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Original article

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

CLINICAL SCIENCE

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 screener, 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

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 behavioural 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 ($\alpha = 0.78$) 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 ($\alpha = 0.82$) 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 48, with higher scores indicating higher approach or lower avoidance coping styles. This scale demonstrated acceptable internal consistency ($\alpha = 0.68$) 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 ($\alpha = 0.82$). 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 reflects 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 found to have high test–retest reliability ($r = 0.87$) and internal consistency ($\alpha = 0.95$) in patients with hyperchondriasis, 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, post code, 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.

Kruskal–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 (di)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 indended 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

Table 1 Distribution of scores for FDRs' interest in taking a predictive test

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 ($n = 396$)

FDRs' characteristics	Descriptive statistics	Association with interest in predictive testing	
		Statistics	*P*
Age, median (IQR), years ($n = 16$ missing)	42 (30–53)	−0.07 [rs]	0.16
Deprivation index, median (IQR) ($n = 82$ missing)	4 (2–7)	−0.05 [rs]	0.41
Gender, *n* (%) ($n = 6$ missing)			0.15
Male	137 (35.1)	3 (2–3) [U]	
Female	253 (64.9)	3 (2–3) [U]	
Employment, *n* (%) ($n = 6$ missing)			0.08
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)			0.76
White	328 (83.2)	3 (2–3) [H]	
Mixed	15 (3.8)	3 (2–3) [H]	
Asian	36 (9.1)	3 (2–3) [H]	
Black	14 (3.6)	3 (2–3) [H]	
Other	1 (0.3)	3 (3–3) [H]	
Smoking, *n* (%) ($n = 8$ missing)			0.62
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)			0.65
A-level or lower	187 (49.3)	3 (2–3) [U]	
Higher than A-level	192 (50.7)	3 (2–3) [U]	
Type of relative, *n* (%) ($n = 4$ missing)			<0.001
Child	295 (75.3)	3 (2–3) [U]	
Sibling	97 (24.7)	2 (2–3) [U]	
Living with index patient, *n* (%) ($n = 2$ missing)			0.45
Yes	77 (19.5)	2 (2–3) [U]	
No	317 (80.5)	3 (2–3) [U]	
Frequency of talking to index patient, *n* (%) ($n = 4$ missing)		0.12 [rs]	0.02
Never	0		
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]	<0.001
Very unlikely	5 (1.3)		
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]	<0.001
Much less likely	6 (1.5)		
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]	<0.001
Strongly disagree	3 (0.8)		
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]	<0.001
Strongly disagree	12 (3.0)		
Disagree	42 (10.6)		

(continued)

TABLE 2 Continued

FDRs' characteristics	Descriptive statistics	Association with interest in predictive testing	
		Statistics	*P*
Neither agree nor disagree	116 (29.4)		
Agree	166 (42.0)		
Strongly agree	59 (14.9)		
Health literacy, *n* (%) (*n* = 4 missing)	0 (0–0)	0.004 ^{rs}	0.95
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)			
Consequences (*n* = 5 missing)	8 (7–9)	0.14 ^{rs}	0.006
Timeline (*n* = 5 missing)	10 (9–10)	0.14 ^{rs}	0.007
Personal control (*n* = 5 missing)	5 (3–7)	–0.03 ^{rs}	0.52
Treatment control (*n* = 5 missing)	7 (5–8)	–0.02 ^{rs}	0.72
Identity (*n* = 4 missing)	8 (7–8)	0.11 ^{rs}	0.03
Concern (*n* = 2 missing)	8 (7–10)	0.21 ^{rs}	<0.001
Understanding (*n* = 2 missing)	7 (6–9)	0.10 ^{rs}	0.04
Emotional (*n* = 2 missing)	7 (6–9)	0.11 ^{rs}	0.03
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)			
Desire for risk knowledge (*n* = 62 missing)	1.08 (0.72–1.37)	0.47 ^{rs}	<0.001
Psychological harm to self as a result of knowing risk (*n* = 49 missing)	1.00 (0.66–1.41)	–0.18 ^{rs}	0.001
Increased empowerment over health (*n* = 7 missing)	1.98 (1.79–2.35)	0.42 ^{rs}	<0.001
Family (di)stress associated with experience of getting a test (*n* = 2 missing)	1.29 (0.79–1.84)	–0.15 ^{rs}	0.003
Accuracy of predictive testing (*n* = 6 missing)	1.72 (0.86–2.58)	0.17 ^{rs}	0.001
Social consequences as a result of testing (*n* = 4 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.

