagnosed PsA, a more specific cohort than all patients with possible PsA. Misclassification of the outcome is not a major concern as mortality is unlikely to be subject to surveillance bias because it has near complete ascertainment.(13) This population-based study draws from a larger cohort, THIN, which is felt to be representative of the UK but may over-represent more affluent areas.(11) However, adjusting for socio-economic status (via Townsend deprivation score) did not change the results. Finally, use of DMARDs is difficult to model in an observational study and can be performed in numerous ways, though all are limited by confounding by indication.(35,36) We chose to classify patients as “ever” or “never” users because we were using DMARDs as a stratification variable and we hypothesized that patients prescribed therapy may be different than patients who had not been prescribed therapy. There may be under-reporting of DMARD use in cases where the consultant is the primary prescriber, despite the fact that this may be recorded by the GP in the medical record, and this could

result in misclassification. However, increasing the number of DMARD users by 25% did not significantly change the results.

In conclusion, we present the results of a large population-based study demonstrating elevated mortality in severe psoriasis and rheumatoid arthritis but no statistically significant elevation in mortality among patients with psoriatic arthritis. The lack of higher mortality in patients with PsA has been previously demonstrated in smaller population-based cohorts. Despite a lack of higher mortality, there is still significant morbidity in patients with PsA including concomitant illnesses and impaired quality of life. Future research efforts are needed to identify mechanisms by which we can improve comorbidities and quality of life for patients with psoriatic arthritis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Gladman D, Antoni C, Mease P, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis. 2005; 64(Suppl II):ii14–ii17. [PubMed: 15708927]
2. Gladman DD. Mortality in psoriatic arthritis. Clin Exp Rheumatol. 2008; 26(Suppl 51):S62–S65. [PubMed: 19026145]
3. Gelfand JM, Troxel AB, Lewis JD, et al. Risk of Mortality in Patients with Psoriasis: Results from a population-based study. Arch Dermatol. 2007; 143(12)
4. Sokka T, Abelson B, Pincus T. Mortality in rheumatoid arthritis: 2008 Update. Clin Exp Rheumatol. 2008; 26(S51):S35–61. [PubMed: 19026144]
5. deLusignan S, Stephens P, Naeema N, et al. Does feedback improve the quality of computerized medical records in primary care? J American Medical Informatics Assoc. 2002; 9:395–403.
6. Ogdie, A.; Langan, S.; Parkinson, J., et al. Medical Record Databases. In: Strom, B.; Kimmel, S.; Hennessy, S., editors. Pharmacoepidemiology. 5th. Oxford, UK: Wiley-Blackwell; 2012. p. 224-243.
7. Cegedim Strategic Data. [Accessed Nov 8, 2012] THIN Data Quality Assurance. Available at: http://csdmruk.cegedim.com/our-data/data-quality.shtml
8. Cegedim Strategic Data. [Accessed Nov 8, 2012] The Health Improvement Network: Our Data. Available at: http://csdmruk.cegedim.com/our-data/our-data.shtml
9. Lewis JD, Schinnar R, Bilker WB, et al. Validation studies of the health improvement network (THIN) database for pharmacoepidemiology research. Pharmacoepidemiol Drug Saf. 2007; 16:393–401. [PubMed: 17066486]
10. Haynes K, Bilker WB, Tenhave TR, et al. Temporal and within practice variability in the health improvement network. Pharmacoepidemiol Drug Saf. 2011; 20(9):948–55. [PubMed: 21755569]
11. Blak B, Thompson M, Dattani H, et al. Generalisability of The Health Improvement Network (THIN) database: demographics, chronic disease prevalence and mortality rates. Informatics in Primary Care. 2011; 19(4):251–55.

