Predictors of interest in predictive testing for rheumatoid arthritis among first degree relatives of rheumatoid arthritis patients

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Abstract

Objectives. There is increasing interest in prediction and prevention of RA. It is important to understand the views of those at risk to inform the development of effective approaches. First-degree relatives (FDRs) of RA patients are at increased risk of RA. This study assessed predictors of their interest in predictive testing for RA.

Methods. Questionnaires were completed by RA patients (provided with their questionnaire by a healthcare professional) and their FDRs (provided with their questionnaire by their RA proband). FDR surveys assessed interest in taking a predictive test, demographic variables, perceived RA risk, attitudes about predictive testing, autonomy preferences, illness perceptions, avoidance coping and health anxiety. Patient surveys included demographic variables, disease impact, RA duration and treatment. Ordinal logistic regression examined the association between FDRs’ characteristics and their interest in predictive testing. Generalized estimating equations assessed associations between patient characteristics and FDRs’ interest in predictive testing.

Results. Three hundred and ninety-six FDRs responded. Paired data from the RA proband were available for 292. The proportion of FDRs interested in predictive testing was 91.3%. Information-seeking preferences, beliefs that predictive testing can increase empowerment over health and positive attitudes about risk knowledge were associated with increased interest. Beliefs that predictive testing could cause psychological harm predicted lower interest. Patient characteristics of the proband were not associated with FDRs’ interest.

Conclusions. FDRs’ interest in predictive testing for RA was high, and factors associated with interest were identified. These findings will inform the development of predictive strategies and informational resources for those at risk.

Key words: RA, predictive testing, first degree relatives, survey, risk perception

Rheumatology key messages

- The majority of first-degree relatives were interested in taking a predictive test for RA.
- Information-seeking preferences, beliefs that predictive testing can increase empowerment over health, and attitudes towards risk knowledge predicted increased interest.
- Beliefs that predictive testing could lead to psychological harm predicted lower levels of interest.

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Introduction

Over recent decades, research has focused on early RA and those at risk of developing RA, to facilitate early intervention and stratified approaches [1–3].

Several prospective studies recruiting first-degree relatives (FDRs) are assessing the value of genetic and environmental variables with autoantibodies and inflammatory markers to predict RA development [4–6]. Interventions to reduce RA risk have also been tested in this group. These include 200–400 mg hydroxychloroquine taken daily for 12 months (trial data awaited) [7] and disclosure of personalized risk information [8]. FDRs who received such information were more likely to alter risk-related behaviours, and less concerned about their risk of RA [9] than a control group receiving standard risk education [8].

The clinical translation of research to predict and prevent RA will mean that at-risk groups will be offered risk assessment. It is therefore important to understand their views to ensure risk information is communicated in a way that is sensitive to recipients’ needs and concerns [10].

One qualitative study investigated FDRs’ perceptions of predictive testing for RA [11]. The majority had positive views towards predictive testing, feeling that it could increase awareness of early RA symptoms. Negative views related to uncertainty about test accuracy and potential for anxiety [11]. Further quantitative studies are needed to provide a robust understanding, including the impact of demographic and psychosocial characteristics on willingness to undergo predictive testing.

Studies in other diseases have found that witnessing a family member being affected by that disease increased perceived vulnerability and motivation to engage in predictive approaches [12, 13]. No studies have examined the influence of patients’ characteristics on FDRs’ perceptions towards predictive testing for RA.

The aim of the current study is to define predictors of interest in predictive testing for RA among FDRs of patients with a diagnosis of RA.

Methods

Design

Two cross-sectional surveys, one for patients with RA and another for their FDR, assessed interest in predictive testing and potential demographic and psychosocial predictors of such interest. This paper focuses on FDRs’ interest in predictive testing.

Procedure

Patients with a confirmed diagnosis of RA were identified via outpatient clinics in the West Midlands, England between March 2017 and January 2020. FDRs were eligible if they (i) were biological children and/or full siblings of a patient with RA; (ii) were aged 18 years or over; (iii) did not have a diagnosis of RA; and (iv) could complete a survey in English. All participants provided written, informed consent by completing a series of checkboxes to indicate that they agreed to take part.

Patients were provided with a pack containing a survey for them and two for FDRs. Patients were invited to pass the latter onto FDRs and could request additional surveys if they wished to invite more than two. Patients were advised that FDRs could take part in the survey even if they themselves did not wish to. All participants were provided with a freepost envelope to return completed surveys. Surveys within each pack were labelled with a unique code, allowing FDR and patient surveys to be linked.

This study was approved by the Research Ethics Committee (Berkshire B): 16/SC/0369.

Measures

Primary outcome measure

Interest in predictive testing was assessed using one item: ‘If, in the next 6 months your doctor offered you a test that predicted your risk of developing rheumatoid arthritis, would you take the test?’ Responses were measured on a four-point Likert scale ranging from 0 (‘no definitely not’) to 3 (‘yes definitely’).

