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2 DR. JAMES ANDREW PRIOR (Orcid ID : 0000-0001-9213-2796)

3 DR. ZOE PASKINS (Orcid ID : 0000-0002-7783-2986)

4 DR. RAM BAJPAI (Orcid ID : 0000-0002-1227-2703)

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10 **Title:** Rheumatological conditions as risk factors for self-harm: A retrospective cohort study  
11 James A. Prior<sup>1,2</sup>, Zoe Paskins<sup>1,3</sup>, Rebecca Whittle<sup>1</sup>, Alyshah Abdul-Sultan<sup>1</sup>, Carolyn A. Chew-  
12 Graham<sup>1,2</sup>, Sara Muller<sup>1</sup>, Ram Bajpai<sup>1</sup>, Tom A. Shepherd<sup>1</sup>, Athula Sumathipala<sup>1,2</sup> & Christian D.  
13 Mallen<sup>1</sup>

14

15 **Authors:**

16 James A. Prior, Lecturer, PhD- j.a.prior@keele.ac.uk

17 Zoe Paskins, Senior Lecturer and Honorary Consultant in Rheumatology, PhD -

18 z.paskins@keele.ac.uk

19 Rebecca Whittle, Research Associate, MSc - r.l.whittle@keele.ac.uk

20 Alyshah Abdul-Sultan, Honorary Senior Research Fellow, PhD - alyshah.sultan@hotmail.com

21 Carolyn A. Chew-Graham, Professor of General Practice Research, MD - c.a.chew-

22 graham@keele.ac.uk

23 Sara Muller, Senior Lecturer, PhD – s.muller@keele.ac.uk

24 Ram Bajpai, Research Fellow, PhD r.bajpai@keele.ac.uk

25 Tom A. Shepherd, Lecturer, PhD - t.a.shepherd1@keele.ac.uk

26 Athula Sumathipala, Professor of Psychiatry, PhD - a.sumathipala@keele.ac.uk

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27 Christian D. Mallen, NIHR Research Professor in General Practice, PhD -  
28 c.d.mallen@keele.ac.uk  
29

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33 **Affiliations:**

34 <sup>1</sup>School of Primary, Community and Social Care, Keele University, UK;

35 <sup>2</sup>Midlands Partnership NHS Foundation Trust, Stafford,

36 <sup>3</sup>Haywood Academic Rheumatology Centre, Midland Partnership NHS Foundation Trust,  
37 Stoke-on-Trent, ST6 7AG, UK

38

39 **\*Corresponding author:**

40 James A. Prior, BSc, MSc, PhD

41 <sup>1</sup>School of Primary, Community and Social Care, Keele University, Staffordshire,

42 ST5 5BG, United Kingdom, E-mail: j.a.prior@keele.ac.uk; Tel: +44(0)1782 734847

43

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57 **Abstract**

58 **Objective**

59 To examine the risk of self-harm in rheumatological conditions

60 **Methods**

61 Retrospective cohort study using data from the Clinical Practice Research Datalink. Patients  
62 with ankylosing spondylitis, fibromyalgia, osteoarthritis or rheumatoid arthritis were  
63 identified between 1990–2016 and matched to patients without these conditions. Incident  
64 self-harm was defined by medical record codes following a rheumatological diagnosis.  
65 Incidence rates (per 10,000 person-years(PY)) were reported for each condition, both  
66 overall and year-on-year(2000-2016). Cox regression analysis determined risk (hazard  
67 ratios(HR), 95% confidence interval(CI)) of self-harm for each rheumatological cohort  
68 compared to the matched unexposed cohort. Initial crude analysis was subsequently  
69 adjusted and stratified by age and gender. Due to non-proportionality over time,  
70 osteoarthritis was also stratified by disease duration(<1 year, ≥1-<5 years, ≥5-<10 years,  
71 ≥10 years).

72 **Results**

73 Incidence of self-harm was highest in patients with fibromyalgia (25.12 (95%CI 22.45,28.11)  
74 per 10,000 PY) and lowest for osteoarthritis (6.48 (6.20, 6.76)). There was a crude  
75 association with each rheumatological condition and self-harm, except for ankylosing  
76 spondylitis. Though attenuated, these associations remained after adjustment for  
77 fibromyalgia (HR 2.06(95%CI 1.60,2.65)), rheumatoid arthritis (1.59(1.20,2.11)) and  
78 osteoarthritis (1-<5years: 1.12 (1.01,1.24); ≥5-<10 years: 1.35 (1.18,1.54)). Age and gender  
79 were weak effect modifiers for these associations.

80 **Conclusions**

81 Primary care patients with fibromyalgia, osteoarthritis or rheumatoid arthritis (but not  
82 ankylosing spondylitis) are at increased risk of self-harm compared to people without these  
83 rheumatological conditions. Clinicians need to be aware of the potential for self-harm in  
84 patients with rheumatological conditions (particularly fibromyalgia), explore mood and risk  
85 with them, and offer appropriate support and management.

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**Significant findings**

- Patients with fibromyalgia, osteoarthritis or rheumatoid arthritis are at increased risk of self-harm.
- Age and gender do not act as strong effect modifiers in the relationship between these rheumatological conditions and self-harm
- In these patients, healthcare professionals need to be aware of this risk and offer appropriate management.

