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Original article

Predictors of poor function in RA based on two prospective UK inception cohorts. Do comorbidities matter?

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Abstract

Objectives. Evidence suggests that factors beyond disease activity associate with functional disability in RA. The primary study objective was to explore associations between comorbidities, sociodemographic factors and functional outcomes at five and 10 years.

Methods. RA patients from two UK prospective cohorts were grouped into low (<1.5) and high (≥1.5) five- and 10-year health assessment questionnaire (HAQ) score. Clinical variables (e.g. disease activity, rheumatoid nodules, erosions) and sociodemographic factors (e.g. ethnicity, deprivation) were recorded at baseline and yearly thereafter. Comorbidity was measured using the Rheumatic Diseases Comorbidity Index (RDCI). Binary logistic regression models were fitted using multiple imputation.

Results. In total, 2701 RA patients were recruited (mean age 56.1 years, 66.9% female). A total of 1718 (63.4%) had five-year and 820 (30.4%) 10-year follow-up data. In multivariable analysis, no association was found between RDCI and HAQ ≥ 1.5 at five or 10 years. Sociodemographic factors (increased age at disease onset, female gender, minority ethnicity) were associated with higher odds of HAQ ≥ 1.5 at five and 10 years, with worse deprivation additionally associated with HAQ ≥ 1.5 at 10 years (OR 0.79, 95% CI: 0.69, 0.90).

Conclusion. Comorbidities at baseline have not been found to be associated with worse RA functional outcome in the long-term. On the other hand, sociodemographic factors, independently of disease measures, are associated with worse functional outcome in RA at five and 10 years, in models adjusting for comorbidity burden. Tailoring management interventions according to not only clinical disease parameters but also patient sociodemographic factors may improve long-term outcomes including functional disability.

Key words: sociodemographic factors, comorbidity, multimorbidity, Health Assessment Questionnaire, rheumatoid arthritis

CLINICAL SCIENCE

Rheumatology key messages

- Sociodemographic factors, independently of disease activity, are associated with worse functional outcome in RA.
- Identifying patients at increased risk of functional disability at initial review enables targeted management.

Introduction

Functional disability in RA is a well-recognised and historically reported debilitating outcome of disease, adding significantly to the overall global burden of RA [1]. Worsening functional ability in RA has been linked to the ongoing, progressive course of this chronic, inflammatory musculoskeletal condition and comes at both physical and psychological cost to patients. Indeed,

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functional measures are often used as a substitute for quality of life in RA [2].

Generally, it is accepted that poor disease control negatively impacts functional ability, especially in early disease, but some studies have shown this is not always the case. Functional deterioration has been reported in 10–21% of early RA patients with moderate disease activity when following standard treatment [3]. Beyond inflammation, other factors that may cause worse function need to be considered.

The comorbidity burden in RA is substantial, even on first presentation of disease [4]. Yet, this observation does not seem to be accompanied by increasing disease severity, whether measured by markers of high disease activity or worse physical function [4]. Additionally, the presence of comorbidities has been associated with unfavourable functional and disease activity outcomes over two years, despite intensive treatment strategies aiming for remission [5]. Disentangling the underlying mechanisms and understanding potential causal links between comorbidities and disease outcomes including function in RA is challenging. Associations between comorbidities and poor health outcomes including physical disability have been traditionally studied alongside other disease-related factors, e.g. inflammation, but not in relation to non-biological, sociodemographic factors.

Sociodemographic determinants of health play a crucial role in health and disease and have gained much attention in recent times, where there is an expectation to manage patients more holistically, with care tailored to their individual physical and psychosocial needs. To achieve this, we have argued for a better understanding of the role of sociodemographic factors, alongside important clinical factors including comorbidities, as drivers of adverse outcomes in RA [6]. In seeking to unravel these so-called 'syndemic' elements [6], this study stems from a larger research initiative to understand multimorbidity in the disease and risk-stratify patients according to individual need.