12. Maguire A, Blak B, Thompson M. The importance of defining periods of complete mortality reporting for research using automated data from primary care. Pharmacoepidemiol Drug Saf. 2009; 18:76–83. [PubMed: 19065600]
13. Hall GC. Validation of death and suicide recording on THIN UK primary care database. Pharmacoepidemiol Drug Saf. 2009; 18(2):120–31. [PubMed: 19109801]
14. Chishom J. The Read clinical classification. BMJ. 1990; 300:1092. [PubMed: 2344534]
15. Watson DJ, Rhodes T, Bing C, et al. Lower Risk of Thromboembolic Cardiovascular Events with Naproxen Among Patients with Rheumatoid Arthritis. Arch Intern Med. 2002; 162:1105–1110. [PubMed: 12020179]
16. Garcia Rodriguez LA, Tolosa LB, et al. Rheumatoid arthritis in UK primary care: incidence and prior morbidity. Scand J Rheumatol. 2009; 38:173–177. [PubMed: 19117247]
17. Seminara NM, Abuabara K, Shin DB, et al. Validity of The Health Improvement Network (THIN) for the study of psoriasis. Br J Dermatol. 2011; 164(3):602–9. [PubMed: 21073449]
18. Ogdie A, Langan S, Love T, et al. Prevalence and treatment patterns of psoriatic arthritis in the United Kingdom. Rheumatology. 2012 In Press.
19. Love T, Zhu Y, Zhang Y, et al. Obesity and the risk of psoriatic arthritis: a population-based study. Ann Rheum Dis. 2012; 71(8):1273–7. [PubMed: 22586165]
20. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chron Dis. 1987; 40(5):373–383. [PubMed: 3558716]
21. Bursac Z, Gauss CH, Williams DK, et al. Purposeful selection of variables in logistic regression. Source Code Biol Med. 2008; 3(17)
22. Shbeeb M, Uramoto KM, Gibson LE, et al. The epidemiology of psoriatic arthritis in Olmsted County, Minnesota, USA 1982-1991. J Rheumatol. 2000; 27:1247–50. [PubMed: 10813295]
23. Watson DJ, Rhodes T, Guess HA. All-cause mortality and vascular events among patients with rheumatoid arthritis, osteoarthritis, or no arthritis in the UK General Practice Research Database. J Rheumatol. 2003; 30:1196–202. [PubMed: 12784389]
24. Bjornadal L, Baecklund E, Yin L, et al. Decreasing mortality in patients with rheumatoid arthritis: results from a large population based cohort in Sweden, 1964-95. J Rheumatol. 2002; 29:906–12. [PubMed: 12022348]
25. Doran MF, Pond GR, Crowson CS, et al. Trends in incidence and mortality in rheumatoid arthritis in Rochester, Minnesota, over a forty-year period. Arthritis Rheum. 2002; 46:625–31. [PubMed: 11920397]
26. Myllykangas-Luosujarvi R, Aho K, Kautianien H, et al. Shortening of life span and causes of excess mortality in a population-based series of subjects with rheumatoid arthritis. Clin Exp Rheumatol. 1995; 13:149–53. [PubMed: 7656460]
27. Mikuls TR, Saag KG, Criswell LA, et al. Mortality risk associated with rheumatoid arthritis in a prospective cohort of older women: results from the Iowa Women's Health Study. Ann Rheum Dis. 2002; 61:994–9. [PubMed: 12379522]
28. Thomas E, Symmons DP, Brewster DH, et al. National study of cause-specific mortality in rheumatoid arthritis, juvenile chronic arthritis, and other rheumatic conditions: a 20 year follow up study. J Rheumatol. 2003; 30:958–65. [PubMed: 12734889]
29. Sihvonen S, Korpela M, Mustonen J, et al. Renal disease as a predictor of increased mortality among patients with rheumatoid arthritis. Nephron Clin Pract. 2004; 96:c107–14. [PubMed: 15122064]
30. Card TR, Solaymani-Dodaran M, Hubbard R, et al. Is an internal comparison better than using national data when estimating mortality in longitudinal studies? J Epidemiol Community Health. 2006; 60:819–21. [PubMed: 16905729]
31. Wong K, Gladman DD, Husted J, et al. Mortality studies in psoriatic arthritis: results from a single outpatient clinic; causes and risk of death. Arthritis Rheum. 1997; 40(10):1868–72. [PubMed: 9336423]
32. Ali Y, Tom BDM, Schentag CT, et al. Improved survival in psoriatic arthritis with calendar time. Arthritis Rheum. 2007; 56(8):2708–14. [PubMed: 17665458]

33. Gordis, L. Measuring the Occurrence of Disease: Mortality Epidemiology. 4th. Philadelphia, PA: Saunders Elsevier; 2004. p. 59-84.

34. Ibrahim G, Waxman R, Helliwell PS. The prevalence of psoriatic arthritis among patients with psoriasis. Arth Care & Research. 2009; 61(10):1373–1378. [PubMed: 19790120]

35. Strom, B.; Melmon, KL. The Use of Pharmacoepidemiology to Study Beneficial Drug Effects. In: Strom, B.; Kimmel, S.; Hennessy, S., editors. Pharmacoepidemiology. 5th. Oxford, UK: Wiley-Blackwell; 2012. p. 224-243.