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131 **Introduction**

132 Prevention of self-harm, a key risk factor for suicide, is an international public health priority  
133 (1). However, data from the UK between 2001 to 2013 showed a significant rising trend in  
134 primary care consultations for self-harm for men and women (2). A potential approach to  
135 preventing self-harm is the targeting of high-risk groups, with the World Health  
136 Organization (WHO) recommending that healthcare professionals assess the potential for  
137 self-harm in patient groups with symptoms of chronic pain and depression (3). Though these  
138 factors can apply to patients with rheumatological conditions, it remains unclear whether  
139 patients in these disease groups are at an increased risk of self-harm.

140

141 Our interest lies in examining and comparing the risk of self-harm in specific  
142 rheumatological conditions (ankylosing spondylitis, fibromyalgia, osteoarthritis and  
143 rheumatoid arthritis). These are some of the most prevalent rheumatological conditions  
144 with known relationships to chronic pain and depression. Poor mental health, especially a  
145 history of a depressive disorder, is a strong risk factor for self-harm (4) and comorbid  
146 depression is frequently experienced by patients with these common rheumatological  
147 conditions, to varying degrees (5-9). Although pain is on the causal pathway for depression,  
148 pain is itself an independent risk factor for self-harm (10) and is commonly experienced by  
149 those with rheumatological conditions (11).

150

151 Previous research into the role of a range of chronic health conditions on the risk of self-  
152 harm has shown conflicting findings (12-15). However, investigation into the role of  
153 rheumatological conditions as risk factors for self-harm is currently very limited, despite  
154 these conditions being among the leading causes of disability worldwide (16). Webb et al  
155 reported an initial unadjusted increased risk of self-harm in patients with osteoarthritis, but  
156 this association was not retained after adjustment (12). Singhal et al did find an increased  
157 relative risk (RR) of self-harm for patients with inflammatory polyarthropathies (RR 1.4  
158 (1.3–1.4) after the first year since diagnosis, but this group contained a wide mix of  
159 rheumatological conditions (ICD-10 code: (M05–M09, M12–M14)) limiting the clinical  
160 usefulness of such information (14). Our aim was to examine and compare the risk of self-  
161 harm in several rheumatological conditions from a primary care population over time and  
162 consider the role of age and gender on such risk.

163

## 164 **Patients and Methods**

### 165 *Study design*

166 We undertook a matched retrospective cohort study using Read-coded patient consultation  
167 data (the clinical coding system used in UK primary care) from the Clinical Practice Research  
168 Datalink (CPRD), a database of anonymised primary care records covering around 7% of the  
169 UK population (17). This provides both coded consultation and prescription data and is  
170 representative of the UK population, with regards to age, sex and ethnicity (17).

171

### 172 *Study Population*

173 We identified patients aged  $\geq 18$  years with one of four rheumatological conditions  
174 (ankylosing spondylitis, fibromyalgia, osteoarthritis or rheumatoid arthritis) between 1st  
175 January 1990 and 31st December 2016. Each exposed cohort was identified by specified  
176 Read codes, identified and refined from an internal code list repository  
177 ([www.keele.ac.uk/mrr](http://www.keele.ac.uk/mrr)) and assigned an index date corresponding to the date of their  
178 diagnosis. Where a patient had consulted for more than one of the rheumatological  
179 conditions of interest, they were placed into the rheumatological cohort for which they had  
180 first consulted. A single matched unexposed cohort was constructed to be a comparison  
181 cohort for all rheumatological conditions. The unexposed cohort included individuals

182 without a previous coded diagnosis of the rheumatological conditions of interest in their  
183 medical record, but no further exclusion was made based on the presence of other chronic  
184 disease. Cases were grouped by 10-year age range and gender and then within these  
185 categories' frequency matched to unexposed patients. Each control was assigned a pseudo-  
186 index date, generated at random from between their 18th birthday and the end of the study.  
187 All individuals were subsequently examined for a self-harm Read code, based on the Read  
188 code list used in previous CPRD research (2) (Code list available at [www.keele.ac.uk/mrr](http://www.keele.ac.uk/mrr)  
189 upon request). Patients with a self-harm code prior to index date were excluded and  
190 incidence based only on the first self-harm code reported post-rheumatological diagnosis.

191

### 192 *Statistical Analysis*

193 Descriptive statistics were initially used to characterise the sample of each rheumatological  
194 condition, including age, gender, practice-level deprivation, BMI, smoking status, alcohol  
195 consumption and previous diagnosis for anxiety and/or depression (the latter four defined  
196 by the closest value recorded before the index date). Incidence rates of self-harm per 10,000  
197 person-years (PY) were determined for each rheumatological condition from 01/01/1990 to  
198 31/12/2016 and year-on-year incidence trends were reported for 01/01/2000 to  
199 31/12/2016 (reduced time-period used due to low incidence in earlier years). Patients  
200 contributed data after the latest of three events: (1) the study start date, (2) the date they  
201 registered at a participating practice, plus 6 months or (3) the date at which the practice was  
202 adjudged to reach internal quality standards, known as the 'up-to-standard' date.