Measures of potential predictors of FDRs’ interest in predictive testing

Selection of measures was informed by a literature review on interest in predictive testing and guided by the self-regulation model of health behaviour [14]. Brief versions of relevant measures were included where available in response to patient partner assessment of cognitive burden for participants. FDRs reported gender, age, ethnicity, post code, employment status, level of education, smoking status, relationship to index patient (child or sibling), whether they live with this patient and how often they talk to them. Demographic variables were found by previous studies to predict interest in predictive testing in other diseases such as cardiovascular disease and type 2 diabetes [15].

The survey included the following questionnaires. (i) The Brief Illness Perceptions Questionnaires (Brief IPQ) measured perceptions of RA in eight domains: consequences, timeline, personal control, treatment control, identity, concern, understanding and emotion. Items were scored on an 11-point scale, with higher scores indicating a more threatening view of RA [16]. The wording of items was modified for at-risk individuals, for example [17]: ‘If you were to develop rheumatoid arthritis, how much do you think your treatment would help it?’ This scale was shown to have good internal reliability and test–retest reliability in healthy individuals [17] and predict interest in predictive testing for cancer and heart disease [18].

(ii) The single item literacy screen, assessed health literacy. Responses were measured on a five-point scale from 0 (‘never’) to 4 (‘always’). This scale demonstrates good sensitivity (54%) and specificity (83%) in patients with diabetes [19]. Scores above 2 indicate difficulty...
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reading health-related material [19]. Health literacy has been shown to be associated with health behaviours and self-reported health status [20], and interventions to increase health literacy improve health outcomes [21].

(iii) The three-item subjective numeracy scale (SNS-3) was also included [22]. Each item was scored on a six-point scale with scores ranging from 3 to 18. Higher scores indicate stronger perceived numeracy. This scale has good internal reliability (α = 0.78) in patients with diseases such as chronic kidney disease and diabetes [22]. Understanding of numerical information has been shown to affect medical decision-making [23].

(iv) The Autonomy Preference Index, measured health-related decision-making (six items) and information-seeking preferences (eight items) [24] using a five-point scale ranging from 0 ('strongly disagree') to 4 ('strongly agree'). For each subscale, scores were converted into a scale from 0 to 100, with higher scores indicating greater autonomy preferences. This index has been found to have good internal consistency (α = 0.82) in a sample of diabetic patients [24] and predict interest in predictive testing for other conditions [25, 26].

(v) The Brief Approach/Avoidance Coping Questionnaire measured approach/avoidant coping style in stressful situations in cognitive, socioemotional and action-related domains [27]. This measure has 12 items, each measured using a five-point scale ranging from 0 ('strongly disagree') to 4 ('strongly agree'). Total scores range from 0 to 18, with higher scores indicating higher approach or lower avoidance coping styles. This scale demonstrated acceptable internal consistency (α = 0.68) in a large sample of primary care patients [27]. Coping styles have been found to be associated with health-related behaviour [28].

(vi) Dispositional optimism was assessed using three items from the Life Orientation Test–Revised (LOT-R). Each item was assessed using a scale ranging from 0 ('strongly disagree') to 4 ('strongly agree'). Total scores ranged from 0 to 12, with higher scores indicating increased optimism [29]. This scale was shown to have strong internal consistency (α = 0.82). Individuals with higher levels of optimism reported greater interest in taking a predictive genetic test, and greater intentions to use this information to change health behaviours [30].

(vii) The Short Health Anxiety Inventory assessed worry about health, awareness of bodily sensations and feared consequences of illness using 18 items and is associated with increased health information-seeking [31]. For each item, participants select one of four statements that best reflect their feelings over the past 6 months. Total scores range from 0 to 54, with scores above 27 indicating health anxiety [32]. This scale has been shown to have high test–retest reliability (r = 0.87) and internal consistency (α = 0.95) in patients with hypercholesterolaemia, panic disorder and social phobia [31].

Four items assessed perceived lifetime risk of RA: absolute risk, relative risk, experiential risk and concern about risk. These were adapted from previous studies examining the association between perceived risk and interest in predictive testing or engagement in health behaviours [18, 30, 33, 34]. Each was scored on a five-point response scale, with higher scores indicating higher perceived risk.

Twenty-three attitudinal statements measuring perceived advantages (12 items) and disadvantages (11 items) of ‘finding out how likely it is that you will develop rheumatoid arthritis in the future’ were adapted from Cameron et al. [18], with additional items based on themes identified in previous qualitative investigations [11, 35, 36] (a list of these statements is provided in Supplementary Data Section S1, available at Rheumatology online). Participants indicated the extent to which they agreed with each statement using a five-point scale ranging from ‘strongly disagree’ to ‘strongly agree’.