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 3 Final ordinal logistic regression model to predict FDRs' interest in predictive testing

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.

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

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

Patients' characteristics	Patients	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 ($n = 7$ missing)	64 (55–73)	64 (55–73)	64 (54–70)	65 (60–75)	0.20	0.66
Deprivation index, median (IQR) ($n = 32$ missing)	4 (2–6)	4 (2–6)	4 (2–7)	3 (2–4.75)	10.60	0.31
Gender, *n* (%) ($n = 6$ missing)					3.98	0.05
Male	50 (24)	39 (26.7)	23 (20.7)	2 (7.7)		
Female	158 (76)	107 (73.3)	88 (79.3)	24 (92.3)		
Employment, *n* (%) ($n = 1$ missing)					0.84	0.36
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)					6.90	0.08
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)					1.43	0.49
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)					2.38	0.12
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 score[a], median (IQR) ($n = 8$ missing)	5.00 (3.00–7.00)	5.23 (2.95–7.00)	5.30 (2.07–7.03)	5.30 (2.85–7.26)	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

[a]RA Impact of Disease score. FDR: first-degree relative; GEE: generalized estimating equation; IQR: interquartile range; RAID: Rheumatoid Arthritis Impact of Disease.

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. 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.

References

1 Sahbudin I, Pickup L, Nightingale P *et al.* The role of ultrasound-defined tenosynovitis and synovitis in the prediction of rheumatoid arthritis development. Rheumatology (Oxford) 2018;57:1243–52.

2 Lübbers J, Vosslamber S, van de Stadt LA *et al.* B cell signature contributes to the prediction of RA development in patients with arthralgia. Ann Rheum Dis 2015;74:1786–8.

3 Lübbers J, Brink M, van de Stadt LA *et al.* The type I IFN signature as a biomarker of preclinical rheumatoid arthritis. Ann Rheum Dis 2013;72:776–80.

4 Pre-clinical EValuation of Novel Targets in RA (PREVeNT-RA): a nationwide register of first-degree relatives of patients with rheumatoid arthritis to evaluate predictors of the development of RA. http://www.preventra.net/ (22 August 2020, date last accessed).

5 Arthritis-Checkup: study of an early detection of the disease. http://www.arthritis-checkup.ch/index_gb.html (22 August 2020, date last accessed).

6 Kolfenbach JR, Deane KD, Derber LA *et al.* A prospective approach to investigating the natural history of preclinical rheumatoid arthritis (RA) using first-degree relatives of probands with RA. Arthritis Rheum 2009;61: 1735–42.

7 Strategy to Prevent the Onset of Clinically-Apparent Rheumatoid Arthritis. https://stop-ra.org/ (17 June 2021, date last accessed).

8 Sparks JA, Iversen MD, Yu Z *et al.* Disclosure of personalized rheumatoid arthritis risk using genetics, biomarkers, and lifestyle factors to motivate health behavior improvements: a randomized controlled trial. Arthritis Care Res (Hoboken) 2018;70:823–33.

9 Marshall AA, Zaccardelli A, Yu Z *et al.* Effect of communicating personalized rheumatoid arthritis risk on concern for developing RA: a randomized controlled trial. Patient Educ Couns 2019;102:976–83.

10 Falahee M, Finckh A, Raza K, Harrison M. Preferences of patients and at-risk individuals for preventive approaches to rheumatoid arthritis. Clin Ther 2019;41: 1346–54.

11 Stack RJ, Stoffer M, Englbrecht M *et al.* Perceptions of risk and predictive testing held by the first-degree relatives of patients with rheumatoid arthritis in England, Austria and Germany: a qualitative study. BMJ Open 2016;6:e010555.

12 Walter FM, Emery J. Perceptions of family history across common diseases: a qualitative study in primary care. Fam Pract 2006;23:472–80.

13 Evans JP, Skrzynia C, Burke W. The complexities of predictive genetic testing. BMJ 2001;322:1052–6.

14 Leventhal H, Brissette I, Leventhal EA. The common-sense model of self-regulation of health and illness. In: LD Cameron, H Leventhal, eds. The Self-Regulation of Health and Illness Behaviour. London: Routledge, 2003, 42–65.

15 Sanderson SC, Wardle J, Jarvis MJ, Humphries SE. Public interest in genetic testing for susceptibility to heart disease and cancer: a population-based survey in the UK. Prev Med 2004;39:458–64.