The aim was to identify predictors of worse five- and 10-year functional outcome, measured using the HAQ, using information available at first outpatient appointment. Of particular interest was whether patients affected by comorbidities have an elevated risk of poor functional ability, taking into account sociodemographic factors.

Methods

Study population

This study used data collected within the Early RA Study (ERAS, 1986–2001) and Early RA Network (ERAN, 2002–2012). These are consecutive prospective cohorts, designed similarly regarding recruitment, variables collected and follow-up timings, often studied together and previously described in detail [7]. ERAS patients were recruited from nine hospitals in England and ERAN patients from 23 centres across England, Wales and Northern Ireland. Dates of deaths occurring in the UK were reported by NHS Digital for all participants who consented to follow-up. ERAS patients gave informed consent as required at time of enrolment [prior to Good Clinical Practice (GCP) implementation], approved by the East Hertfordshire Local Research Ethics Committee. ERAN patients gave informed, written consent, approved by the Trent Research Ethics Committee.

Baseline measures

Comorbidities

The variable of interest was baseline comorbidity, measured using the Rheumatic Disease Comorbidity Index (RDCI [8]). Scores ranged from 0 to 9, where higher scores indicated a higher comorbidity burden, and were used as a continuous variable in the analysis. The RDCI arranges 11 illness types into eight categories (lung disease, heart attack/other cardiovascular/stroke), fracture, depression, cancer, ulcer/stomach problem, hypertension, diabetes), defined using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. As well as overall RDCI values, individual disease categories were assessed to determine association with high HAQ outcome.

Sociodemographic and clinical variables

At baseline, standard demographic data were recorded including age at onset, gender and ethnicity. Patient postcodes were used to derive an Index of Multiple Deprivation [9] (IMD), Welsh Index of Multiple Deprivation [10] (WIMD) or Northern Ireland Multiple Deprivation Measure [11] (NIMDM) rank, then grouped into quintiles to enable comparison across regions. Clinical data collected at each appointment included HAQ, BMI, haemoglobin, ESR and presence of erosions, rheumatoid nodules, RF and anti-cyclic citrullinated peptide autoantibodies (anti-CCP). Disease activity was measured using the 28-joint Disease Activity Score DAS28 [12] for ERAN and the Disease Activity Score (DAS [13]) in the ERAS cohort. DAS scores were transformed so they could be directly comparable to the DAS28 using a formula previously tested and applied on the same data (Carpenter *et al.* [14]). Months from onset of symptoms to first rheumatology outpatient appointment and from first appointment to prescription of the first DMARD were each recorded. Variables were continuous (e.g. age, haemoglobin, ESR) or categorical, e.g. IMD (quintiles; 1, most deprived to 5, least deprived), smoking status (ever/never), serostatus (positive/negative RF and/or anti-CCP), ethnicity (white/minority ethnic).

Outcome measures

Five-year and 10-year HAQ

HAQ scores above 1.5 indicate considerable levels of disability, shown to be the value above which progressive damage to large joints (shoulder, elbow, hip, knee, ankle) is expected to increase [15]. Therefore, the primary outcome of interest in this analysis was HAQ score studied as a binary outcome to indicate high ($\geq$1.5) *vs* low ($<$1.5)

HAQ at five years. HAQ at 10 years was investigated in secondary analysis.

Statistical analysis

Five-year and 10-year HAQ

The statistical analysis was prespecified (Supplementary Data S1, available at *Rheumatology* online) for HAQ outcomes. Descriptive statistics were calculated for patients with HAQ <1.5 and HAQ ≥ 1.5 values at five and 10 years; medians and interquartile ranges (IQR) for continuous variables, frequencies and proportions for binary/ordinal. Odds ratios comparing the groups were obtained using binary logistic regression models for each covariate under consideration, fitting separate models for five- and 10-year HAQ. Five-year outcomes were not used in 10-year models, because only baseline factors were of interest. Variables with a likelihood ratio test *P*-value <0.2 were tested in multivariable analysis.

