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Original article

Worse outcomes linked to ethnicity for early inflammatory arthritis in England and Wales: a national cohort study

Maryam A. Adas [1,*], Sam Norton [1,2,*], Sathiyaa Balachandran[1,*], Edward Alveyn[1], Mark D. Russell [1], Thomas Esterine[3], Paul Amlani-Hatcher[3], Sarah Oyebanjo[4], Heidi Lempp[1], Joanna Ledingham[5], Kanta Kumar[6], James B. Galloway[1,†] and Shirish Dubey [7,†]

Abstract

Objective. To assess variability in care quality and treatment outcomes across ethnicities in early inflammatory arthritis (EIA).

Methods. We conducted an observational cohort study in England and Wales from May 2018 to March 2020, including patients with a suspected/confirmed EIA diagnosis. Care quality was assessed against six metrics defined by national guidelines. Clinical outcomes were measured using DAS28. Outcomes between ethnic groups ('White', 'Black', 'Asian', 'Mixed', 'Other') were compared, and adjusted for confounders.

Results. A total of 35 807 eligible patients were analysed. Of those, 30 643 (85.6%) were White and 5164 (14.6%) were from ethnic minorities: 1035 (2.8%) Black; 2617 (7.3%) Asian; 238 (0.6%) Mixed; 1274 (3.5%) Other. In total, 12 955 patients had confirmed EIA, of whom 11 315 were White and 1640 were from ethnic minorities: 314 (2.4%) Black; 927 (7.1%) Asian; 70 (0.5%) Mixed; 329 (2.5%) Other. A total of 14 803 patients were assessed by rheumatology within three weeks, and 5642 started treatment within six weeks of referral. There were no significant differences by ethnicity. Ethnic minority patients had lower odds of disease remission at three months [adjusted odds ratio 0.79 (95% CI: 0.65, 0.96)] relative to White patients. Ethnic minorities were significantly less likely to receive initial treatment withMTX[0.68 (0.52, 0.90)] or with glucocorticoids [0.63 (0.49, 0.80)].

Conclusion. We demonstrate that some ethnic minorities are less likely to achieve disease remission in three months following EIA diagnosis. This is not explained by delays in referral or time to treatment. Our data highlight the need for investigation into the possible drivers of these inequitable outcomes and reappraisal of EIA management pathways.

Key words: early inflammatory arthritis, ethnic minorities, Black, Asian, Mixed, Other, disease outcome, DAS28, care quality, DMARD

Rheumatology key messages

- Ethnic minority patients with EIA were less likely to achieve remission by three months compared to White.
- There were no differences in referral time, baseline-DAS28 and time to treatment across different ethnicities.
- Ethnic minority patients were more likely to be non-smokers and seropositive.

[1]Centre for Rheumatic Disease, Department of Inflammatory Biology, [2]Psychology Department, Institute for Psychiatry, Psychology & Neuroscience, King's college London, [3]British Society for Rheumatology, NEIAA Patient Panel, [4]British Society of Rheumatology, NEIAA, London, [5]Rheumatology Department, Portsmouth Hospitals University NHS Trust, Portsmouth, [6]Institute of Clinical Sciences, University of Birmingham, Birmingham and [7]Oxford University Hospitals NHS Foundation Trust, Oxford, UK

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Correspondence to: James Galloway, Weston Education Centre, 10 Cutcombe Road, SE5 9RJ London, UK.
E-mail: james.galloway@kcl.ac.uk

*Joint first authors.

†Joint senior authors.

CLINICAL SCIENCE

Introduction

Across the UK population, the opportunity to live a long and healthy life is not evenly distributed. Multiple studies have consistently demonstrated that patients from racial or ethnic minority backgrounds experience considerable health inequality, having generally poorer health outcomes compared with White patients [1, 2]. Evidence shows that there is a systematic relationship between good health and several social determinants, including education, deprivation, income and employment. An imbalance within that relationship is known as health inequality [3, 4].

RA is the commonest form of early inflammatory arthritis (EIA), affecting 0.5–1% of the worldwide population. RA mainly affects the lining of the synovial joints, and can cause progressive disability, reducing patients' quality of life [5]. The care for patients with EIA has evolved dramatically over the past decades [6]. Early treatment within three to six months of symptom onset improves long-term clinical outcomes [5]. Barriers to starting treatment early include delays in seeking medical advice (which is linked to health cognition), slow referral between primary and secondary care, and lengthy rheumatology service waiting times [7, 8].

Ethnic minority patients with a diagnosis of EIA have been shown to have less favourable health outcomes compared with White patients [9]. Recent data show differential engagement in accessing healthcare services in non-White patients [8].

Previous research into the role of ethnicity in inflammatory arthritis has yielded conflicting results. One observational cohort study using data from a Singaporean early RA registry demonstrated patients of Malay origin were more likely to be in high disease activity groups at presentation, compared with Chinese patients [10]. A prospective cohort study demonstrated that Native American populations were more likely to be seropositive and have higher inflammatory markers compared with White patients, findings that persisted throughout treatment [11]. Conversely, a cross-sectional study of male US veterans showed no significant differences in disease characteristics or markers of severity after adjustment, aside from the presence of fewer rheumatoid nodules, in African-American compared with White patients [12]. Further data from US cohorts have revealed more adverse disease activity, disability and pain scores among minority ethnic groups [13, 14], which do not remain statistically significant when adjusted for socioeconomic, demographic and other potential confounding factors, with the exception of higher pain scores among African-American patients in one large cross-sectional study [14].

There is a paucity of published data characterizing the response to treatment among patients of different ethnic backgrounds. A multi-ethnic cross-sectional study of 371 patients in Malaysia comparing patients with RA who achieved treatment targets against those who did not, identified Malay ethnicity is an independent predictor of not achieving treatment target, after confounder adjustment (OR 2.96; 95% CI 1.4, 5.96) [15]. A US cohort using registry data from 2010–2012 showed higher disease activity among ethnic minority patients compared with White patients [16].

In this study, we aimed to provide information to help clinicians and decision makers reach informed choices about the management of patients and services, to reduce health inequalities in EIA care. The specific objectives of this study were to use the National Early Inflammatory Arthritis Audit (NEIAA) to: (i) assess the relationship between ethnicity and achievement of six quality metrics, derived from the 2013 and 2020 editions of the National Institute for Health and Clinical Excellence (NICE) Quality Standard 33 (QS33) [17]; and (ii) report the impact of ethnicity on achieving DAS28 remission at three months following diagnosis.