16 Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. J Psychosom Res 2006; 60:631–7.

17 Figueiras MJ, Alves NC. Lay perceptions of serious illnesses: an adapted version of the Revised Illness Perception Questionnaire (IPQ-R) for healthy people. Psychol Health 2007;22:143–58.

18 Cameron LD, Sherman KA, Marteau TM, Brown PM. Impact of genetic risk information and type of disease on perceived risk, anticipated affect, and expected consequences of genetic tests. Health Psychol 2009;28: 307–16.

19 Morris NS, MacLean CD, Chew LD, Littenberg B. The Single Item Literacy Screener: evaluation of a brief instrument to identify limited reading ability. BMC Fam Pract 2006;7:21.

20 Aaby A, Friis K, Christensen B, Rowlands G, Maindal HT. Health literacy is associated with health behaviour and self-reported health: a large population-based study in individuals with cardiovascular disease. Eur J Prev Cardiol 2017;24:1880–8.

21 Walters R, Leslie SJ, Polson R *et al.* Establishing the efficacy of interventions to improve health literacy and health behaviours: a systematic review. BMC Public Health 2020;20:1040.

22 McNaughton CD, Cavanaugh KL, Kripalani S, Rothman RL, Wallston KA. Validation of a short, 3-item version of the subjective numeracy scale. Med Decis Making 2015; 35:932–6.

23 Reyna VF, Nelson WL, Han PK, Dieckmann NF. How numeracy influences risk comprehension and medical decision making. Psychol Bull 2009;135:943–73.

24 Ende J, Kazis L, Ash A, Maskowitz MA. Measuring patients' desire for autonomy: decision making and information-seeking preferences among medical patients. J Gen Intern Med 1989;4:23–30.

25 Hildt E. Predictive genetic testing, autonomy and responsibility for future health. Med Stud 2009;1:143–53.

26 Gooding HC, Linnenbringer EL, Burack J *et al.* Genetic susceptibility testing for Alzheimer disease: motivation to obtain information and control as precursors to coping with increased risk. Patient Educ and Couns 2006;64:259–67.

27 Finset A, Steine S, Haugli L, Steen E, Laerum E. The brief approach/avoidance coping questionnaire: development and validation. Psychol Health Med 2002;7:75–85.

28 Litzelman K, Kent EE, Rowland JH. Interrelationships between health behaviors and coping strategies among informal caregivers of cancer survivors. Health Educ Behav 2018;45:90–100.

29 Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. J Pers Soc Psychol 1994;67:1063–78.

30 Taber JM, Klein WM, Ferrer RA *et al.* Dispositional optimism and perceived risk interact to predict intentions to learn genome sequencing results. Health Psychol 2015;34:718–28.

31 Salkovskis PM, Rimes KA, Warwick HMC, Clark DM. The Health Anxiety Inventory: development and validation of scales for the measurement of health anxiety and hypochondriasis. Psychol Med 2002;32: 843–53.

32 Olatunji BO, Etzel EN, Tomarken AJ, Ciesielski BG, Deacon B. The effects of safety behaviors on health anxiety: an experimental investigation. Behav Res Ther 2011;49:719–28.

33 Cameron LD, Reeve J. Risk perceptions, worry, and attitudes about genetic testing for breast cancer susceptibility. Psychol Health 2006;21:211–30.

34 Dillard A, Ferrer RA, Ubel PA, Fagerlin A. Risk perception measures' associations with behavior intentions, affect, and cognition following colon cancer screening messages. Health Psychol 2012;31:106–13.

35 Falahee M, Simons G, Raza K, Stack RJ. Healthcare professionals' perceptions of risk in the context of genetic testing for the prediction of chronic disease: a qualitative metasynthesis. J Risk Res 2018;21:129–66.

36 Bayliss K, Raza K, Simons G *et al.* Perceptions of predictive testing for those at risk of developing a

chronic inflammatory disease: a meta-synthesis of qualitative studies. J Risk Res 2018;21:167–89.

37 Gossec L, Dougados M, Rincheval N *et al.* Elaboration of the preliminary Rheumatoid Arthritis Impact of Disease (RAID) score: a EULAR initiative. Ann Rheum Dis 2009;68:1680–5.

38 Homish GG, Edwards EP, Eiden RD, Leonard KE. Analyzing family data: A GEE approach for substance use researchers. Addict Behav 2010;35:558–63.