Models for five-year and 10-year HAQ were built using forward selection based on clinical relevance and statistical robustness to obtain odds ratios (ORs) and 95% CIs. Age at onset, gender and RDCI were included *a priori*. Interaction testing was undertaken as appropriate to determine inclusion of interaction terms and is described in detail in Supplementary Data S2, available at *Rheumatology* online. Once model building was complete, multicollinearity between covariates was assessed, excluding variables with centred variance inflation factors >10. After models were determined using complete cases, multiple imputation by chained equations was used. All baseline variables in the complete case model and HAQ outcomes were imputed. Baseline and five-year values of clinical covariates (measured annually) were included in the imputation model for the five-year HAQ model, similarly baseline and 10-year values in the 10-year HAQ model, if available. Patients who had died before year five/10, respectively, were excluded from imputation models. Each model was performed with 20 imputations. Continuous variables were modelled using linear regression, binary using logistic regression and ordinal using predictive mean matching.

Although two-sided *P*-values of <0.05 are referred to as significant, a multiple testing correction was not applied. Thus, *P*-values should be interpreted with caution and significant results seen as hypothesis-generating rather than confirmatory.

HAQ sensitivity analyses

In these analyses, five- and 10-year HAQ were used in their continuous form. In addition, a binary RDCI variable was formed, comparing patients with no comorbidities (RDCI $= 0$) to those with at least one (RDCI ≥ 1).

Supplementary analyses: Short-Form 36 health questionnaire

To support the HAQ findings, the effect of baseline comorbidity burden on health-related quality of life (HRQoL) at five years was assessed, using the Short-Form 36 Health Questionnaire (SF-36). Full details of the methods used can be found in Supplementary Data S2, available at *Rheumatology* online.

Results

The ERAS and ERAN cohorts recruited 2701 patients, mean age 56.1 years and 66.9% female. Median time from onset to first outpatient appointment was 6 months. By year five, 1718 (63.4%) patients remained enrolled, 185 (6.8%) were known to have died and a further 798 (29.5%) were no longer in follow-up. At year 10, 820 (30.4%) were enrolled, 454 (16.8%) had died and 1427 (52.8%) were not in follow-up. Comparisons between those still enrolled and those no longer followed up are shown in Supplementary Tables S1 and S2, available at *Rheumatology* online. Those remaining enrolled at five years had median age of onset of 55.5 years (IQR 45–65) compared with 62 (IQR 50–70) years for those no longer followed up.

Five-year HAQ

Table 1 summarises baseline characteristics for patients with HAQ <1.5 and HAQ ≥ 1.5 at five years, with scores available for 1441 (83.9%) of those still in follow-up. A higher age of onset was seen among the HAQ ≥ 1.5 group (median 58, IQR 48–68 compared with median 55, IQR 43–63). A larger proportion of females had HAQ ≥ 1.5 (75.3% compared with 63.9% for HAQ <1.5). More patients had a minority ethnic background with HAQ ≥ 1.5 (4.7% compared with 1.7%), although just 37 patients identified as belonging to a minority ethnic group. A larger proportion of patients with HAQ ≥ 1.5 were in the most deprived IMD quintile (15.8% compared with 11.0%). Conversely, 28.8% of patients with HAQ <1.5 were in the least deprived group compared with 20.2% with HAQ ≥ 1.5.

More patients with HAQ ≥ 1.5 had at least one comorbidity (with 18.2% having an RDCI score of 1 and 11.8% scoring ≥ 2, compared with the HAQ <1.5 group, where 13.5% had RDCI score of 1 and 9.9% had a score of ≥ 2). The median RDCI score for both groups was 0, although the IQR was slightly wider for HAQ ≥ 1.5 group. Each comorbidity category was slightly more prevalent among the HAQ ≥ 1.5 group. Hypertension was the most common comorbidity, present in 9.0% of patients with HAQ <1.5 and 12.2% of patients with HAQ ≥ 1.5. Baseline HAQ was higher for those with high five-year HAQ (median 1.5, IQR 1.00–2.13 compared with 0.88, IQR 0.38–1.38) and DAS was similarly elevated (5.30, IQR 4.47–6.08 compared with 4.51, IQR 3.68–5.49).