Methods

Study design and data sources

In this national observational cohort study, we used a dataset compiled from the Health Quality Improvement Partnership (HQIP)-commissioned National Early Inflammatory Arthritis Audit (NEIAA). NEIAA has data on adults (aged >16 years) referred to secondary care rheumatology services in England and Wales with a suspected EIA. Patients with a confirmed EIA diagnosis are eligible for further follow-up. Patients' demographics and clinical information are collected in NEIAA. Full methodology on data collection has been described previously in the project annual report [18]. The data for this report were collected from patients seen within specialist rheumatology services between 8 May 2018 and 27 March 2020. Informed patient consent was not required for this study, as the NEIAA has Secretary of State for Health permission to collect data for the purpose of a national audit (Clinical Advisory Group Reference 19/CAG/0059). In parallel, ethics approval for secondary use of NEIAA data for research has been obtained: Research Ethics Committee reference 19/EE/0082; 06/Dec/2019.

Outcomes

We assessed care quality according to the six metrics defined by NICE QS33 (Supplementary Table S1, available at *Rheumatology* online) and achievement of disease remission by three months. For metrics 1 and 2, data were used for all referred patients with a suspected EIA. For assessing other metrics and disease remission, analyses were limited to patients with a confirmed EIA diagnosis (patients with peripheral arthritis mainly) that were eligible for follow-up. Disease remission was defined by a Disease Activity Score using a 28-joint count (DAS28) below 2.6 measured by three months [19].

We coded ethnicity using the Office for National Statistics categorization system from the 2001 UK census [20]. Ethnic origin was collapsed into five main groups: White, Black (Black British/Caribbean/African),

Asian (Asian/Asian British), Mixed (White and Black Caribbean/White and Black African/White and Asian/any other mixed or multiple ethnic backgrounds), and Other (Arab/any other ethnic group). Ethnicity information was entered by treating clinicians.

Statistical analysis

Patient characteristics were tabulated according to ethnic groups, as described above. For continuous measures, data were described as medians and interquartile ranges (IQR). For categorical measures, absolute number and percentages were applied.

We used logistic regression models to estimate associations between ethnicity and (i) expected performance against NICE quality metrics and (ii) disease remission. Models were adjusted for confounder variables including age, gender, smoking, comorbidity, rheumatoid factor (RF) or anti-CCP positivity, and disease severity at presentation. Robust standard errors were estimated to account for clustering of patients within centres. Data were presented as odds ratio (OR) for achieving the outcome, relative to the reference group (typically the White ethnic group), with 95% CI.

Social deprivation has a complex relation with ethnicity, and we considered deprivation a path or a mediator variable that can mask the relation between ethnicity and disease outcome. Additional expletory analyses were performed where we adjusted for deprivation (to assess the relation between quality metrics, disease remission and ethnicity) and for the working diagnosis (to assess disease remission and ethnicity) in the confounder model using logistic regression. Deprivation level was assessed using Index of Multiple Deprivation (IMD). Scores were then grouped into 10 categories according to the English IMD 2015 guidance [21].

To examine the association with process measures in more detail, we considered the NICE quality measures in models as continuous measures (e.g. time to starting treatment in days rather than a binary 'treated within 6 weeks'). To examine the relationship with disease outcome, we analysed results for each subcomponent of the DAS28 score (swollen joint count, tender joint count, patient global visual analogue score, ESR, or CRP separately). These analyses used linear regression following the same approach as described above. We also used logistic regression to identify whether ethnicity associated with treatment choice (MTX-based therapy, with or without glucocorticoids).

Analyses were restricted to people with recorded ethnicity. Other demographic information was mostly complete; however, imputation was used for missing data in NICE quality metrics, comorbidity, RF and CCP results, and baseline and three-month DAS28. Multivariate sequential imputation model using 20 chained equations (at the end of each cycle, one imputed dataset was generated and then the process was repeated to generate 20 imputed datasets) was used for adjusted analyses for quality metrics 3–6. For analysis of disease remission and treatment choice, in addition to imputation for the missing variables mentioned above, models were weighted by inverse probability of completing a three-month clinical visit data return.

All missing data were imputed regardless of the reason/second they were missing. Linear and logistic regression were performed to impute the missing variables. The following variables with complete data were utilized for the imputation: age; gender; smoking status; and ethnicity.

Statistical significance was assessed at the 5% level. No correction for multiple hypothesis testing was made. All statistical analyses were performed using Stata version 17.0 (StataCorp, College Station, TX, USA).