Measures of patients’ characteristics
For those FDRs for whom linked survey data were available from their index patient, measures of patients’ demographic and clinical characteristics were assessed, including reported gender, age, ethnicity, postcode, employment status, level of education, smoking status, years with RA, current treatment for RA and RA status measured using the Rheumatoid Arthritis Impact of Disease (RAID) scale (includes seven domains: pain, ability, fatigue, sleep, physical wellbeing, emotional wellbeing and coping; higher scores indicate worse disease status) [37]. Each domain was measured on an 11-point scale from 0 to 10, where 0 indicates no impact, and 10 indicates extreme impact. A total score was calculated taking into account the weight of each domain (pain 0.21, ability 0.16, fatigue 0.15, sleep 0.12, emotional wellbeing 0.12, physical wellbeing 0.12 and coping 0.12). Total scores range between 0 and 10, where higher scores indicate worse reported disease status [37].

Analysis
Analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA).

Association between FDR characteristics and their interest in predictive testing
Descriptive statistics were used to summarize demographic and psychosocial characteristics. Principal component analysis with direct oblimin rotation was conducted to reduce the 23 attitudinal items into a smaller number of underlying factors. Original scores for each item were multiplied by factor loadings to obtain a weighted score. From this, a mean score was calculated.

Kruskall-Wallis H- and Mann–Whitney U-tests assessed the effects of categorical variables on interest in predictive testing. Spearman’s rank correlations were used to investigate associations between ordinal variables and interest in predictive testing. All predictor variables with a significance level <0.05 informed an ordinal logistic regression model using backward elimination, with interest in predictive testing recoded as ‘definitely interested’, ‘probably interested’ and ‘not interested’.
Association between patients’ characteristics and FDRs’ interest in predictive testing

Where possible, FDRs’ interest in predictive testing was paired with measures of index patients’ demographic and clinical characteristics. Descriptive statistics summarized patients’ characteristics. Generalized estimating equations (GEEs) using an exchangeable working correlation matrix assessed the ability of patient characteristics to predict FDRs’ interest in predictive testing allowing for possible non-independence of FDRs paired with the same patient. This method of analysis offers a flexible tool for dealing with correlated data; in this case responses from a single patient could be related to more than one FDR [38, 39].

Sample size calculation

A sample size of 288 FDRs provides 95% confidence that an estimate of the proportion of positive and negative responses for the primary outcome variable was within 0.06 of the true value. Our multivariate ordinal regression analysis included 316 FDRs.

Patient and public involvement

Three patient research partners (PRPs) contributed to survey development, commenting on drafts of the protocol, study documents and surveys (via email), and attending a focus group to discuss survey design and content. They highlighted that issues raised in the survey might cause anxiety for some patients and FDRs, who may not have considered that they or their relatives might have an elevated risk status. As a result, potential patient participants were approached during clinic appointments by a member of the healthcare team rather than by mail, so they had the opportunity to raise any concerns. Participants were provided with an information resource about RA risk for family members of RA patients as part of a debriefing letter at the end of the survey. Patients diagnosed with RA within the previous six months were not approached, as PRPs felt that such patients may be experiencing anxiety associated with adjusting to diagnosis and treatment, and that it was not appropriate to invite these patients to take part in a study that may raise additional concern about the possibility of other family members developing RA. As a result of further PRP input, a subjective rather than an objective measure of numeracy was used, the patients’ survey was divided into two parts to allow for a break if necessary, tables of contents were included so participants were aware of the nature of survey questions before deciding to respond, and opportunities for open-ended responses were included.

Results

Survey packs were provided to 1720 patients; 396 FDRs returned a survey; for 292 of these, paired data from 214 patients were available. In some cases, FDRs who returned a survey did not have a linked patient. In other cases, multiple FDRs were associated with one patient survey. For 148 patients one FDR completed the survey, 56 had two, eight had three and two had four. Analyses are presented separately for predictors relating to FDRs and to index patients.

The distribution of scores for FDRs’ interest in taking a predictive test within the following 6 months is described in Table 1. The majority (91.3%) reported being definitely or probably interested in taking a predictive test.

In the principal component analysis of the 23 items describing advantages and disadvantages of predictive testing, factor loadings < 0.3 were disregarded [40]. The Kaiser–Meyer–Olkin measure of sampling adequacy was 0.84. Bartlett’s test of sphericity was significant (P < 0.001). A six-factor solution (Supplementary Table S1, available at Rheumatology online) explained 64.44% of the variance. Interpretation of the factor loadings labelled the factors as: (i) desire for risk knowledge; (ii) psychological harm to self; (iii) increased empowerment over health; (iv) family (dis)stress; (v) accuracy of predictive testing; and (vi) social consequences.

FDRs’ demographic and psychosocial characteristics, and univariate analyses of their relationships with interest in predictive testing, are summarized in Table 2; 20 predictors were significantly associated with interest in predictive testing.

Measures of perceived risk were highly intercorrelated. Risk framed in absolute, rather than relative terms is less likely to affect health behaviour [41]. Therefore, as these results were intended to be informative for the development of information to support shared decision-making rather than intended to influence behaviour, absolute risk was the measure of risk perception included in the multivariate analysis.