Results of univariable analyses are shown in Supplementary Table S3, available at *Rheumatology* online. Increased age at onset, being female, or of minority ethnicity were associated with high HAQ, with $P < 0.2$. The two least deprived IMD quintiles were associated with a reduction in odds of HAQ ≥ 1.5. Several clinical and treatment variables were associated with

Table 1 Patient, comorbidity and disease characteristics according to elevated HAQ status

	Five-year HAQ <1.5	Five-year HAQ ≥1.5	Ten-year HAQ <1.5	Ten-year HAQ ≥1.5
Total *n* (%)	1007 (69.9)	434 (30.1)	438 (60.9)	281 (39.1)
Sociodemographic				
Age at onset (years): median (IQR)	55 (45–63)	58 (48–68)	52 (43–61)	55 (45–64)
Female: *n* (%)	643 (63.9)	327 (75.3)	280 (63.9)	215 (76.5)
White ethnicity: *n* (%)	982 (98.3)	410 (95.3)	426 (98.6)	263 (94.9)
Ever smoked: *n* (%)	394 (48.1)	177 (50.1)	165 (41.9)	110 (44.0)
IMD quintiles: *n* (%)				
1 (Most deprived)	97 (11.0)	61 (15.8)	40 (9.7)	57 (20.7)
2	123 (14.0)	68 (17.6)	48 (11.7)	50 (18.1)
3	211 (24.0)	101 (26.2)	87 (21.1)	64 (23.2)
4	196 (22.3)	78 (20.2)	91 (22.1)	43 (15.6)
5 (Least deprived)	253 (28.8)	78 (20.2)	146 (35.4)	62 (22.5)
Comorbidity				
RDCI (continuous): Median (IQR)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)
Lung disease: *n* (%)	58 (5.8)	28 (6.5)	22 (5.0)	13 (4.6)
Heart attack, other CV, stroke: *n* (%)	44 (4.4)	25 (5.8)	12 (2.7)	3 (1.1)
Fractures: *n* (%)	3 (0.3)	2 (0.5)	2 (0.5)	1 (0.4)
Depression: *n* (%)	15 (1.5)	10 (2.3)	4 (0.9)	6 (2.1)
Cancer: *n* (%)	13 (1.3)	10 (2.3)	4 (0.9)	4 (1.4)
Ulcer or stomach problem: *n* (%)	24 (2.4)	18 (4.1)	8 (1.8)	8 (2.8)
Hypertension: *n* (%)	91 (9.0)	53 (12.2)	24 (5.5)	17 (6.0)
Diabetes: *n* (%)	16 (1.6)	9 (2.1)	8 (1.8)	6 (2.1)
Clinical measures				
Onset to 1st appt: median (IQR)	6 (4–12) *n* = 1002	7 (4–12) *n* = 431	7 (4–12) *n* = 438	6 (4–12) *n* = 281
1st appt to 1st DMARD: median (IQR)	2 (0–4) *n* = 894	1 (0–4) *n* = 415	2 (1–8) *n* = 378	2 (1–6) *n* = 268
HAQ: median (IQR)	0.88 (0.38–1.38) *n* = 998	1.50 (1.00–2.13) *n* = 428	0.75 (0.25–1.25) *n* = 438	1.38 (0.88–2.00) *n* = 281
DAS28: median (IQR)	4.51 (3.68–5.49) *n* = 988	5.30 (4.47–6.08) *n* = 427	4.46 (3.60–5.29) *n* = 433	5.11 (4.30–5.93) *n* = 279
BMI (kg/m^2): median (IQR)	25.40 (22.80–28.40) *n* = 920	26.20 (23.05–29.76) *n* = 397	25.0 (22.6–27.4) *n* = 400	25.2 (22.5–28.7) *n* = 251
Erosions: *n* (%)	251 (25.5)	120 (28.2)	92 (21.2)	75 (27.6)
Nodules: *n* (%)	62 (6.2)	26 (6.0)	24 (5.5)	22 (7.8)
Haemoglobin (g/dl): median (IQR)	12.8 (11.8–13.8) *n* = 1001	12.6 (11.7–13.8) *n* = 427	12.8 (11.9–13.8) *n* = 434	12.5 (11.4–13.5) *n* = 279
Seropositive: *n* (%)	702 (73.4)	327 (77.9)	315 (73.3)	209 (76.0)
ESR (mm/h): median (IQR)	30 (15–54) *n* = 956	36 (18–60) *n* = 416	30 (14–50) *n* = 430	40 (24–64) *n* = 279