203

204 Using Cox proportional-hazards regression analysis over the full time-period (1990-2016),  
205 crude hazard ratios (HR) were initially reported with 95% confidence intervals (CIs) to  
206 examine the association between the presence of each of the four rheumatological  
207 conditions and the subsequent incidence of self-harm compared to the matched unexposed  
208 cohort. Adjusted analysis was then undertaken, accounting for age, gender, practice-level  
209 deprivation, BMI, smoking status, alcohol consumption, anxiety and depression. Cases with  
210 missing data for smoking, BMI and alcohol consumption were included within analysis using  
211 a missing category approach. Imputation was not considered sensible in this case, as data  
212 were unlikely to be missing at random (18, 19). Proportionality of hazards was examined for

213 each model using Schoenfeld's residuals. Where variables showed evidence of non-  
214 proportionality, they were included as time varying covariates. Further analyses were  
215 conducted for each rheumatological cohort, stratifying by median age of the relevant  
216 exposed cohort and gender. We defined our dichotomized age subgroups as "younger" or  
217 "older" patients. This study was approved by the CPRD Independent Scientific Advisory  
218 Committee (reference number 18\_018R3). Data were analyzed with Stata software (version  
219 15.1, StataCorp, College Station, TX, USA). A two-sided p-value <0.05 was considered for  
220 statistical significance.

221

## 222 **Results**

### 223 *Sample characteristics*

224 The number of cases in each rheumatological condition group identified were: ankylosing  
225 spondylitis 10,484, fibromyalgia 17,546; osteoarthritis 410,384 and rheumatoid arthritis  
226 23,205, with a matched unexposed cohort of the same size for each condition. Patient  
227 cohorts with fibromyalgia, osteoarthritis or rheumatoid arthritis were predominantly female  
228 (85.5%, 59.5% & 66.7% respectively) and the mean age across the four condition cohorts  
229 (similar in their unexposed cohorts) ranged from the youngest of 47 years (fibromyalgia) to  
230 the oldest at 65 years (osteoarthritis) (**Table 1**).

231

### 232 *Incidence of self-harm in rheumatological cohorts*

233 Incidence of self-harm was highest in the fibromyalgia cohort at 25.12 (95%CI 22.45, 28.11)  
234 per 10,000 PY, but lower at 11.37 (9.37, 13.81) for ankylosing spondylitis, 9.70 (8.32, 11.29)  
235 for rheumatoid arthritis and 6.48 (6.20, 6.76) for osteoarthritis (**Table 2**). Over a 16-year  
236 period (2000-2016), and despite fluctuations, the year-on-year incidence rates of self-harm  
237 across each rheumatological condition changed little, with incidence rates in 2016 similar to  
238 those in 2000 (**Figure 1**).

239

### 240 *Risk of self-harm in rheumatological conditions*

241 The risk of self-harm in patients with osteoarthritis was not proportional over the study  
242 period. As such, risk in this condition group was examined over four separate time-periods  
243 of disease duration,  $\leq 1$  year, 1-<5years,  $\geq 5$ -<10 years and  $\geq 10$  years. There was a significant



244 crude association between fibromyalgia (HR 3.01 (95%CI 2.42, 3.76)), rheumatoid arthritis  
245 (1.72 (1.34, 2.22)) and for the majority of categories of osteoarthritis patients (excluding  
246 those with a disease duration of less than 1 year (1.07 (0.90, 1.26)) and subsequent self-  
247 harm compared to their matched unexposed counterparts. There was no association  
248 between ankylosing spondylitis and self-harm compared to the unexposed matched cohort  
249 (1.21 (0.90, 1.64)).

250

251 After adjustment, the association in each cohort was attenuated. Patients with fibromyalgia  
252 remained twice as likely to self-harm as those without a rheumatological condition and  
253 rheumatoid arthritis patients had an increased self-harm risk of 59%. The increased risk of  
254 self-harm in osteoarthritis with a disease duration of 1-<5years and  $\geq 5$ -<10 years was 12%  
255 and 35% respectively; however, patients with osteoarthritis for  $\geq 10$  years no longer had a  
256 significant risk of self-harm (1.17 (0.98, 1.40)) (**Table 2**).

257

#### 258 *Age-specific risk of self-harm in rheumatological conditions*

259 After stratifying by median age, we found there to be a similar association between the risk  
260 of self-harm across the younger and older strata for the rheumatoid arthritis cohort.  
261 However, this association was only statistically significant for the younger cohort (Younger:  
262 1.67 (1.18, 2.36), Older: (1.52 (0.92, 2.52))). In the fibromyalgia cohort, both age categories  
263 experienced a significant increase in risk of self-harm with older patients experiencing a  
264 slightly greater risk (Younger: 2.28 (1.66, 3.13), Older 2.58 (1.67, 3.99)). There was a  
265 somewhat mixed picture for osteoarthritis, with some younger patients seeing an increase in  
266 risk (1-<5years: 1.18 (1.03, 1.34);  $\geq 5$ -<10 years: 1.34 (1.13, 1.58), as did older patients with  
267 osteoarthritis (1.22 (1.07, 1.38), across all disease durations). There remained no increased  
268 risk of self-harm in patients with ankylosing spondylitis when stratified by age (**Table 3**).

269

#### 270 *Gender-specific risk of self-harm in rheumatological conditions*

271 There were similar levels of increased risk of self-harm across the genders in those with  
272 osteoarthritis, rheumatoid arthritis or fibromyalgia compared to those without a  
273 rheumatological condition. Men and women who had had osteoarthritis for between  $\geq 5$ -<10  
274 years had a significantly increased risk of self-harm of 42% and 35% respectively. However,

275 though the risk estimates for men with rheumatoid arthritis or fibromyalgia were similar to  
276 that of women with the same condition, the increase was not statistically significant in either  
277 gender (fibromyalgia men: 2.16 (0.91, 5.31); rheumatoid arthritis men 1.63 (0.98, 2.68))

278 (Table 4).