39 Hanley JA, Negassa A, Edwardes MD, Forrester JE. Statistical analysis of correlated data using generalized estimating equations: an orientation. Am J Epidemiol 2003;157:364–75.

40 Tabachnick B, Fidell L. Using Multivariate Statistics. 6th edn. Boston, MA, USA: Pearson Education, 2013.

41 Malenka DJ, Baron JA, Johansen S, Wahrenberger JW, Ross JM. The framing effect of relative and absolute risk. J Gen Intern Med 1993;8:543–8.

42 Mosor E, Stoffer-Marx M, Steiner G *et al.* I would never take preventive medication! Perspectives and information needs of people who underwent predictive tests for rheumatoid arthritis. Arthritis Care Res (Hoboken) 2020;72:360–8.

43 Falahee M, Simons G, Buckley CD *et al.* Patients' perceptions of their relatives' risk of developing rheumatoid arthritis and of the potential for risk communication, prediction, and modulation. Arthritis Care Res (Hoboken) 2017;69:1558–65.

44 McAllister M. Personal theories of inheritance, coping strategies, risk perception and engagement in hereditary non-polyposis colon cancer families offered genetic testing. Clin Genet 2003;64:179–89.

45 Meiser B, Butow P, Barratt A *et al.* Attitudes to genetic testing for breast cancer susceptibility in women at increased risk of developing hereditary breast cancer. J Med Genet 2000;37:472–6.

46 Amin TT, Al-Wadaani HA, Al-Quaimi MM *et al.* Saudi women's interest in breast cancer gene testing: possible influence of awareness, perceived risk and socio-demographic factors. Asian Pac J Cancer Prev 2012;13:3879–87.

47 Simons G, Mason A, Falahee M *et al.* Qualitative exploration of illness perceptions of rheumatoid arthritis in the general public. Musculoskeletal Care 2017;15:13–22.

48 Reid EP, Forbes A, Sanderson J *et al.* Recruiting first-degree relatives for prevention research: a comparison of clinician and proband-led methods of contact in Crohn's disease. Eur J Hum Genet 2006;14:1263–8.

49 van Boheemen L, ter Wee MM, Seppen B *et al.* How to enhance recruitment of individuals at risk of rheumatoid arthritis into trials aimed at prevention: understanding the barriers and facilitators. RMD Open 2021;7:e001592.

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References: 1. JYSELECA SPC. Available at: www.medicines.org.uk. Last accessed: June 2022. **2.** Angelini J, *et al.* Biomolecules 2020;10(7):E1002. **3.** Banerjee S, *et al.* Drugs 2017;77:521–546. **4.** O'Shea JJ, *et al.* Nat Rev Rheumatol 2013;9(3):173–182. **5.** Traves PG, *et al.* Ann Rheum Dis 2021;0:1–11. **6.** McInnes IB, *et al.* Arthr Res Ther 2019;21:183. **7.** Combe B, *et al.* Ann Rheum Dis 2021;doi:10.1136/annrheumdis-2020-219214. **8.** Genovese MC, *et al.* JAMA 2019;322 (4):315–325. **9.** Westhovens R, *et al.* Ann Rheum Dis 2021;doi:10.1136/annrheumdis-2020-219213. **10.** Combe B, *et al.* Arthritis Rheumatol 2021;73(suppl 10). https://acrabstracts.org/abstract/clinical-outcomes-up-to-week-48-of-filgotinib-treatment-in-an-ongoing-long-term-extension-trial-of-ra-patients-with-inadequate-response-to-mtx-initially-treated-with-filgotinib-or-adalimumab-during-th/. Last accessed: June 2022. **11.** Buch MH, *et al.* Arthritis Rheumatol 2021;73 (suppl 10). https://acrabstracts.org/abstract/clinical-outcomes-up-to-week-48-of-ongoing-filgotinib-ra-long-term-extension-trial-of-biologic-dmard-inadequate-responders-initially-on-filgotinib-or-placebo-in-a-phase-3-trial/. Last accessed: June 2022. **12.** Winthrop K, *et al.* Arthritis Rheumatol 2021;73(suppl 10). Available at: https://acrabstracts.org/abstract/integrated-safety-analysis-update-for-filgotinib-in-patients-with-moderately-to-severely-active-rheumatoid-arthritis-receiving-treatment-over-a-median-of-2-2-years/. Last accessed: June 2022.

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