Results

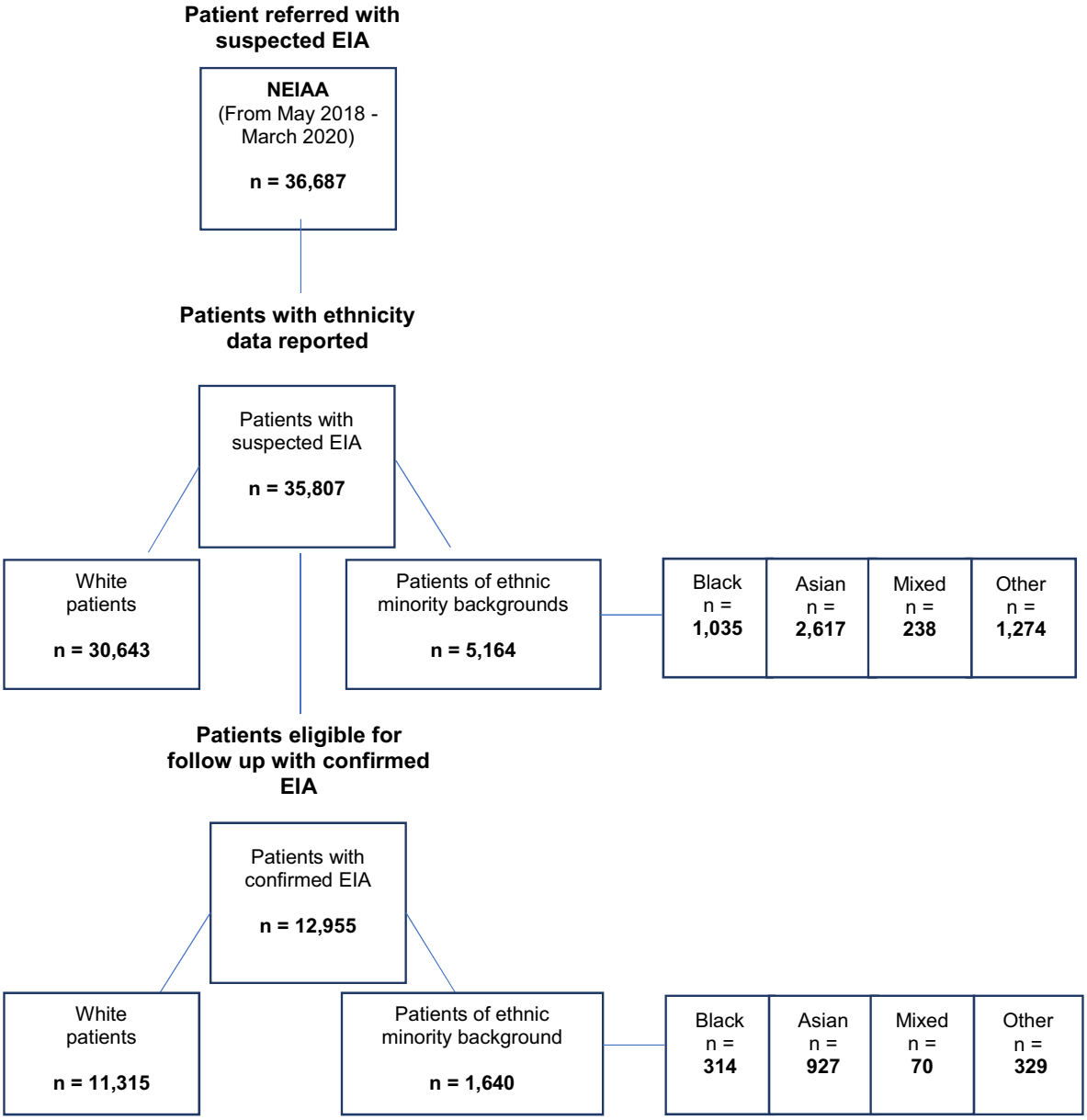
In total, 36 687 patients were enrolled into NEIAA between May 2018 and March 2020. Of those, 35 807 had information on ethnicity: 5164 (14.4%) were from an ethnic minority background and 30 643 (85.6%) were White. Of the 12 955 patients with a confirmed EIA diagnosis, 1640 (12.7%) were from ethnic minority backgrounds and 11 315 (87.3%) were White. Within the ethnic minority groups, 314 (2.4%) were from Black backgrounds, 927 (7.1%) patients from Asian backgrounds, 70 (0.5%) were from Mixed ethnic backgrounds, and 329 (2.5%) were from Other minority backgrounds (Fig. 1).

Baseline characteristics are presented in Table 1. On average, compared with White ethnic groups, patients from ethnic minority backgrounds tended to be younger, more likely to be female, and less likely to have cigarette smoke exposure. Those from ethnic minority backgrounds were more likely to receive a working diagnosis of RA than people from White ethnic groups. Of those with confirmed inflammatory arthritis, compared with White ethnic groups, patients from ethnic minority backgrounds were less likely to have a comorbidity, but more likely to have positive RF and CCP serology. No major difference was observed between ethnic groups in terms of duration of EIA symptoms prior to referral or baseline DAS28.

Quality of care for all patients with suspected EIA

The proportion of patients referred by their primary care provider to a rheumatologist within 3 working days (metric 1) was 42.7% for White ethnicity and 47.0% for ethnic minority groups. Patterns across ethnic groups are shown in Table 2 and Fig. 2A. The proportions of patients seen in rheumatology services within 3 weeks of referral (metric 2) were similar across ethnic groups (White 41.9%, ethnic minority groups 43.1%, see Table 2). In regression models adjusted for age and gender, there was no significant difference in odds of meeting either metric 1 or 2 according to White *vs* ethnic minority group, nor was the variation across ethnic groups significant ($P = 0.473$). However, pairwise contrasts indicated significant differences between the Other

Fig. 1 Population flow chart



EIA: early inflammatory arthritis; NEIAA: national early inflammatory arthritis audit.

ethnic group compared with White (Supplementary Table S2, available at *Rheumatology* online).

Quality of care for patients with confirmed inflammatory arthritis diagnoses

The proportions of patients started on treatment within six weeks of referral (metric 3) was similar across ethnic categories, and there was no significant difference between any of the ethnic minority groups, compared with White ethnicity, in logistic regression models (see Fig. 2B, Table 2, Supplementary Table S2, available at *Rheumatology* online).

Overall, the majority of patients were provided with disease education (metric 4) (94.3%), had a treatment target set (metric 5) (86.1%), and were given information about emergency access to advice (metric 6) (92.8%) (Table 2). Performance for these metrics was consistently lowest for the Mixed ethnicity group (86.8%, 76.5% and 83.8%,