279

## 280 Discussion

281 We found that primary care patients with rheumatological conditions of fibromyalgia,  
282 rheumatoid arthritis or osteoarthritis are at increased risk of self-harm compared to  
283 matched unexposed patients, that this risk varies across the three conditions, but that age  
284 and gender are weak effect modifiers. In contrast there was no association between  
285 ankylosing spondylitis and self-harm. Finally, the year-on-year incidence of self-harm in  
286 these patient groups remained relatively consistent from 2000 to 2016.

287

288 Overall, patients with fibromyalgia had the greatest risk of self-harm with a 2-fold increase  
289 compared to the unexposed cohort. This propensity to self-harm was greater than that seen  
290 for the rheumatoid arthritis and osteoarthritis cohorts and may relate to different effects of  
291 similar mechanisms. Patients with fibromyalgia have been shown to experience more  
292 depression (6, 7, 20) and poorer health outcomes, particularly bodily pain (21) and fatigue  
293 (22), than patients with osteoarthritis and rheumatoid arthritis. Furthermore, in contrast to  
294 osteoarthritis and rheumatoid arthritis, psychological factors play a major role in the origin  
295 of this disorder as both physical and childhood trauma are associated with fibromyalgia and  
296 self-harm (4, 23). Though the risk of self-harm in different rheumatological conditions has  
297 not been previously described, a meta-analysis by Li et al did find the prevalence of suicidal  
298 ideation (of which self-harm is a risk factor (24)) to be greater in patients with fibromyalgia  
299 compared to the other rheumatological conditions (systemic lupus erythematosus and  
300 osteoarthritis) (25). This suggests the greatest risk we observed in patients with  
301 fibromyalgia is plausible.

302

303 Our initial findings on osteoarthritis were in-line with those of Webb et al, who examined the  
304 risk of self-harm in several physical illnesses using CPRD (12) and found an unadjusted  
305 increase in the risk of self-harm in patients with osteoarthritis. However, in contrast, we

306 found that after adjustment the risk of self-harm remained for certain disease duration  
307 categories. In our study, the risk remained increased in those having had osteoarthritis for  
308 between 1 and 10 years. Our contrasting findings to Webb et al are potentially due to our  
309 increased sample size from a much longer time-period of the CPRD, and thus greater  
310 statistical power. However, it is clear that the risk of self-harm in osteoarthritis is relatively  
311 modest, especially compared to fibromyalgia and rheumatoid arthritis. This may reflect a  
312 different experience in terms of pain duration, frequency and location; osteoarthritis is  
313 typically a more localised pain condition, unlike the generalized pain and systemic  
314 symptoms caused by fibromyalgia and rheumatoid arthritis, and therefore may have less  
315 impact on patients' lives leading to self-harm behaviour. Furthermore, the violation of the  
316 proportional hazards assumption in our study suggests that the risk of self-harm is  
317 influenced by disease duration, this may have been masked in the study of Webb et al (12)  
318 where data were from a case-control study and so the effect of disease duration could not be  
319 assessed. Though there is mixed evidence around the association between disease duration  
320 and progression of osteoarthritis (26), we found that those with newly diagnosed  
321 osteoarthritis ( $\leq 1$  year) or those with long-standing disease ( $\geq 10$  years) were not at  
322 significantly increased risk of self-harm. This could be due to patients with a recent  
323 diagnosis not yet having a prolonged negative experience of osteoarthritis, which could be a  
324 contributing factor to self-harm, or those with very long-standing osteoarthritis having  
325 developed coping mechanisms (27).

326  
327 Despite crude analysis demonstrating an initial association, adjusted analysis did not show  
328 ankylosing spondylitis to be a risk factor for self-harm. These findings may be related to this  
329 cohort having the greatest proportion of men, with a reduced incidence of self-harm  
330 compared to women (2). However, our matching, adjustment and stratification should have  
331 countered for the majority of confounding for gender. Though not examining self-harm, Wu  
332 et al. found no association between ankylosing spondylitis and subsequent suicide ideation  
333 or attempt (9). Although Wu et al., used a different group of patients, their sample was from  
334 a large population-based cohort which suggests our findings are conceivable and not just an  
335 artifact of our ankylosing spondylitis cohort being the smallest sample.

336

337 Overall, we found age and gender to be weak effect modifiers of the relationship between all  
338 rheumatological cohorts and subsequent self-harm. For patients with fibromyalgia or  
339 rheumatoid arthritis, we found little difference in the strength of association between  
340 younger and older, or male and female patients and the subsequent risk of self-harm.  
341 However, this finding is tempered by relatively small participant numbers, which meant that  
342 the association was not statistically significant for men with fibromyalgia or rheumatoid  
343 arthritis and older patients with rheumatoid arthritis. Therefore, further study on the role of  
344 these factors is required to clarify this association.

345  
346 Our findings suggest that primary care clinicians, rheumatologists and allied health  
347 professionals need to be especially aware of the potential for self-harm in people with  
348 fibromyalgia and rheumatoid arthritis, exploring mood and risk, and offering appropriate  
349 support and management. Interventions to reduce this serious comorbidity in  
350 rheumatological patients are important because, as our incident data show, little has  
351 changed in the proportion of patients who self-harm in recent years.