Six variables were included in the final multivariate regression. A flow chart detailing this process is provided

| Interest in taking a predictive test | Number of relatives (n = 393)a | Percentage |
|-------------------------------------|-------------------------------|------------|
| Yes definitely                      | 218                           | 55.5       |
| Yes probably                        | 141                           | 35.9       |
| No probably not                     | 29                            | 7.4        |
| No definitely not                   | 5                             | 1.3        |

a n = 3 (0.8%) missing responses from relatives. FDR: First-degree relative.
### Table 2: Descriptive statistics and univariate analyses for FDRs’ characteristics and associations with interest in testing

| FDRs' characteristics                           | Descriptive statistics | Association with interest in predictive testing |
|-------------------------------------------------|------------------------|-----------------------------------------------|
| Age, median (IQR), years (n = 16 missing)       | 42 (30–53)             | –0.07 rs                                     |
| Deprivation index, median (IQR) (n = 82 missing) | 4 (2–7)                | –0.05 rs                                     |
| Gender, n (%) (n = 6 missing)                    |                        |                                               |
| Male                                            | 137 (35.1)             | 3 (2–3) H                                   |
| Female                                          | 253 (64.9)             | 3 (2–3) H                                   |
| Employment, n (%) (n = 6 missing)                |                        |                                               |
| Employed                                        | 297 (76.2)             | 3 (2–3) H                                   |
| Unemployed                                      | 62 (15.9)              | 3 (2–3) H                                   |
| Other                                           | 31 (7.9)               | 3 (2–3) H                                   |
| Ethnic group, n (%) (n = 2 missing)              |                        |                                               |
| White                                           | 328 (83.2)             |                                               |
| Mixed                                           | 15 (3.8)               |                                               |
| Asian                                           | 36 (9.1)               |                                               |
| Black                                           | 14 (3.6)               |                                               |
| Other                                           | 1 (0.3)                |                                               |
| Smoking, n (%) (n = 8 missing)                   |                        |                                               |
| Current                                         | 40 (10.3)              | 3 (2–3) H                                   |
| Ever                                            | 111 (28.6)             | 3 (2–3) H                                   |
| Never                                           | 237 (61.1)             | 3 (2–3) H                                   |
| Education, n (%) (n = 17 missing)                |                        |                                               |
| A-level or lower                                | 187 (49.3)             | 3 (2–3) H                                   |
| Higher than A-level                             | 192 (50.7)             | 3 (2–3) H                                   |
| Type of relative, n (%) (n = 4 missing)          |                        |                                               |
| Child                                           | 295 (75.3)             | 3 (2–3) H                                   |
| Sibling                                         | 97 (24.7)              | 2 (2–3) H                                   |
| Living with index patient, n (%) (n = 2 missing) |                        |                                               |
| Yes                                             | 77 (19.5)              | 2 (2–3) H                                   |
| No                                              | 317 (80.5)             | 3 (2–3) H                                   |
| Frequency of talking to index patient, n (%) (n = 4 missing) |                        |                                               |
| Never                                           | 0                      | 0.12 rs                                     |
| Rarely                                          | 4 (1)                  |                                               |
| Sometimes                                       | 20 (5.1)               |                                               |
| Often                                           | 154 (39.3)             |                                               |
| Daily                                           | 214 (54.6)             |                                               |
| Perceived absolute risk, n (%) (n = 2 missing)   | 3 (2–3)                | 0.33 rs                                     |
| Very unlikely                                   | 5 (1.3)                | <0.001                                       |
| Unlikely                                        | 31 (7.9)               |                                               |
| Neither likely nor unlikely                     | 101 (25.6)             |                                               |
| Likely                                          | 202 (51.3)             |                                               |
| Very likely                                     | 55 (14.0)              |                                               |
| Perceived relative risk, n (%) (n = 2 missing)   | 3 (2–3)                | 0.34 rs                                     |
| Much less likely                                | 6 (1.5)                | <0.001                                       |
| Less likely                                     | 17 (4.3)               |                                               |
| About the same                                  | 155 (39.3)             |                                               |
| More likely                                     | 174 (44.2)             |                                               |
| Much more likely                                | 42 (10.7)              |                                               |
| Perceived experiential risk, n (%) (n = 1 missing) | 3 (2–3)                | 0.32 rs                                     |
| Strongly disagree                               | 3 (0.8)                | <0.001                                       |
| Disagree                                        | 28 (7.1)               |                                               |
| Neither agree nor disagree                      | 92 (23.3)              |                                               |
| Agree                                           | 211 (53.4)             |                                               |
| Strongly agree                                  | 61 (15.4)              |                                               |
| Worry about risk, n (%) (n = 1 missing)          | 3 (2–3)                | 0.29 rs                                     |
| Strongly disagree                               | 12 (3.0)               | <0.001                                       |
| Disagree                                        | 42 (10.8)              |                                               |

(continued)
In Supplementary Fig. S1 (available at Rheumatology online). The final model is outlined in Table 3. Desire to obtain risk knowledge, information-seeking preferences and beliefs that predictive testing would increase empowerment over health predicted increased interest in predictive testing. Those who perceived themselves to be ‘neither likely nor unlikely to develop RA’, or ‘unlikely to develop RA’ had lower interest in predictive testing than those who perceived themselves to be ‘very likely to develop RA’. However, those who perceived themselves to be ‘very unlikely to develop RA’ did not have a lower interest in predictive testing compared with those who felt ‘very likely to develop RA’. Finally, FDRs’ beliefs that predictive testing would result in psychological harm predicted decreased interest in testing.