Table 1 Baseline characteristics

Patients with suspected EIA and with ethnic data reported	Total patients	White	All ethnic minority backgrounds	Black	Asian	Mixed	Other
	n = 35 807	*n* = 30 643	*n* = 5164	*n* = 1035	*n* = 2617	*n* = 238	*n* = 1274
Age: median (IQR)	55 (42,67)	56 (44,68)	48 (37,58)	51 (40,59)	46 (37,57)	46 (34,55)	49 (38,60)
Age-band: *n* (%)							
16–24	1226 (3.4%)	1004 (3.3%)	222 (4.3%)	43 (4.2%)	105 (4.0%)	15 (6.3%)	59 (4.6%)
25–39	6188 (17.3%)	4888 (16.0%)	1300 (25.2%)	210 (20.3%)	733 (28.0%)	72 (30.3%)	285 (22.4%)
40–64	18 024 (50.3%)	15 132 (49.4%)	2892 (56.0%)	617 (59.6%)	1447 (55.3%)	124 (52.1%)	704 (55.3%)
65–74	6081 (17.0%)	5564 (18.2%)	517 (10.0%)	98 (9.5%)	242 (9.2%)	20 (8.4%)	157 (12.3%)
75+	4286 (12.0%)	4053 (13.2%)	233 (4.5%)	67 (6.5%)	90 (3.4%)	7 (2.9%)	69 (5.4%)
Gender: n (%)							
Male	12 307 (34.4%)	10 926 (35.7%)	1381 (26.7%)	239 (23.1%)	710 (27.1%)	62 (26.1%)	370 (29.0%)
Female	23 500 (65.6%)	19 717 (64.3%)	3783 (73.3%)	796 (76.9%)	1907 (72.9%)	176 (73.9%)	904 (71.0%)
Patient in paid work >20h/week: *n* (%)							
No	17 336 (50.6%)	14 903 (50.7%)	2433 (49.6%)	455 (45.7%)	1350 (53.3%)	90 (40.2%)	538 (46.5%)
Yes	16 941 (49.4%)	14 466 (49.3%)	2475 (50.4%)	541 (54.3%)	1182 (46.7%)	134 (59.8%)	618 (53.5%)
Smoking status: *n* (%)							
Current smoker	6053 (16.9%)	5502 (18.0%)	551 (10.7%)	129 (12.5%)	215 (8.2%)	37 (15.5%)	170 (13.3%)
Ex-smoker	8920 (24.9%)	8376 (27.3%)	544 (10.5%)	126 (12.2%)	170 (6.5%)	40 (16.8%)	208 (16.3%)
Never smoked	16 873 (47.1%)	13524 (44.1%)	3349 (64.9%)	632 (61.1%)	2012 (76.9%)	121 (50.8%)	584 (45.8%)
Not known	3961 (11.1%)	3241 (10.6%)	720 (13.9%)	148 (14.3%)	220 (8.4%)	40 (16.8%)	312 (24.5%)
Duration symptoms: *n* (%)							
<1 month	2687 (7.8%)	2337 (7.9%)	350 (7.0%)	67 (6.7%)	205 (8.0%)	19 (8.4%)	59 (5.0%)
1–3 months	9009 (26.0%)	7783 (26.3%)	1226 (24.7%)	235 (23.4%)	636 (24.9%)	61 (27.1%)	294 (24.8%)
3–6 months	6774 (19.6%)	5798 (19.6%)	976 (19.6%)	191 (19.0%)	522 (20.4%)	48 (21.3%)	215 (18.1%)
6–12 months	6454 (18.6%)	5568 (18.8%)	886 (17.8%)	183 (18.2%)	437 (17.1%)	30 (13.3%)	236 (19.9%)
1–5 years	6801 (19.6%)	5699 (19.2%)	1102 (22.2%)	236 (23.5%)	552 (21.6%)	43 (19.1%)	271 (22.8%)
5–10 years	1705 (4.9%)	1439 (4.9%)	266 (5.4%)	62 (6.2%)	125 (4.9%)	14 (6.2%)	65 (5.5%)
>10 years	1186 (3.4%)	1022 (3.4%)	164 (3.3%)	30 (3.0%)	78 (3.1%)	10 (4.4%)	46 (3.9%)
Referral via EIA pathway: *n* (%)	23 431 (67.1%)	19 818 (66.4%)	3613 (71.3%)	775 (76.3%)	1760 (68.4%)	151 (65.4%)	927 (74.4%)
EIA – eligible for follow up	**Total**	**White**	**All ethnic minority backgrounds**	**Black**	**Asian**	**Mixed**	**Other**
	n =12 955	*n* =11 315	*n* =1640	*n*=314	*n*=927	*n*=70	*n*=329
Age: median (IQR)	58 (46,70)	59 (47,71)	49 (39,60)	53 (42,62)	47 (38,58)	47 (35,56)	53 (41,64)
Age-band: *n* (%)							
16–24	336 (2.6%)	277 (2.4%)	59 (3.6%)	11 (3.5%)	30 (3.2%)	6 (8.6%)	12 (3.6%)
25–39	1886 (14.6%)	1504 (13.3%)	382 (23.3%)	56 (17.8%)	243 (26.2%)	19 (27.1%)	64 (19.5%)
40–64	6125 (47.3%)	5213 (46.1%)	912 (55.6%)	178 (56.7%)	521 (56.2%)	38 (54.3%)	175 (53.2%)
65–74	2700 (20.8%)	2510 (22.2%)	190 (11.6%)	36 (11.5%)	97 (10.5%)	4 (5.7%)	53 (16.1%)
75+	1908 (14.7%)	1811 (16.0%)	97 (5.9%)	33 (10.5%)	36 (3.9%)	3 (4.3%)	25 (7.6%)

(continued)