352  
353 With regard to the strengths and limitations of our work, this is the first study to examine  
354 several rheumatological conditions as risk factors for incident self-harm. Our use of a large  
355 UK primary care dataset has allowed us to examine the incidence of self-harm over a 26-year  
356 time-period, year-on-year incidence trends over a 16-year time-period and examine the role  
357 of age and gender on risk of self-harm. Our analysis also takes account of clinically recorded  
358 depression, a key risk factor for self-harm. However, several limitations to our work need to  
359 be considered. Across these rheumatological conditions of interest, pain is likely to be an  
360 important contributory factor in the risk of self-harm (28), but could not be determined from  
361 consultation record data. Furthermore, it remains unclear to what extent use of medications  
362 influence the risk of self-harm, though the potential causal mechanism of such medications  
363 means this would be difficult to disentangle. We also found large proportions of missing data  
364 for BMI, smoking and alcohol consumption within the CPRD dataset, particularly in the  
365 unexposed patients. As such data is not “missing at random”, we were unable to impute for  
366 these variables. However, we included missing data as a separate category in the Cox model  
367 and reported the extent of missing data in descriptive tables to ensure transparency. There

368 may also be some residual confounding. Firstly for psychological comorbidities, though our  
369 adjustment for anxiety and depression will have covered the majority of these, and secondly  
370 for additional rheumatological comorbidities, where patients went on to develop a further  
371 rheumatological condition of interest (most likely the common condition of OA) after they  
372 had been grouped into a cohort based on their first rheumatological consultation. However,  
373 the small increased risk of self-harm in patients with OA that we found would suggest that  
374 any confounding would have a minimal impact on the risk experienced by those with the  
375 other rheumatological conditions of interest. Our original intention within this analysis had  
376 also been to examine the risk of suicide, as well as self-harm, in these rheumatological  
377 conditions. However, available samples were too small to conduct such analysis. The  
378 available sample also proved problematic when stratifying by gender. As the majority of  
379 included participants were female, stratification by gender lead to small numbers of events  
380 in the male cohorts (e.g. only 35 incidents of self-harm in men with fibromyalgia). However,  
381 stratification remains justified, as it highlights the role of age and gender.

382

383 In conclusion, patients with rheumatological conditions have increased risk of self-harm  
384 compared to matched unexposed patients, but age and gender do not act as strong effect  
385 modifiers. The incidence of self-harm in these conditions has remained relatively consistent  
386 over the last decade and a half and therefore clinicians should be vigilant, explore mood,  
387 assess risk, and offer appropriate support and management, especially to patients with  
388 fibromyalgia.

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#### 394 **Acknowledgments**

#### 395 **Data**

396 This study is based in part on data from the Clinical Practice Research Datalink obtained  
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401

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#### 419 **Author contributions**

420 JAP was involved with conceptualisation of the project idea, the subsequent acquisition of  
421 funding, overall study design and the undertaking and interpretation of analysis. ZP came up  
422 with the initial idea, was a funding co-applicant and involved in overall study design. RW was  
423 a funding co-applicant, curated the data and conducted analysis. AAS was a funding co-  
424 applicant and supported RW in data curation. CCG was involved with conceptualization of  
425 the project idea and the subsequent acquisition of funding. SM & RB provided support to JAP  
426 in undertaking data analysis. TS and AS were co-applicants in the acquisition of funding and  
427 CDM was involved with conceptualization of the project idea, the funding application and  
428 overall study design. All authors were involved in manuscript writing, have read, and  
429 approved the final version.

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Table 1: Characteristics of patients with rheumatological conditions and their matched cohorts (1990-2016)