The multivariate model was replicated using relative risk instead of absolute risk as a sensitivity analysis. One small difference was found in results: for relative risk, those who felt they were ‘less likely to develop RA compared with other people their age, gender and race’ did not have a lower interest in predictive testing compared with those who felt they were ‘much more likely to develop RA compared with other people their age, gender and race’. The relative risk multivariate model can be found in Supplementary Table S2 (available at Rheumatology online). The association between patients’ characteristics and FDRs’ interest in predictive testing

Descriptive statistics summarizing demographic and clinical characteristics of index patients, and tests for

| Table 2 Continued |
|--------------------|
| FDRs’ characteristics | Descriptive statistics | Association with interest in predictive testing |
| -------------------- | ---------------------- | --------------------------------------------- |
|                     |                       | Statistics | P               |
| Neither agree nor disagree | 116 (29.4) | 0.004 rs | 0.95 |
| Agree               | 166 (42.0) |           |                 |
| Strongly agree      | 59 (14.9)  |           |                 |
| Health literacy, n (%) (n = 4 missing) | 0 (0–0) |           |                 |
| Never               | 306 (78.1) |           |                 |
| Rarely              | 49 (12.5)  |           |                 |
| Sometimes           | 26 (6.6)   |           |                 |
| Often               | 6 (1.5)    |           |                 |
| Always              | 5 (1.3)    |           |                 |
| Subjective numeracy, median (IQR) (n = 4 missing) | 15.00 (11.25–17.75) | –0.05 rs | 0.33 |
| Brief illness perception questionnaire, median (IQR) (n = 5 missing) | 8 (7–9) | 0.14 rs | 0.006 |
| Consequences (n = 5 missing) | 10 (9–10) | 0.14 rs | 0.007 |
| Timeline (n = 5 missing) | 5 (3–7) | –0.03 rs | 0.52 |
| Personal control (n = 5 missing) | 7 (5–8) | –0.02 rs | 0.72 |
| Treatment control (n = 5 missing) | 8 (7–8) | 0.11 rs | 0.03 |
| Identity (n = 4 missing) | 8 (7–10) | 0.21 rs | <0.001 |
| Concern (n = 2 missing) | 7 (6–9) | 0.10 rs | 0.04 |
| Understanding (n = 2 missing) | 7 (6–9) | 0.11 rs | 0.03 |
| Emotional (n = 2 missing) | 7 (6–9) |           |                 |
| Information seeking, median (IQR) (n = 4 missing) | 84.38 (75.00–93.75) | 0.34 rs | <0.001 |
| Decision making, median (IQR) (n = 1 missing) | 58.33 (45.83–70.83) | –0.02 rs | 0.73 |
| Brief Avoidance Coping Questionnaire, median (IQR) (n = 9 missing) | 30 (26–34) | 0.12 rs | 0.02 |
| Optimism, median (IQR) (n = 5 missing) | 7 (6–9) | 0.06 rs | 0.25 |
| Health anxiety overall, median (IQR) (n = 17 missing) | 12 (8–18) | 0.14 rs | 0.006 |
| Attitudes towards testing, median (IQR) | 1.08 (0.72–1.37) | 0.47 rs | <0.001 |
| Desire for risk knowledge (n = 62 missing) | 1.00 (0.66–1.41) | –0.18 rs | 0.001 |
| Psychological harm to self as a result of knowing risk (n = 49 missing) | 1.98 (1.79–2.35) | 0.42 rs | <0.001 |
| Increased empowerment over health (n = 7 missing) | 1.29 (0.79–1.84) | –0.15 rs | 0.003 |
| Family (di)stress associated with experience of getting a test (n = 2 missing) | 1.72 (0.86–2.58) | 0.17 rs | 0.001 |
| Accuracy of predictive testing (n = 6 missing) | 1.24 (0.82–1.64) | –0.06 rs | 0.27 |

Correlation coefficients are reported for Spearman’s rank correlations, medians and IQRs are reported for Kruskal–Wallis H- and Mann–Whitney U-tests. rs: Spearman’s rank correlation; H: Kruskal–Wallis H-test; U: Mann–Whitney U-test. FDR: first-degree relative; IQR: interquartile range.

Descriptive statistics summarizing demographic and clinical characteristics of index patients, and tests for
the relationships between patients’ characteristics and FDRs’ interest in predictive testing for RA are presented in Table 4.

FDRs were more interested in taking a predictive test if their index patient was male compared with female ($P = 0.05$) and reported higher levels of RA pain ($P = 0.04$). However, these characteristics only weakly predicted their FDRs’ interest in predictive testing and would not remain statistically significant when corrected for multiple comparisons.