Table 1 Continued

EIA – eligible for follow up	Total	White	All ethnic minority backgrounds	Black	Asian	Mixed	Other
	n =12 955	*n* =11 315	*n* =1640	*n*=314	*n*=927	*n*=70	*n*=329
Gender: *n* (%)							
Male	4956 (38.3%)	4486 (39.6%)	470 (28.7%)	78 (24.8%)	273 (29.4%)	19 (27.1%)	100 (30.4%)
Female	7999 (61.7%)	6829 (60.4%)	1170 (71.3%)	236 (75.2%)	654 (70.6%)	51 (72.9%)	229 (69.6%)
Smoking status: *n* (%)							
Current smoker	2506 (19.3%)	2316 (20.5%)	190 (11.6%)	43 (13.7%)	83 (9.0%)	13 (18.6%)	51 (15.5%)
Ex-smoker	3773 (29.1%)	3577 (31.6%)	196 (12.0%)	41 (13.1%)	73 (7.9%)	11 (15.7%)	71 (21.6%)
Never smoked	5798 (44.8%)	4681 (41.4%)	1117 (68.1%)	201 (64.0%)	720 (77.7%)	39 (55.7%)	157 (47.7%)
Not known	878 (6.8%)	741 (6.5%)	137 (8.4%)	29 (9.2%)	51 (5.5%)	7 (10.0%)	50 (15.2%)
Referral via EIA pathway: *n* (%)	8334 (65.0%)	7207 (64.4%)	1127 (69.3%)	231 (74.8%)	614 (66.5%)	49 (72.1%)	233 (71.7%)
Working diagnosis: *n* (%)							
Rheumatoid arthritis	9051 (70%)	7874 (70%)	1177 (72%)	252 (80%)	641 (69%)	42 (60%)	242 (74%)
Psoriatic arthritis	1639 (13%)	1497 (13%)	142 (9%)	14 (4%)	97 (10%)	10 (14%)	21 (6%)
Axial spondyloarthritis	243 (2%)	210 (2%)	33 (2%)	5 (2%)	18 (2%)	0 (0%)	10 (3%)
Undifferentiated arthritis	1544 (12%)	1325 (12%)	219 (13%)	39 (12%)	129 (14%)	15 (21%)	36 (11%)
Other	478 (4%)	409 (4%)	69 (4%)	4 (1%)	42 (5%)	3 (4%)	20 (6%)
Symptom duration: *n* (%)							
<1 month	1099 (8.5%)	969 (8.6%)	130 (8.0%)	23 (7.3%)	80 (8.7%)	6 (8.8%)	21 (6.6%)
1–3 months	4143 (32.2%)	3668 (32.6%)	475 (29.3%)	77 (24.6%)	299 (32.4%)	18 (26.5%)	81 (25.5%)
3–6 months	3031 (23.6%)	2626 (23.4%)	405 (25.0%)	83 (26.5%)	223 (24.1%)	22 (32.4%)	77 (24.2%)
6–12 months	2348 (18.3%)	2033 (18.1%)	315 (19.4%)	78 (24.9%)	158 (17.1%)	6 (8.8%)	73 (23.0%)
>12 months	2239 (17.5%)	1941 (17.3%)	298 (18.1%)	54 (16.6%)	164 (17.7%)	16 (23.5%)	66 (20.7)
Comorbidity: *n* (%)							
None	7450 (58.2%)	6376 (57.0%)	1074 (66.9%)	184 (60.3%)	640 (69.8%)	42 (61.8%)	208 (66.0%)
One	2757 (21.6%)	2484 (22.2%)	273 (17.0%)	50 (16.4%)	146 (15.9%)	16 (23.5%)	61 (19.4%)
Two or more	2585 (20.2%)	2327 (20.8%)	258 (16.1%)	71 (23.3%)	131 (14.3%)	10 (14.7%)	46 (14.6%)
Diabetes mellitus: *n* (%)							
No	11 678 (91%)	10 278 (92%)	1400 (87%)	247 (81%)	803 (88%)	57 (84%)	293 (93%)
Yes	1114 (9%)	909 (8%)	205 (13%)	58 (19%)	114 (12%)	11 (16%)	22 (7%)
Hypertension: *n* (%)							
No	10 361 (81%)	9032 (81%)	1329 (83%)	220 (72%)	788 (86%)	56 (82%)	265 (84%)
Yes	2431 (19%)	2155 (19%)	276 (17%)	85 (28%)	129 (14%)	12 (18%)	50 (16%)
Lung disease: *n* (%)							
No	11 538 (90%)	10 019 (90%)	1519 (95%)	287 (94%)	874 (95%)	66 (97%)	292 (93%)
Yes	1254 (10%)	1168 (10%)	86 (5%)	18 (6%)	43 (5%)	2 (3%)	23 (7%)
Disease severity:							
Baseline DAS28: median (IQR)	4.7 (3.6,5.7)	4.7 (3.6,5.7)	4.8 (3.6,5.7)	5.2 (4.2,6.3)	4.7 (3.5,5.6)	4.6 (3.7,5.2)	4.7 (3.3,5.5)
Baseline ESR mm/hr: median (IQR)	24.0 (10.0,41.0)	24.0 (10.0,41.0)	27.0 (13.0,46.0)	36.0 (18.0,60.0)	26.0 (13.0,43.0)	20.0 (10.0,28.0)	26.0 (9.0,42.0)
Baseline CRP mg/l: median (IQR)	10.0 (4.0,27.0)	11.0 (4.0,28.0)	8.0 (3.0, 20.0)	10.0 (4.0,27.0)	7.0 (3.0,18.0)	6.0 (2.0,19.0)	7.0 (4.0,20.0)
RhF or CCP positive: *n* (%)							
No	5027 (43.0%)	4480 (43.8%)	547 (37.1%)	94 (33.8%)	315 (37.1%)	26 (40.6%)	112 (39.6%)
Yes	6671 (57.0%)	5744 (56.2%)	927 (62.9%)	184 (66.2%)	534 (62.9%)	38 (59.4%)	171 (60.4%)

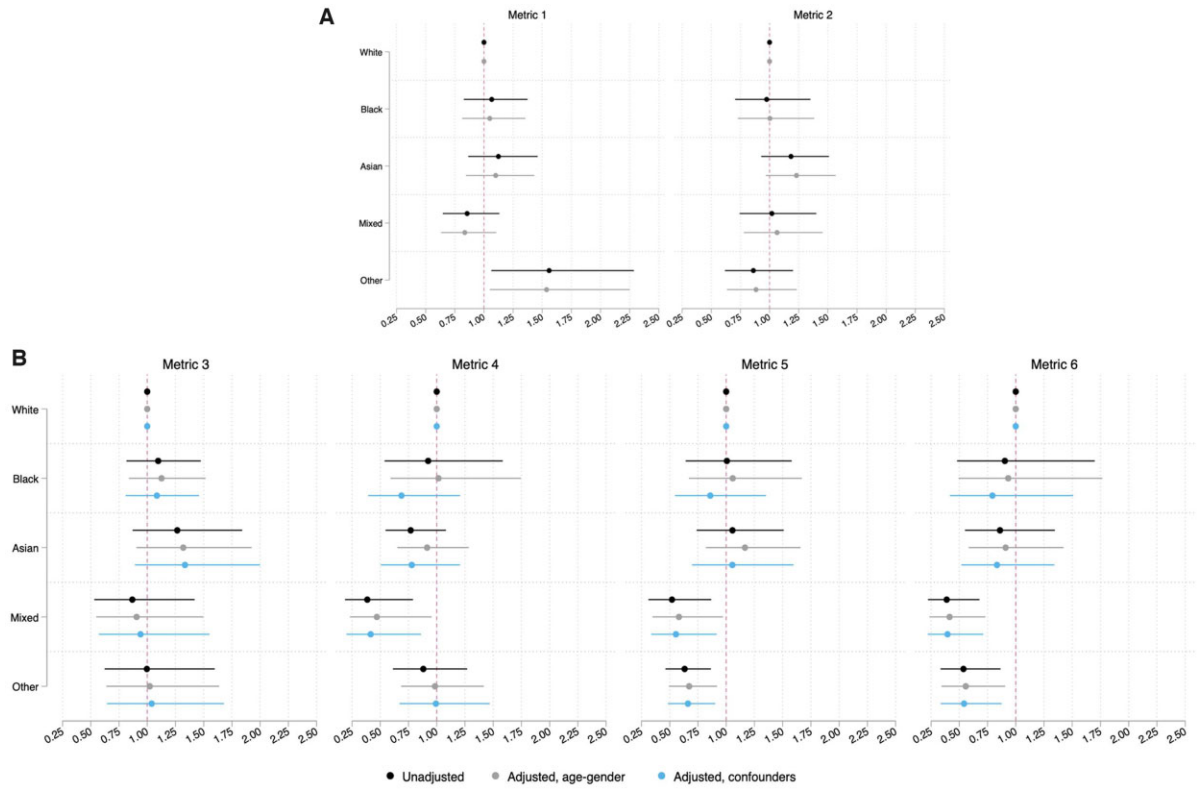
Baseline characteristics for patients with ethnicity data reported, shown for patients with suspected EIA diagnoses and patients who had confirmed EIA diagnoses, recruited to NEIAA from May 2018 to March 2020. CCP: anti-citrullinated c-peptide antibody; DAS28: disease activity score for 28 joints; EIA: early inflammatory arthritis; IQR: interquartile range; *n*: population size; NEIAA: National Early Inflammatory Arthritis Audit.