36. Dixon WG, Bansback N. Understanding the side effects of glucocorticoid therapy: shining a light on a drug everyone thinks they know. Ann Rheum Dis. 2012; 71(11):1761–4. [PubMed: 22851467]

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Table 1

Demographics

N		**Control 82,258**	**PsA 8,706**	**RA 41,752**	**Psoriasis 138,424**
Male Sex (%)		45%	51%	29%	49%
Age (mean)		49.9	50.7	61.4	47.6
Cohort Time (yrs)		5.25	5.21	5.29	5.38
Start Year (Median)		2003	2003	2002	2003
Townsend* (Median)		2.57	2.53	2.68	2.66
DMARD N (%)		0	4213 (48%)	21,910 (52%)	3,577 (3%)
Hospitalized in baseline period		11,558 (14%)	1,383 (16%)	8,094 (19%)	16,861 (12%)
Disabled		2,106 (2.6%)	447 (5.1%)	3,053 (7.3%)	3,611 (2.6%)
Smoking	Never	39,529 (55%)	4,117 (52%)	18,854 (51%)	54,437 (45%)
N (%)	Past	13,823 (19%)	1,878 (24%)	8,865 (24%)	26,375 (22%)
	Current	18,025 (25%)	1,857 (24%)	9,193 (25%)	40,820 (34%)
	Missing	*10,881 (13%)*	*854 (10%)*	*4,840 (12%)*	*16,792 (12%)*
BMI	Normal	21,639 (43%)	2,274 (34%)	13,391 (40%)	44,819 (41%)
N (%)	Underweight	1,472 (3%)	83 (1%)	1,008 (3%)	2,879 (3%)
	Overweight	16,854 (34%)	2,439 (36%)	11,442 (34%)	37,219 (34%)
	Obese	9,924 (20%)	1,993 (29%)	7,433 (22%)	23,409 (22%)
	Missing	*32,369 (39%)*	*1,917 (22%)*	*8,478 (20%)*	*30,098 (22%)*
Comorbidities	Mean Charlson				
N (%)	Comorbidity Index	0.44	0.41	0.65	0.39
	Diabetes	4,619 (6%)	608 (7%)	3,307 (8%)	7,087 (5%)
	Heart Disease	6,169 (7%)	576 (7%)	5,767 (14%)	9,761 (7%)
	Hypertension	15,349 (19%)	1,901 (22%)	11,895 (28%)	22,899 (17%)
	Dyslipidemia	6,919 (8%)	849 (10%)	4,432 (11%)	10,879 (8%)
	Stroke	2,586 (3%)	219 (3%)	2,372 (6%)	3,987 (3%)
	Kidney Disease	1,730 (2%)	196 (2%)	1,608 (4%)	2,275 (2%)
	Cancer	6,982 (8%)	601 (7%)	4,465 (11%)	10,006 (7%)
	Liver Disease	1,039 (1%)	208 (2%)	750 (2%)	2,075 (1%)

N		Control 82,258	PsA 8,706	RA 41,752	Psoriasis 138,424
	Depression	14,447 (18%)	1,908 (22%)	8,874 (21%)	26,180 (19%)
	Substance Abuse	2,583 (3%)	355 (4%)	1,090 (3%)	6,216 (4%)

*Socioeconomic status was assessed by Townsend deprivation scores using quintiles (1-5) with higher quintiles representing more deprivation.

Table 2

Incidence of Death

		Deaths	Person-Years	Incidence (deaths/1000 PY)
Control		**5330**	**431,730**	**12.35**
PsA	All	470	45,334	10.37
	DMARD	159	20,377	7.80
	No DMARD	311	24,958	12.46
RA	All	7004	220,855	31.71
	DMARD	2903	113,859	24.50
	No DMARD	4101	106,996	38.33
Psoriasis	All	9021	744,318	12.12
	DMARD	328	14,781	22.19
	No DMARD	8693	729,537	11.92

Table 3

Cox Proportional Hazards Models

		HR - Unadjusted	HR – Age and Sex Adjusted	HR - Unadjusted Stratified*	HR – Age and Sex Adjusted, Stratified*
Control		**Ref**	**Ref**	**Ref**	**Ref**
PsA	All	0.84 (0.77-0.92)	1.02 (0.92-1.12)		
	No DMARD			1.00 (0.90-1.13)	1.06 (0.95-1.19)
	DMARD			0.64 (0.55-0.75)	0.94 (0.80-1.10)
RA	All	2.57 (2.48-2.67)	1.56 (1.51-1.62)		
	No DMARD			3.09 (2.97-3.22)	1.54 (1.48-1.61)
	DMARD			2.08 (1.99-2.18)	1.59 (1.52-1.66)
Psoriasis	All	0.98 (0.95-1.01)	1.10 (1.06-1.13)		
	No DMARD			0.96 (0.93-1.00)	1.08 (1.04-1.12)
	DMARD			1.85 (1.65-2.07)	1.75 (1.56-1.95)
Age			1.10 (1.10-1.10)		1.10 (1.10-1.10)
Sex			0.71 (0.69-0.73)		0.71 (0.69-0.73)

* Interaction p-value < 0.001 (likelihood ratio/Wald test)