1st appt to 1st DMARD: time (months) from first appointment to starting DMARD; DAS28: Disease Activity Score (28 count); IMD: Index of Multiple Deprivation; Onset to 1st appt: time (months) from symptom onset to first outpatient appointment; RDCI: Rheumatic Diseases Comorbidity Index.

HAQ ≥ 1.5, with $P < 0.2$. Notably, increasing baseline HAQ was associated with a large increase in odds of high five-year HAQ.

Multivariable analyses

Results of multivariable analyses are shown in Table 2. No association was found between baseline RDCI and HAQ ≥ 1.5 at five years in models fully adjusted for all relevant covariates (OR 1.06, 95% CI: 0.90, 1.26). Patients of minority ethnicity were at higher risk of high five-year HAQ, but with a wide CI (OR 4.29, 95% CI: 2.13, 8.64). A strong association between baseline HAQ and five-year HAQ was seen (OR 3.62, 95% CI: 3.01, 4.35). Increased age at onset, female gender, increased onset to first outpatient time and seropositive status at baseline were all associated with five-year HAQ ≥ 1.5 scores. Worse deprivation levels were associated with increased HAQ values, but including ethnicity attenuated

Table 2 Sociodemographic and clinical factors associated with HAQ outcomes

	5-year HAQ ($n = 2516$)	10-year HAQ ($n = 2247$)
	Odds ratio (95% CI)	Odds ratio (95% CI)
Baseline RDCI (continuous)	1.06 (0.90, 1.26)*	0.94 (0.73, 1.22)*
Age at onset	1.02 (1.01, 1.03)	1.02 (1.00, 1.03)
Gender (female)	1.48 (1.11, 1.97)	1.58 (1.10, 2.25)
Baseline HAQ	3.62 (3.01, 4.35)	2.47 (1.80, 3.41)
Minority ethnicity	4.29 (2.13, 8.64)	3.65 (1.55, 8.59)
Onset to 1st OPD (months)	1.03 (1.01, 1.05)	[a]
IMD quintiles	0.95 (0.85, 1.05)**	0.79 (0.69, 0.90)
Seropositive	1.67 (1.21, 2.30)	[a]
ESR (mm/h)	0.99 (0.99, 1.00)	[b]

Variables tested in univariable analysis shown in Supplementary Table S2, available at *Rheumatology* online. IMD: index of multiple deprivation; RDCI: rheumatic diseases comorbidity index. Variables tested in multivariable analyses: *Five-year HAQ*: RDCI, age at onset, gender, HAQ, disease activity score, seropositive status, haemoglobin, ethnicity, IMD, time (months) from symptom onset to first outpatient appointment, time (months) from first appointment to commencing DMARD, BMI, ESR. *Ten-year HAQ*: RDCI and each component individually, age at onset, gender, HAQ, disease activity score, presence of erosions, BMI, haemoglobin, ethnicity, IMD, time (months) from first appointment to commencing DMARD. [a]Not selected in univariable analysis ($P > 0.2$). [b]Not selected in multivariable analysis ($P > 0.05$). Multivariable logistic regression models; gender, age at onset and RDCI included *a priori*. *$P > 0.05$ (not significant). **All $P < 0.02$ except IMD ($P = 0.316$) at five years.

this association, suggesting a potential confounding effect. Evidence of association with ESR and odds of high HAQ was found but with an extremely small effect size.