Table 2 Clinical process measures by ethnicity (quality metrics 1–6)

Patients with suspected EIA and with ethnic data reported	Total patients	White	All ethnic minority backgrounds	Black	Asian	Mixed	Other
	n = 35 807	*n* = 30 643	*n* = 5164	*n* = 1035	*n* = 2617	*n* = 238	*n* = 1274
Referral within 3 days of EIA—M1: *n* (%)	14 894 (43.3%)	12 561 (42.7%)	2333 (47.0%)	445 (44.3%)	1160 (45.6%)	88 (38.9%)	640 (53.7%)
Missing M1 data: *n*	1420	1223	197	30	72	12	83
Seen within 3 weeks—M2: *n* (%)	14 803 (42.1%)	12 619 (41.9%)	2184 (43.1%)	422 (41.3%)	1187 (46.1%)	98 (42.4%)	477 (38.3%)
Missing M2 data: *n*	647	554	93	14	42	7	30
EIA-eligible for follow-up	**Total**	**White**	**All ethnic minority backgrounds**	**Black**	**Asian**	**Mixed**	**Other**
	n=12 955	*n*=11 315	*n*=1640	*n*=314	*n*=927	*n*=70	*n*=329
Treatment within 6 weeks—M3: *n* (%)	5642 (57.0%)	4919 (56.6%)	723 (60.6%)	140 (58.8%)	422 (62.2%)	26 (53.1%)	135 (56.5%)
Missing M3 data: *n*	3055	2619	436	76	249	21	90
Education provided—M4: *n* (%)	11 912 (94.3%)	10 447 (94.4%)	1465 (93.0%)	283 (94.0%)	838 (92.9%)	59 (86.8%)	285 (93.8%)
Missing M4 data: *n*	319	254	65	13	25	2	25
Treatment target set—M5: *n* (%)	10 824 (86.1%)	9494 (86.2%)	1330 (84.9%)	258 (86.3%)	779 (86.8%)	52 (76.5%)	241 (79.8%)
Missing M5 data: *n*	377	303	74	15	30	2	27
Emergency access to care—M6: *n* (%)	11 676 (92.8%)	10 251 (93.0%)	1425 (90.9%)	277 (92.3%)	826 (92.0%)	57 (83.8%)	265 (87.7%)
Missing M6 data: *n*	367	295	72	14	29	2	27

Performance in quality metrics 1–6 for patients recruited to NEIAA from May 2018 to March 2020 who had ethnicity data for analysis. Data on metrics 1 and 2 were available for patients with suspected EIA diagnoses, while data on metrics 3–6 were available for patients with confirmed EIA diagnoses. EIA: early inflammatory arthritis; M: metric; *n*: population size; NEIAA: national early inflammatory arthritis audit.

Fig. 2 Association between ethnicity and performance in quality metrics at three months



(**A**) Quality metric 1 and 2; (**B**) Quality metrics 3–6. Logistic regression coefficient plots demonstrating the relationship between ethnicity and performance in care quality metrics 1–6 at three months in patients with confirmed EIA diagnoses. Metric 1: primary care provider to a rheumatologist within 3 working days; metric 2: seen within Rheumatology services within 3 weeks; metric 3: started treatment within 6 weeks of referral; metric 4: providing education; metric 5: having a treatment target set; accessing emergency rheumatology services. White patients were used as the reference group. All models were clustered by England and Wales Hospital Trust codes (clustered standard errors were estimated to account for within-centre correlations). The confounder-adjusted model was adjusted for age, gender, smoking, comorbidities, DAS28 at baseline, seropositivity for RF or CCP. Data are presented as odds ratios and 95% CIs. CCP: anti-citrullinated c-peptide antibody; DAS28: disease activity score for 28 joints; EIA: early inflammatory arthritis; M: metric.

respectively). The differences for this group were statistically significant when compared with White patients in regression models. The Other ethnicity group was also less likely to have a treatment target set or be provided with information on emergency access to advice when compared with White patients (see Fig. 2B and Supplementary Table S2, available at *Rheumatology* online). When adjusting for social deprivation in the sensitivity analysis, similar findings were observed (Supplementary Table S3, available at *Rheumatology* online).

Analysis of delays in referrals and treatment, using time as a continuous measure rather than the binary attainment of the quality metrics, revealed that there were no significant differences in absolute referral time to rheumatology services from primary care, and no significant differences in the time to treatment initiation for any ethnic group compared with White ethnicity (see Supplementary Table S4, available at *Rheumatology* online).