### Discussion

This study is the first quantitative assessment of perceptions of predictive testing for RA among FDRs, and the impact of RA patients’ characteristics on FDRs’ interest in predictive testing.

FDRs expressed high levels of interest in predictive testing for RA. This aligns with results from qualitative studies [11, 42]. This study also confirms qualitative findings [11, 43] that interest in predictive testing for RA was associated with beliefs that such tests would be extremely accurate, and able to rule in/out future RA development. Such beliefs may help individuals to manage potentially complex risk information [43, 44]. However, these mechanisms may impede understanding of risk information provided by healthcare professionals. Therefore, effective communication of the probabilistic nature of risk information for diseases such as RA presents a challenge for approaches to support shared decision-making in this context.

Several predictors were associated with FDRs’ interest in predictive testing, including greater information-seeking preferences, beliefs that predictive testing would increase empowerment and attitudinal items reflecting a desire to obtain risk knowledge about RA. The influence of FDRs’ desire to obtain risk knowledge of RA and beliefs that tests would increase control over health on interest in testing is consistent with findings from studies in other diseases [18, 33]. Increased health information-seeking preferences were previously found to be associated with testing for Alzheimer’s disease [26], but not for hereditary breast or ovarian cancer [45].

The association between perceived risk and interest in predictive testing contradicts findings in other disease areas [46]. However, this finding should be interpreted with caution since few participants perceived themselves to be very unlikely to develop RA.

FDRs were less interested in taking a predictive test if they agreed that risk information could cause psychological harm. This aligns with previous qualitative research highlighting concerns about the potential for anxiety about risk status [11, 43]. Predictive approaches therefore should incorporate appropriate information and support.

Patients’ characteristics were not associated with FDRs’ interest in predictive testing. It is possible that an assessment of impact of the patient’s RA over time, rather than over the previous week as captured by the RAID questionnaire, may have been predictive. However, long term impact of RA is reflected by whether or not the proband is taking biologic drugs for RA, which was not associated with FDRs’ interest in predictive testing in the current study.

These findings increase understanding of perceptual variation among those at risk of developing RA. Further research is needed to explore interest in different types of predictive tests for RA (e.g. multi-omics technologies) and tests with different performance characteristics (e.g. high positive predictive value vs high negative predictive value).

### Strengths and limitations

This study has several methodological strengths, including a large sample, paired data linking FDRs with index patients.

### Table 3

| FDRs’ predictors                                      | OR (95% CI)       | P-value       |
|------------------------------------------------------|------------------|---------------|
| Desire for RA risk knowledge                         | 7.03 (3.51, 14.12) | <0.001        |
| Information seeking preferences                      | 1.03 (1.01, 1.06)  | 0.005         |
| Increased empowerment over health                    | 2.64 (1.25, 5.59)  | 0.011         |
| Perceived absolute risk (reference category—very likely) |                 |               |
| Likely                                               | 0.44 (0.16, 1.23)  | 0.118         |
| Neutral                                              | 0.20 (0.07, 0.58)  | 0.003         |
| Unlikely                                              | 0.22 (0.06, 0.75)  | 0.016         |
| Very unlikely                                        | 0.24 (0.02, 3.07)  | 0.270         |
| Psychological harm to self as a result of knowing risk| 0.36 (0.23, 0.58)  | <0.001        |
| Frequency of talking to index patient (reference category—everyday) |         |               |
| Rarely                                                | 0.49 (0.05, 5.36)  | 0.561         |
| Sometimes                                             | 0.39 (0.13, 1.14)  | 0.085         |
| Often                                                 | 1.43 (0.84, 2.43)  | 0.186         |

$n = 80/396$ missing cases. FDR: first-degree relative; OR: odds ratio.
patients, multidisciplinary contributors, and extensive patient involvement. Six predictors were included, and the sample size was sufficient using the rule of thumb of a minimum of 10 cases per predictor, although it is acknowledged that the fraction of patients in the 'Not interested' category was lower than expected. A further strength includes recruitment of FDRs via patients with a confirmed diagnosis, rather than individuals self-reporting family history. This is important as people often confuse RA with other conditions, such as osteoarthritis [47].

As FDR recruitment relied on patients passing the survey to their FDRs, the study may be subject to selection bias.