Factor	Ankylosing Spondylitis		Fibromyalgia		Osteoarthritis		Rheumatoid Arthritis	
	Exposed (%)	Unexposed (%)	Exposed (%)	Unexposed (%)	Exposed (%)	Unexposed (%)	Exposed (%)	Unexposed (%)
N	10,484	10,484	17,546	17,546	410,384	410,384	23,205	23,205
Mean age at index (SD)	46.9 (15.6)	46.6 (15.9)	46.9 (12.1)	46.6 (12.7)	64.6 (12.7)	64.2 (13.2)	56.7 (15.2)	56.4 (15.6)
Males	4,376 (41.7)	4,376 (41.7)	2,552 (14.5)	2,552 (14.5)	166,241 (40.5)	166,241 (40.5)	7,728 (33.3)	7,728 (33.3)
Median years follow-up (IQR)	7.4 (3.8, 12.2)	5.3 (2.7, 10.6)	5.8 (3.0, 9.9)	5.7 (2.7, 11.3)	6.8 (3.6, 11.0)	5.9 (2.9, 11.0)	6.2 (3.1, 10.5)	5.9 (2.8, 11.2)
Deprivation status								
Q1 (Least deprived)	1,986 (18.9)	1,917 (18.3)	3,002 (17.1)	3,218 (18.3)	72,018 (17.6)	73,347 (17.9)	3,774 (16.3)	4,186 (18.1)
Q2	1,806 (17.2)	1,782 (17.0)	2,960 (16.9)	3,227 (18.4)	71,941 (17.5)	72,068 (17.5)	4,070 (17.5)	4,042 (17.4)
Q3	2,109 (20.1)	2,190 (20.9)	3,337 (19.0)	3,571 (20.4)	79,179 (19.3)	85,833 (20.8)	4,752 (20.5)	4,824 (20.8)
Q4	1,925 (18.4)	2,259 (21.5)	3,786 (21.6)	3,766 (21.5)	85,826 (20.9)	90,589 (22.1)	4,892 (21.1)	5,041 (21.7)
Q5 (Most deprived)	2,658 (25.4)	2,336 (22.3)	4,461 (25.4)	3,764 (21.4)	101,420 (24.7)	89,047 (21.7)	5,717 (24.6)	5,112 (22.0)
BMI (kg/m <sup>2</sup> )								
Underweight (<18.5)	164 (1.5)	123 (1.2)	286 (1.6)	218 (1.2)	3,013 (0.7)	3,587 (0.9)	389 (1.7)	234 (1.0)
Healthy weight (<18.5-24.9)	3,707 (35.4)	2,294 (21.9)	5,602 (31.9)	4,371 (24.9)	99,869 (24.3)	79,731 (19.4)	7,491 (32.3)	4,920 (21.2)
Overweight (25.0-29.9)	2,800 (26.7)	1,587 (15.1)	4,983 (28.4)	2,638 (15.0)	136,070 (33.2)	72,724 (17.7)	6,600 (28.4)	3,960 (17.1)
Obese (>30.0)	1,595 (15.2)	886 (8.4)	4,817 (27.5)	1,747 (10.0)	104,776 (25.5)	37,063 (9.2)	4,474 (19.3)	2,137 (9.2)
Missing	2,218 (21.2)	5,594 (53.4)	1,858 (10.6)	8,572 (48.9)	66,656 (16.3)	216,739 (52.8)	4,251 (18.3)	11,954 (51.5)
Smoking								
Never/Ex smoked	6,680 (63.7)	4,212 (40.2)	12,163 (69.3)	7,696 (43.9)	308,795 (75.2)	170,633 (41.6)	15,332 (66.1)	9,660 (41.6)
Current smoker	2,540 (24.2)	1,494 (14.2)	4,636 (26.4)	2,416 (13.8)	63,869 (15.6)	48,963 (11.9)	5,566 (24.0)	3,037 (13.1)
Missing	1,264 (12.1)	4,778 (45.6)	747 (4.3)	7,434 (42.4)	37,720 (9.2)	190,788 (46.5)	2,307 (9.9)	10,508 (45.3)
Alcohol consumption								
Never/Ex-drinker	1,493 (14.2)	942 (9.0)	4,104 (23.4)	1,735 (9.9)	72,098 (17.6)	42,065 (10.2)	4,229 (18.2)	2,225 (9.6)
Current 1-9	4,923 (47.0)	3,000 (28.6)	9,355 (53.3)	5,824 (33.2)	200,504 (48.9)	116,325 (28.4)	11,178 (48.2)	6,891 (29.7)
Current >=10	1,6223 (15.5)	869 (8.5)	1,692 (9.6)	1,236 (7.0)	66,935 (16.3)	32,979 (8.0)	3,120 (13.5)	1,891 (8.1)
Missing	2,445 (23.3)	5,646 (53.9)	2,395 (13.7)	8,751 (49.9)	70,847 (17.2)	219,016 (53.4)	4,678 (20.1)	12,198 (52.6)
Anxiety	1,757 (16.8)	879 (8.4)	5,944 (33.9)	1,865 (10.6)	67,894 (16.5)	36,568 (8.9)	3,385 (14.6)	2,229 (9.6)
Depression	2,356 (22.5)	1,263 (12.1)	8,784 (50.1)	2,786 (15.9)	90,354 (22.0)	51,631 (12.6)	5,035 (21.7)	3,064 (13.2)

Table 2: Risk of self-harm associated with each rheumatological condition

Condition	Exposed		Unexposed		Hazard ratios (95% CI)	
	n	Incidence rate, per 10,000 (95% CI)	n	Incidence rate, per 10,000 (95% CI)	Crude	Adjusted*
<i>Total</i>						
Ankylosing Spondylitis	102	11.37 (9.37, 13.81)	72	9.57 (7.60, 12.06)	1.21 (0.90, 1.64)	0.95 (0.69, 1.31)
Fibromyalgia	303	25.12 (22.45, 28.11)	108	8.24 (6.82, 9.95)	<b>3.01 (2.42, 3.76)</b>	<b>2.06 (1.60, 2.65)</b>
Osteoarthritis	2,060	6.48 (6.20, 6.76)	1,528	5.02 (4.77, 5.28)		
≤1 year	277	6.75 (6.00, 7.60)	260	6.34 (5.61, 7.16)	1.07 (0.90, 1.26)	1.02 (0.86, 1.21)
1-<5 years	844	6.36 (5.95, 6.80)	664	5.36 (4.97, 5.78)	<b>1.19 (1.07, 1.31)</b>	<b>1.12 (1.01, 1.24)</b>
≥5-<10 years	629	6.72 (6.22, 7.27)	376	4.46 (4.03, 4.91)	<b>1.51 (1.33, 1.72)</b>	<b>1.35 (1.18, 1.54)</b>
10≥ years	310	6.11 (5.47, 6.83)	228	4.13 (3.63, 4.70)	<b>1.47 (1.24, 1.74)</b>	1.17 (0.98, 1.40)
Rheumatoid Arthritis	165	9.70 (8.32, 11.29)	96	5.52 (4.52, 6.75)	<b>1.72 (1.34, 2.22)</b>	<b>1.59 (1.20, 2.11)</b>

\*adjusted for age, BMI, smoking status, alcohol consumption, anxiety, depression and practice-level deprivation. **Bold** = statistically significant (p<=0.05).