Clinical outcomes for patients with confirmed inflammatory arthritis diagnoses

Data on clinician-reported outcomes after three months of specialist care are detailed in Table 3. Remission status was achieved in 30.6% for ethnic minority groups, compared with 37.3% for White patients. The odds of remission were significantly lower for ethnic minority patients in unadjusted and adjusted models, compared with the White ethnicity group. Pairwise comparisons indicated significantly lower probabilities of remission in the Black (OR 0.57, 95% CI: 0.41, 0.79) and Asian (OR 0.76, 95% CI: 0.62, 0.93) populations, compared with the White ethnic group (see Fig. 3 and Supplementary Table S5, available at *Rheumatology* online). This remained statistically significant when we adjusted for social deprivation and for the working diagnosis in the

TABLE 3 Clinical outcome measures at three months, by ethnicity

EIA-eligible patients	Total patients	White	All ethnic minority backgrounds	Black	Asian	Mixed	Other
	n = 12 955	*n* = 11 315	*n* = 1640	*n* = 314	*n* = 927	*n* = 70	*n* = 329
Remission by 3 months: n (%)							
No	5090 (63.4%)	4456 (62.7%)	634 (69.4%)	134 (77.0%)	350 (69.4%)	25 (73.5%)	125 (61.9%)
Yes	2934 (36.6%)	2654 (37.3%)	280 (30.6%)	40 (23.0%)	154 (30.6%)	9 (26.5%)	77 (38.1%)
Missing 3-month remission information: *n*	4931	4205	726	140	423	36	127
DAS28 at 3 months: median (IQR)	3.2 (2.2,4.3)	3.1 (2.1,4.2)	3.4 (2.4,4.5)	3.8 (2.7,5.0)	3.5 (2.4,4.4)	3.4 (2.5,4.6)	3.2 (2.0,4.3)
ESR at 3 months mm/hr: median (IQR)	14.0 (6.0,28.0)	14.0 (6.0,27.0)	18.0 (9.0,34.0)	21.0 (11.0,42.0)	19.5 (10.0,32.5)	14.0 (5.0,35.0)	14.0 (5.0,28.0)
CRP at 3 months mg/l: median (IQR)	5.0 (2.0,11.0)	5.0 (2.0,11.0)	4.0 (2.0,9.0)	5.0 (2.0,11.0)	5.0 (2.0,9.0)	3.0 (1.0,9.0)	4.0 (2.0,8.0)

Clinical outcomes at 3 months in patients diagnosed with EIA with different ethnicity backgrounds. DAS28: disease activity score for 28 joints; EIA: early inflammatory arthritis; IQR: interquartile range; *n*: population size.

sensitivity analysis (Supplementary Table S6, available at *Rheumatology* online).

Regression for the individual components of the DAS28 demonstrated ethnic differences for tender joint count, swollen joint count, inflammatory markers (especially ESR) and patient global (see Supplementary Table S7, available at *Rheumatology* online).

The proportion of patients commencing a MTX-based DMARD regimen was higher for White compared with non-White patients (see Supplementary Table S8, available at *Rheumatology* online). In regression models, the odds of commencing a MTX-based regimen were significantly lower for Asian patients compared with White patients. A similar pattern was observed for corticosteroids (see Supplementary Table S9, available at *Rheumatology* online).

Discussion

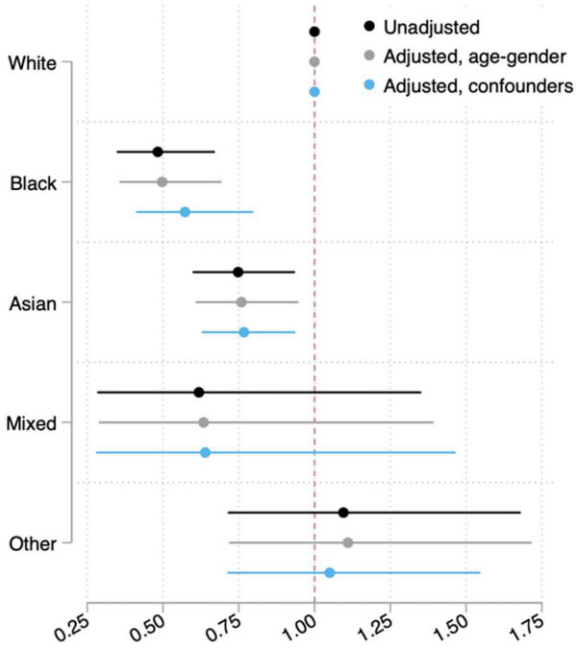
In this study, we have described worse clinical outcomes for patients of non-White ethnicity who are diagnosed with EIA, relative to patients of White ethnicity. Patients from ethnic minority backgrounds were over 25% less likely than White patients to achieve remission by three months. The results are consistent with findings from the USA [16, 22]. Explanatory factors that we could identify included differences in disease phenotype, less provision of disease specific education, differences in treatment targets, and sub-optimal initial treatment strategy.

The explanations for differences in outcomes warrant further consideration. Patients from ethnic minorities were younger and were less likely to smoke. The different disease pattern across ethnicities may be explained by a difference in genetic predisposition evidenced by differences in the rate of seropositivity, environmental exposures, or by a confounded association, or systematic bias in our data capture. Genetic associations between ethnicity and RA severity have been described previously [23, 24]. The HLA-DR4 gene has been strongly correlated with both seropositivity, disease severity and treatment response among White patients, but far less is known for other ethnic groups [25, 26]. Environmental or dietary exposures may be relevant, as alcohol consumption has been shown to be protective [27], and alcohol consumptions varies across ethnic groups [28]. Smoking is an established risk factor for incident disease, disease severity and worse treatment response [29]. However, in our analyses, we were able to adjust for most of these factors, and the impact on the association between ethnicity and remission remained significant.

We considered whether comorbidity burden could be contributing to observed differences. Non-White patients had fewer comorbidities overall. Given that comorbidity would, if anything, correspond with worse outcomes, this is unlikely to be an explanation for differences in remission rates in our study.