10-year HAQ

Table 1 compares sociodemographic, comorbidity and disease characteristics, with HAQ scores recorded for 719 (87.7%) of those in follow up at year 10. Patients with 10-year HAQ ≥ 1.5 scores were more likely to be slightly older (median 55, IQR 45–64 compared with median 52, IQR 43–61), female (76.5% v 63.9%) and of minority ethnic origin (94.9% v 98.6%). Differences in deprivation were more marked than at five years, 35.4% of patients with HAQ < 1.5 compared with just 22.5% of those with HAQ ≥ 1.5 were in the least deprived quintile. No notable differences were seen in RDCI or any comorbidity component. Again, baseline HAQ was higher for those with high 10-year HAQ (median 1.38, IQR 0.88–2.00 compared with 0.75, IQR 0.25–1.25) and similarly for baseline DAS28 (median 5.11, IQR 4.30–5.93 compared with 4.46, IQR 3.60–5.29). More patients with high 10-year HAQ scores had erosions (27.6% *vs* 21.2%) and nodules (7.8% *vs* 5.5%) at baseline.

Results of univariable analysis are shown in Supplementary Table S3, available at *Rheumatology* online. As with five-year HAQ, increased age at onset, female gender, minority ethnicity and more deprived IMD quintiles were individually associated with high 10-year HAQ scores, shown in Table 2. Baseline RDCI was not associated with high 10-year HAQ scores, in contrast with five-year HAQ. Among baseline clinical measures, first appointment to first DMARD time, baseline HAQ, baseline DAS28, BMI, haemoglobin and ESR remained associated with $P < 0.2$. Although associated with five-year HAQ, onset to first appointment time and being seropositive were not associated with 10-year HAQ. Conversely, presence of erosions at baseline were associated with HAQ ≥ 1.5 at 10 but not five years.

Multivariable analyses

Results of models fully adjusted for all covariates are shown in Table 2. Baseline RDCI was not found to be associated with increased odds of high 10-year HAQ (OR 0.94, 95% CI: 0.73, 1.22). In contrast to the five-year model, time from onset to first appointment, being seropositive and ESR were not included. Worse deprivation was associated with increased odds of 10-year HAQ ≥ 1.5 (OR 0.79, 95% CI: 0.69, 0.90). Baseline HAQ remained strongly associated with high 10-year HAQ but with a smaller magnitude than in the five-year model (OR 2.47, 95% CI: 1.80, 3.41).

HAQ sensitivity analyses

Results are shown in Supplementary Table S4, available at *Rheumatology* online. There remained no association between baseline RDCI and baseline HAQ when considered binary and continuous respectively at either five (0.03, 95% CI: −0.06, 0.12) or 10 years (0.01, 95% CI: −0.17, 0.18).

Supplementary analyses: Short-Form 36 health questionnaire

Full results of this analysis are shown in Supplementary Data S2, and model results presented in Supplementary Table S5, both available at *Rheumatology* online. In summary, there was no evidence of an association between RDCI at baseline and five-year SF-36, for either the physical or mental scores.

Discussion

This study shows that baseline comorbidity, measured using the RDCI, is not significantly associated with high HAQ at five or 10 years. In contrast, sociodemographic factors (increased age at disease onset, female gender and minority ethnicity) were significantly associated with higher odds of HAQ $\geq$ 1.5 at five and 10 years. Worse deprivation was associated with HAQ $\geq$ 1.5 at 10 years.