Table 3: Age-specific risk of self-harm associated with each rheumatological condition

Condition	Total incidents of self-harm	Exposed		Non-exposed		Hazard ratios (95% CI)	
		n	Incidence rate, per 10,000 (95% CI)	n	Incidence rate, per 10,000 (95% CI)	Crude	Adjusted*
<b>Ankylosing Spondylitis</b>							
<45.3 years	131	78	17.63 (14.12, 22.01)	53	15.22 (11.62, 19.92)	1.21 (0.85, 1.71)	0.97 (0.68, 1.40)
>= 45.3 years	43	24	5.28 (3.54, 7.88)	19	4.71 (3.00, 7.38)	1.13 (0.62, 2.06)	0.88 (0.46, 1.68)
<b>Fibromyalgia</b>							
<46.7 years	282	205	34.72 (30.27, 39.81)	77	12.30 (9.83, 15.37)	<b>2.77 (2.13, 3.61)</b>	<b>2.28 (1.66, 3.13)</b>
>=46.7 years	129	98	15.92 (13.06, 19.40)	31	4.52 (3.18, 6.43)	<b>3.56 (2.38, 5.32)</b>	<b>2.58 (1.67, 3.99)</b>
<b>Osteoarthritis</b>							
<b>&lt;64.6 years</b>							
≤1 year	380	192	9.36 (8.13, 10.78)	188	8.99 (7.79, 10.37)	1.04 (0.85, 1.27)	1.01 (0.83, 1.24)
1-<5 years	985	561	8.25 (7.59, 8.96)	424	6.53 (5.94, 7.19)	<b>1.26 (1.11, 1.43)</b>	<b>1.18 (1.03, 1.34)</b>
≥5-<10 years	618	393	7.58 (6.86, 8.37)	225	4.73 (6.86, 8.37)	<b>1.60 (1.36, 1.88)</b>	<b>1.34 (1.13, 1.58)</b>
10≥ years	340	194	5.86 (5.09, 6.75)	146	4.06 (3.46, 4.78)	<b>1.43 (1.15, 1.77)</b>	0.99 (0.80, 1.25)
<b>&gt;=64.6 years</b>							
≤1 year	157	85	4.14 (3.35, 5.13)	72	3.58 (2.84, 4.51)	1.16 (0.84, 1.58)	
1-<5 years	523	283	4.38 (3.89, 4.92)	240	4.07 (3.58, 4.61)	1.07 (0.90, 1.27)	
≥5-<10 years	387	236	5.66 (4.98, 6.42)	151	5.66 (4.98, 6.43)	<b>1.38 (1.13, 1.69)</b>	<b>1.22 (1.07, 1.38)†</b>
10≥ years	198	116	6.59 (5.49, 7.91)	82	4.26 (3.43, 5.29)	<b>1.55 (1.17, 2.06)</b>	
<b>Rheumatoid Arthritis</b>							
<57.0 years	184	120	13.20 (11.04, 15.79)	64	7.15 (5.60, 9.13)	<b>1.83 (1.35, 2.48)</b>	<b>1.67 (1.18, 2.36)</b>
>=57.0 years	77	45	5.68 (4.24, 7.60)	32	3.79 (2.68, 5.37)	1.50 (0.95, 2.37)	1.52 (0.92, 2.52)

\*adjusted for gender, BMI, smoking status, alcohol consumption, anxiety, depression and practice-level deprivation. **Bold** = statistically significant (p<=0.05). †Data met assumptions for proportionality and therefore stratification by time was not required

Table 4: Gender-specific risk of self-harm associated with each rheumatological condition

Condition	Total incidents of self-harm	Exposed		Non-exposed		Hazard ratios (95% CI)	
		n	Incidence rate, per 10,000 (95% CI)	n	Incidence rate, per 10,000 (95% CI)	Crude	Adjusted*
<b>Ankylosing Spondylitis</b>							
Men	71	42	11.59 (8.56, 15.68)	29	9.35 (6.50, 13.45)	1.25 (0.78, 2.01)	1.13 (0.69, 1.84)
Women	103	60	11.23 (8.72, 14.46)	43	9.73 (7.22, 13.12)	1.19 (0.80, 1.77)	0.83 (0.55, 1.27)
<b>Fibromyalgia</b>							
Men	48	35	18.34 (13.17, 25.54)	13	6.82 (3.96, 11.74)	<b>2.98 (1.54, 5.75)</b>	2.16 (0.91, 5.13)
Women	363	268	26.39 (23.42, 29.75)	95	8.48 (6.93, 10.37)	<b>3.03 (2.40, 3.83)</b>	<b>2.44 (1.87, 3.18)</b>
<b>Osteoarthritis</b>							
<b>Men</b>							
≤1 year	209	108	6.50 (5.38, 7.85)	101	6.08 (5.00, 7.39)	1.07 (0.82, 1.40)	1.06 (0.81, 1.40)
1-<5 years	568	320	6.01 (5.38, 6.70)	248	4.94 (4.36, 5.59)	<b>1.22 (1.03, 1.44)</b>	1.18 (0.99, 1.40)
≥5-<10 years	382	240	6.53 (5.76, 7.41)	142	4.17 (3.53, 4.91)	<b>1.57 (1.27, 1.93)</b>	<b>1.42 (1.14, 1.76)</b>
10≥ years	191	114	8.80 (4.83, 6.97)	77	3.50 (2.80, 4.38)	<b>1.66 (1.24, 2.22)</b>	1.34 (0.99, 1.81)
<b>Women</b>							
≤1 year	328	169	6.92 (5.96, 8.05)	159	6.51 (5.78, 7.61)	1.06 (0.86, 1.32)	1.08 (0.87, 1.35)
1-<5 years	940	524	6.60 (6.06, 7.19)	416	5.64 (5.13, 6.21)	<b>1.17 (1.03, 1.33)</b>	<b>1.16 (1.02, 1.33)</b>
≥5-<10 years	623	389	6.85 (6.20, 7.56)	234	4.65 (4.09, 5.29)	<b>1.47 (1.25, 1.73)</b>	<b>1.35 (1.14, 1.59)</b>
10≥ years	347	196	6.31 (5.49, 7.26)	151	4.55 (3.88, 5.33)	<b>1.37 (1.11, 1.70)</b>	1.07 (0.85, 1.34)
<b>Rheumatoid Arthritis</b>							
Men	82	53	9.81 (7.50, 12.84)	29	5.03 (3.49, 7.23)	<b>1.89 (1.20, 2.99)</b>	1.63 (0.98, 2.68)
Women	179	112	9.64 (8.01, 11.60)	67	5.77 (4.54, 7.33)	<b>1.65 (1.22, 2.23)</b>	<b>1.56 (1.11, 2.20)</b>