We observed differences in the provision of disease education, having a treatment target set and accessing

Fig. 3 Associations between ethnicity and disease remission at three months



Logistic regression coefficient plots demonstrating the relationship between ethnicity and disease remission (based on DAS28) in three months in patients with confirmed EIA diagnoses. White patients were used as the reference group. All models were clustered by England and Wales Hospital Trust codes (clustered standard errors were estimated to account for within-centre correlations). The confounder-adjusted model was adjusted for age, gender, smoking, comorbidities, DAS28 at baseline, seropositivity for RF or CCP. Data are presented as odds ratios and 95% CIs. CCP: anti-citrullinated c-peptide antibody; DAS28: disease activity score for 28 joints; EIA: early inflammatory arthritis.

emergency services in the Mixed and Other group compared with White patients. This may have occurred because of the availability of language- and culture-appropriate educational material. When educating patients who attend early RA services, individual approaches that consider cultural diversity need to be adopted [30]. It has been reported previously that patients diagnosed with early RA from ethnic minorities have more limited access to education materials in non-English languages [8, 31]. When translations are available, difficulties in effective communication linked to culture or educational background can persist. Recognizing the impact of early disease experiences on long-term outcomes may be particularly relevant to patients from ethnic minority backgrounds who develop RA [32]. Interventions such as Apni Jung (our fight against RA) may have helped South Asian patients, but similar resources are not available for other ethnic groups [33].

White patients were more likely to be treated with MTX in their initial DMARD regimen. This could be part of the explanation for observed differences in remission rates. MTX is a recommended first-line treatment for most patients diagnosed with RA [34]. The decision to commence a particular regimen will depend upon shared decision-making between the clinician and patient. It is relevant that in our data, there was evidence that patients of non-White ethnicity were less likely to have a treatment target set, which is a surrogate for successful shared decision-making. Other researchers have also observed differences in shared decision-making across ethnicities, with clinicians advocating different treatments based upon ethnicity [35, 36].

A major strength of this study is the large sample size, with representation from most rheumatology departments in England and Wales. Patients of ethnic minority accounted for 14% in NEIAA and this is representative of the UK population, based upon the latest ONS report [37]. Our study also has important limitations. First, we must acknowledge that there is likely to be sampling bias in our data collection method. The NEIAA is a mandated national audit programme, but not all trusts return audit data [18]. There is evidence that the return of audit data is directly correlated with centre-level performance [38], and so it is likely that we are missing information on patients in centres where barriers to care may be greater. In addition, we are also making analyses that divide ethnicity into very broad categories; some based upon skin colour (White and Black), while others are based upon enormous geographic areas (Asian). While the nomenclature has a long history, it hinders more granular understanding of how culture interplays with health outcomes. Some evidence suggests that it is culture and social determinants that are the major drivers of differential health outcome, rather than genetics and skin colour [39].

A relationship between social deprivation and disease remission has been shown [40]. Our previous study in early RA reported that patients living in more deprived areas were less likely to achieve remission [3]. Social deprivation is inextricably intertwined with ethnicity in many parts of the UK, and addressing this is one of the major focuses of the NHS long-term plan [4].

Finally, we did not capture information on adherence. Evidence suggests that negative beliefs about treatments and illness perception are related to non-adherence to treatment [41]. Ethnic minorities are more likely to have negative views about DMARDs and RA compared with White patients [9]. It has been reported that non-adherence to DMARDs in South Asian patients for example has been associated with dissatisfaction about DMARD mechanisms of action and potential adverse events [42, 43].

Conclusion

The difference between equality and equity within the NEIAA cohort is an important finding that must be highlighted. Process measure performance suggests that

there is equality in provision of care at the start, but the outcomes highlight an imbalance in equity. Disease remission after three months was different between groups in our cohort. Differences in use and uptake of care may explain our results, or this could be the result of genetics and/or cultural factors. Although equality and equity both promote fairness, equality is achieved through treating all patients the same regardless of need, while equity is accomplished through treating people differently according to need. Understanding this difference is the key to delivering the best care for all and closing the health gap for patients diagnosed with RA.

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J.B.G., J.L. involved in the design. J.B.G., M.A.A., S.B. analysed the data. All authors interpreted the results. J.BG., M.A.A., S.D., S.B., S.N. wrote the report with contributions from all other authors. J.B.G. and S.D. are joint senior authors. J.B.G., S.N. accessed and verified the underlying data. M.A.A., J.BG. had final responsibility for the decision to submit for publication.

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Data availability statement

Data used in this study were collected for the National Early Inflammatory Arthritis Audit and are available on request to the data controllers [the Healthcare Quality Improvement Partnership (HQIP)]. Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article. All figures and tables included in this article are original.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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Infections: Infections, including serious infections such as pneumonia and opportunistic infections e.g. tuberculosis (TB), oesophageal candidiasis, and cryptococcosis have been reported. Risk benefit should be assessed prior to initiating in patients with risk factors for infections (see SmPC). Patients should be closely monitored for the development of signs and symptoms of infections during and after filgotinib treatment. Treatment should be interrupted if the patient is not responding to antimicrobial therapy, until infection is controlled. There is a higher incidence of serious infections in the elderly aged 75 years and older, caution should be used when treating this population. Tuberculosis: Patients should be screened for TB before initiating filgotinib, and filgotinib should not be administered to patients with active TB. Viral reactivation: Cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical studies (see SmPC). If a patient develops herpes zoster, filgotinib treatment should be temporarily interrupted until the episode resolves. Screening for viral hepatitis and monitoring for reactivation should be performed. Malignancy: Immunomodulatory medicinal products may increase the risk of malignancies. Malignancies were observed in clinical studies (see SmPC). Fertility: In animal studies, decreased fertility, impaired spermatogenesis, and histopathological effects on male reproductive organs were observed (see SmPC). The potential effect of filgotinib on sperm production and male fertility in humans is currently unknown. Haematological abnormalities: Do not start therapy, or temporarily stop, if Absolute Neutrophil Count (ANC) <1 × 10^9 cells/L, ALC <0.5 × 10^9 cells/L or haemoglobin <8 g/dL. Temporarily stop therapy if these values are observed during routine patient management. Vaccinations: Use of live vaccines during, or immediately prior to, filgotinib treatment is not recommended. 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For Great Britain and Northern Ireland, reporting forms and information can be found at yellowcard.mhra.gov.uk or via the Yellow Card app (download from the Apple App Store or Google Play Store).
Adverse events should also be reported to Galapagos via email to DrugSafety.UK.Ireland@glpg.com or 00800 7878 1345

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