Previous studies have shown a high comorbidity burden at diagnosis of RA, increasing over time [16, 17]. The recent work of England *et al.* [16] showed higher incidence and poorer trajectory of multimorbidity in patients with RA, particularly after symptom onset. Few studies, however, have examined how comorbidities are associated with RA disease outcomes in later years. Recognising the importance of comorbidities, we took the approach of adjusting for them in our models, allowing for effects of other variables to be seen, possible only because of the wealth of data within these cohorts.

In addition to functional outcome, this study considered patients likely to report poorer health-related quality of life (HRQoL) at five years, measured using the Short-Form Health Survey (SF-36) [18], as described in Supplementary Data S1, available at *Rheumatology* online. HAQ and SF-36 were the focus of this study, recognising the importance of these patient-reported outcomes (PROs) and the growing need to deliver more tailored, holistic patient care that takes into account the patient perspective [19]. The value of using these tools is being increasingly recognised, as focus shifts towards outcomes important to patients as well as clinicians. This study is unique in two principal ways. Firstly, in using two of the largest and longest longitudinal RA cohorts, rich in comorbidity and other clinical and sociodemographic data. Secondly, in attempting to study both biological and non-biological factors using principles of syndemic theory to provide in-depth understanding of associations between these factors and how they could impact on physical function in RA. Evidence suggests that comorbidities negatively impact on the achievement of treat-to-target goals and act as a barrier to optimal outcomes in RA [17, 20, 21]. This study goes a step further, providing evidence that sociodemographic factors potentially play an additional role, beyond comorbidities, which should not be sidelined when managing patients.

The focus of this study has been on using patient features identified at the initial rheumatology appointment to determine those more likely to have worse disease outcome in later years. A previous study [22] found that clinical data three months after onset was more informative, once treatment had begun. This work has shown that, although clinical features can aid identification of those patients for whom treatment failure is more likely, sociodemographic factors, collected at baseline, can also be helpful in guiding specific care pathways. These may relate to drug therapy and or non-drug therapeutic strategies such as more tailored physical therapy (physiotherapy) especially in view of the outcome.

The link between joint damage and physical function is well known and documented [23]. Although relevant to the HAQ outcome, radiographic data were beyond the scope of this study, which had a focus on sociodemographic and clinical factors and their potential role at baseline.

Strengths of this study include the use of large, early RA cohorts designed such that data could be collectively analysed. The long study follow-up and treatment according to best practice allow for useful, real-world information on RA treatment and outcomes. The richness of data has resulted in meaningful analyses focussing on parameters beyond those routinely reported in the literature, including sociodemographic factors. A study limitation is the age of the cohorts, partly due to previous more conservative approaches to disease management including lower use of biologic therapies, especially in the context of comorbidities. Thus, generalisability of study findings is limited. Additionally, few patients identified with a minority ethnic heritage, so their responses could not be meaningfully analysed to represent different communities. Univariable analysis showed a relationship between deprivation (IMD) and HAQ $\geq$ 1.5 outcome; in multivariable analysis this ceased to exist once ethnicity was included at five years. Deprivation and/or ethnicity appear to contribute to poor HAQ outcome, with 28% of minority ethnicity compared with 14% of white patients in the most deprived quintile within these cohorts. However, limited sampling of these subpopulations highlights an important avenue for future study to better delineate these relationships, understand these mechanisms and identify potentially modifiable factors to redress health inequalities. A further limitation is the number of hypotheses tested and lack of multiple testing correction. It is possible that some significant results are false positives, and results should be interpreted as exploratory rather than confirmatory.

In conclusion, this study found no association between baseline comorbidities and later functional outcome. However, in models adjusting for comorbidities, based on their importance and relevance on disease outcomes in RA, sociodemographic factors play a role in functional ability in the longer-term and should be considered. These findings provide ground for risk stratification in RA at first in-clinic patient review, enabling the identification of patients at higher risk of functional disability. Insights on the potential role of patient-related, sociodemographic factors beyond traditional disease measures such as high disease activity allows for more holistic patient management and tailored intervention to be undertaken.

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Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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