\*adjusted for age, BMI, smoking status, alcohol consumption, anxiety, depression and practice-level deprivation. **Bold** = statistically significant (p<=0.05).

AS = Ankylosing Spondylitis, OA = Osteoarthritis, RA = Rheumatoid Arthritis

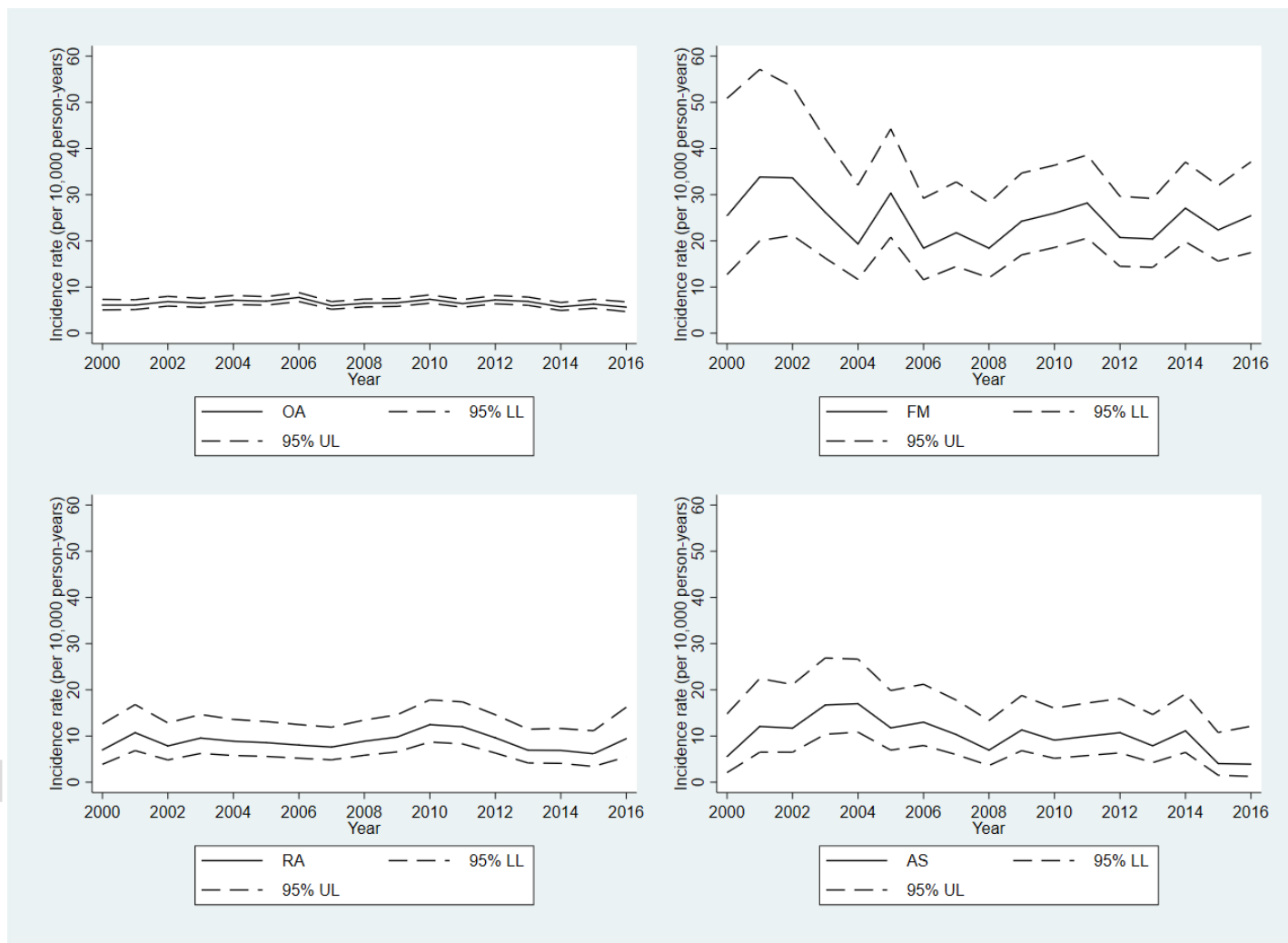


Figure 1 legend: Incidence rates per 10,000 person-years for osteoarthritis (OA), fibromyalgia (FM), rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Solid line = rate, dashed line = 95% confidence intervals, lower and upper bands