### Table 4: Descriptive statistics and GEEs examining impact of patient characteristics on FDRs' interest in testing (n = 214)

| Patients' characteristics | Patients whose relatives were definitely interested in taking a test (n = 150) | Patients whose relatives were probably interested in taking a test (n = 133) | Patients whose relatives were not interested in taking a test (n = 27) | Wald chi-square | P-value |
|---------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|----------------|--------|
| Age, median (IQR), years  | 64 (55–73)                                      | 64 (55–73)                                      | 65 (60–75)                                      | 0.20           | 0.66   |
| Deprivation index, median (IQR) (n = 32 missing) | 4 (2–6)                                          | 4 (2–6)                                          | 3 (2–4.75)                                      | 10.60          | 0.31   |
| Gender, n (%) (n = 6 missing) | Male 50 (24)                                | 39 (26.7)                                       | 23 (20.7)                                       | 3.98           | 0.05   |
|                               | Female 158 (76)                                | 107 (73.3)                                      | 88 (79.3)                                       | 24 (92.3)      |        |
| Employment, n (%) (n = 1 missing) | Employed 63 (29.6)                            | 37 (24.8)                                       | 36 (31.9)                                       | 7 (25.9)       |        |
|                               | Unemployed 148 (69.5)                          | 109 (73.2)                                      | 77 (68.1)                                       | 20 (74.1)      |        |
|                               | Other 2 (0.9)                                   | 3 (2.0)                                          | 0                                               | 0              |        |
| Ethnic group, n (%) (n = 2 missing) | White 180 (84.9)                              | 124 (83.8)                                      | 95 (84.1)                                       | 24 (88.9)      |        |
|                               | Mixed 4 (1.9)                                   | 2 (1.4)                                           | 4 (3.5)                                         | 1 (3.7)        |        |
|                               | Asian 18 (8.5)                                  | 17 (11.5)                                        | 8 (7.1)                                         | 1 (3.7)        |        |
|                               | Black 10 (4.7)                                  | 5 (3.4)                                           | 6 (5.3)                                         | 1 (3.7)        |        |
|                               | Other 0                                         | 0                                                 | 0                                               | 0              |        |
| Smoking, n (%) (n = 3 missing) | Current 17 (8.1)                               | 12 (8.1)                                         | 8 (7.1)                                         | 1 (3.7)        |        |
|                               | Ever 70 (33.2)                                  | 58 (39.2)                                        | 40 (35.7)                                       | 9 (33.3)       |        |
|                               | Never 124 (58.8)                                | 78 (52.7)                                        | 64 (57.1)                                       | 17 (63)        |        |
| Education, n (%) (n = 13 missing) | A level or lower 135 (67.2) | 103 (73)                                      | 70 (63.6)                                       | 16 (66.7)      |        |
|                               | Higher than A level 66 (32.8)                   | 38 (27)                                          | 40 (36.4)                                       | 8 (33.3)       |        |
| RA duration, median (IQR), years (n = 43 missing) | 10 (4–20)                                      | 10 (4–16)                                       | 10 (4–20)                                       | 0.62           | 0.43   |
| RAID scorea, median (IQR) (n=8 missing) | 5.00 (3.00–7.00)                             | 5.23 (2.95–7.00)                               | 5.30 (2.07–7.03)                               | 0.49           | 0.48   |
| Pain                        | 5 (3–7)                                        | 5 (3–7)                                          | 5 (3–8)                                         | 5 (3–7)        | 19.32  | 0.04   |
| Ability                     | 5 (2–7)                                        | 6 (2–8)                                          | 5 (2–8)                                         | 5 (2.75–7.25)  | 14.23  | 0.16   |
| Fatigue                     | 6 (3–8)                                        | 6 (4–8)                                          | 6 (3–8)                                         | 6 (3.75–8)     | 7.66   | 0.66   |
| Sleep                       | 5 (2–8)                                        | 6 (3–8)                                          | 5 (2–8)                                         | 5 (2–7)        | 7.49   | 0.68   |
| Physical wellbeing         | 5 (3–7)                                        | 5 (3–8)                                          | 5 (2–7)                                         | 4 (3–7)        | 10.61  | 0.30   |
| Emotional wellbeing        | 4 (2–7)                                        | 5 (3–7)                                          | 5 (1–7)                                         | 4 (2–7)        | 16.44  | 0.09   |
| Coping                      | 4 (2–6)                                        | 4 (2–6)                                          | 4 (1–6)                                         | 4 (2–6)        | 17.42  | 0.07   |
| Current treatment, n (%)    | No treatment 4 (1.9)                           | 3 (2.0)                                          | 2 (1.8)                                         | 1 (3.7)        | 0.001  | 0.97   |
| Conventional synthetic DMARDs and glucocorticoids | 189 (88.3) | 135 (90)                                      | 95 (84.1)                                       | 23 (85.2)      | 1.40   | 0.24   |
| Biologic DMARDs            | 67 (31.3)                                      | 47 (31.3)                                        | 36 (31.9)                                       | 11 (40.7)      | 0.47   | 0.50   |

aRA Impact of Disease score. FDR: first-degree relative; GEE: generalized estimating equation; IQR: interquartile range; RAID: Rheumatoid Arthritis Impact of Disease.
bias. Recruitment of FDRs is challenging [48, 49] and further research is needed to compare alternative strategies and investigate predictors of the likelihood that patients will pass on RA risk information to their relatives. Additionally, recruiting FDRs in this manner meant that no data were available for FDRs who did not respond to the survey. It would be informative to understand the characteristics and views of this group. Further work using alternative methodologies is needed to understand the views of FDRs who are unlikely to respond to a survey of this kind.

No objective measure assessed patients’ disease activity in this study. Further investigation is needed to examine associations between FDRs’ interest in testing and measures of patients’ disease activity including objective elements (e.g. DAS28). Furthermore, participants in this cross-sectional study were linked with one family member with RA, but may have had experience of other relatives from previous generations who may have been more severely affected by RA. Further investigation is needed to comprehensively assess relationships between FDRs’ interest in predictive testing for RA and their experience of the impact of RA on their family members, and how this varies over time. However, this experience is likely to be reflected in their illness perceptions, which were assessed in this study.

Finally, female participants of white British ethnicity are over-represented in the present sample.

Conclusion

FDRs’ interest in predictive testing for RA was high. Several predictors were identified, including information-seeking preferences, beliefs that predictive testing would increase empowerment over health and desire for RA risk knowledge. FDRs who perceived themselves to be ‘neither likely nor unlikely’, or perceived themselves to be ‘unlikely’ to develop RA were less interested in taking a predictive test compared with those who perceived themselves to be ‘very likely’ to develop RA. Finally, beliefs that testing could lead to psychological harm predicted lower interest. These findings will inform development of effective predictive strategies and information to support decision-making in individuals considering predictive tests for RA or taking part in prospective and preventive research.

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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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Indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs.* May be used as monotherapy or in combination with methotrexate.

*From biochemical assays, the clinical relevance of which is uncertain. JAK, Janus kinase; RA, rheumatoid arthritis; TYK, Tyrosine kinase.

Refer to Summary of Product Characteristics (SmPC) before prescribing, and for full prescribing information.

JYSELECA® filgotinib 100 mg or 200 mg film-coated tablets.

Indications: Jyseleca is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs (DMARDs). Jyseleca may be used as monotherapy or in combination with methotrexate (MTX).

Dosage: Jyseleca is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who respond inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs. May be used as monotherapy or in combination with methotrexate.

Dose: Adults: 200 mg once daily. Taken orally without food. It is recommended that tablets are swallowed whole. Laboratory monitoring refers to the SmPC for information regarding laboratory monitoring and dose initiation or interruption. Therapy: A starting dose of 100 mg once daily is recommended for patients aged 75 years and older as clinical experience is limited. Renal impairment: No dose adjustment required in patients with GFR of ≥ 30 mL/min. Hepatic impairment: Mild/moderate hepatic impairment: no dose adjustment required. Severe hepatic impairment: not recommended. Children (< 18 years): Safety and efficacy not yet established.

Contraindications: Hypersensitivity to the active substance or any of the excipients. Active tuberculosis (TB) or active serious infections. Pregnancy. Warnings: Precautions: See SmPC for full information. Immunosuppression: Combination use with immunosuppressive agents such as cyclophosphamide, biologics, or biologic combinations may increase the risk of infections. Malignancies: Malignancies may occur at any site, including skin. Patients should be closely monitored for the development of signs and symptoms of infections during and after treatment with Jyseleca. Treatment should be interrupted if the 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. Malfunction: Inammatory modulatory 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 neutrophil count (ANC) < 1.0 × 10^9/L, platelets < 50 × 10^9/L, or haemoglobin < 8 g/dL. Temporarily stop therapy if these values are observed during routine patient management. Vaccination: Use of live vaccines during, or immediately prior to, filgotinib treatment is not recommended. Lab tests: With filgotinib was associated with dose-dependent increases in lipid parameters, including total cholesterol, and high-density lipoprotein (HDL) levels, while low density lipoprotein (LDL) levels were slightly increased (see SmPC). Cardiac safety: Rheumatoid arthritis patients have an increased risk for cardiovascular disorders. Patients should have risk factors (e.g., hypertension, hyperlipidaemia) managed as part of usual care. Venous thromboembolism: Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving JAK inhibitors including filgotinib. Caution should be used in patients with risk factors for DVT/PE, such as older age, obesity, a medical history of DVT/PE, or patients undergoing surgery, and prolonged immobilisation.

Labelling: Contains GABA, patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take filgotinib. Pregnancy/Lactation: Filgotinib is contraindicated in pregnancy. Filgotinib should not be used during breastfeeding. Women of childbearing potential must use effective contraception during and for at least 1 week after cessation of treatment. Driving/Using machinery: No or negligible influence; however, dizziness has been reported.

Side effects: See SmPC for full information. Common (≥1/100 to <1/10): dizziness, headache, upper respiratory tract infection and dizziness. Uncommon (≥1/1000 to <1/100): herpes zoster, pneumonia, maculopapular, herpes zoster, and blood creatinine phosphokinase increase. Serious side effects: See SmPC for full information. Legal category: POM. Pack size: 30 film-coated tablets/bottle. Pack size 180 tablets/bottle. Price: 180 tablets: £404.22 (cost price: £331.00) 280 tablets: £565.60 (cost price: £488.00) 360 tablets: £727.12 (cost price: £618.00) 500 tablets: £988.64 (cost price: £828.00).

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