Patients' perceptions of their relatives' risk of developing rheumatoid arthritis and of the potential for risk communication, prediction and modulation

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DOI:
10.1002/acr.23179

Original Article

Arthritis Care & Research
DOI 10.1002/acr.23179

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Running head: Patients' perceptions of relatives' risk of rheumatoid arthritis

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Funders: This research was supported by The Swedish Foundation for Humanities and Social Sciences [grant number M13-0260:1'Mind the Risk' www.crb.uu.se/mind-the-risk] and the European Union's FP7 HEALTH programme [grant agreement FP7-HEALTH-F2-2012-305549 'Euro-TEAM' www.team-arthritis.eu]

Word Count: 3650

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an 'Accepted Article', doi: 10.1002/acr.23179

Received: Jul 25, 2016; Revised: Nov 17, 2016; Accepted: Dec 13, 2016

Abstract

Objectives: To understand the perspectives of patients with rheumatoid arthritis (RA) about the risk of their relatives developing RA in the future, and about communicating with their relatives about risk and its modulation.

Methods: Twenty-one RA patients took part in semi-structured interviews.

Results: Participants reported willingness to communicate with relatives about their risk of developing RA, but described choosing which relatives to communicate with, on the basis of their perceived receptivity to such risk information. Participants described the potential for risk information to cause negative emotions.

Some participants did not consider RA to be hereditable, and few reported smoking as a risk factor. Patients described a lack of public awareness about the causes of RA and the negative impact that RA has on quality of life. Awareness of this negative impact was identified as an important driver for predictive and preventive strategies.

Participants held positive perceptions of predictive testing for RA, though the results of predictive tests were conceptualised as having a high degree of accuracy. Negative views of predictive testing were associated with an appreciation of the probabilistic nature of risk information. Participants felt that their relatives would prefer lifestyle modification over medication as a risk reduction strategy.

Conclusions: Information about risk factors for RA, and the potential impact of RA on quality of life, is needed to support family communication about RA risk. Management of expectations is needed in relation to the probabilistic nature of risk information, and appropriate support should be provided for negative psychological outcomes.

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Significance and Innovations

- This is the first study of the perspectives of existing RA patients relating to the possibility that their relatives might be at an elevated risk of developing RA in the future, and their views on communicating with relatives about their risk status and possibilities for risk quantification and modification.
- The findings of this study will inform the development of predictive / preventive approaches to the management of RA which depend on the willingness of existing patients to pass on information about RA risk to their relatives.

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Rheumatoid arthritis (RA) is a chronic polyarthritis affecting approximately 1% of the population.(1) If its diagnosis and treatment are delayed, irreversible joint destruction and disability are more likely.(2-4) Increased healthcare utilisation, disability and reduced ability to work resulting from RA present considerable personal and economic burdens.(5, 6) Management of established RA involves long-term treatment with disease modifying anti-rheumatic drugs, associated with potential toxicity and consequent intensive monitoring.(7) Research efforts are therefore being directed towards the earliest stages of RA, and towards the identification of biomarkers predictive of future RA development, in order to facilitate early treatment and preventive interventions for those at risk.(8, 9) Clinical trials are underway to evaluate therapeutic intervention for individuals with arthralgia but without clinically manifest arthritis (10-12), and promising early results may herald a paradigm shift from treatment towards prevention of RA.(13)

Genetic factors contribute to the risk of RA;(14, 15) having a family history of RA increases the risk of RA by approximately 3-5 fold.(16, 17) A range of modifiable environmental risk factors including cigarette smoking also contribute to RA risk.(18-20) Both genetic factors and smoking are more strongly associated with seropositive RA. Approximately 25% of all RA and 35% of seropositive RA risk can be attributed to smoking.(20, 21) Demographic, lifestyle and genetic information together with markers of autoimmunity (e.g. the presence of autoantibodies such as rheumatoid factor,(22) anti-cyclic citrullinated (23) and anti-carbamylated protein antibodies (24)) are therefore

increasingly likely to be used to identify individuals suitable for prevention strategies.(25, 26)

The design of preventive approaches to the management of RA should be informed by an understanding of the perspectives of those affected. The importance of understanding stakeholder perspectives in rheumatology research has been reinforced over recent years with the recognition that outcome measures that are identified by patients as important (e.g. fatigue) are reliable and independent predictors of disease activity,(27, 28) and that there are important differences between the perspectives of patients and physicians.(29)

First-degree relatives (siblings or children) of individuals with RA are a likely target population for predictive and preventive approaches, and several prospective studies are currently recruiting from this 'at risk' group.(30-33) Qualitative studies have begun to explore first-degree relatives' views about their susceptibility to RA, and the possibility of predictive testing and preventive action.(34, 35) However, the success of preventive strategies is dependent not only on their acceptability to 'at risk' relatives, but also to their family members who have a diagnosis of RA, as access to first-degree relatives would typically take place indirectly via existing patients. If patients are unwilling or unable to communicate effectively with their relatives about their risk of developing RA or about predictive testing and risk modulation, access to this group may be restricted. Studies of risk communication amongst families in other disease contexts have found that patients do not always communicate risk information in a timely or effective manner (36, 37). With a growing trend towards stratified and preventive approaches to disease management, it is therefore important to understand the perspectives of existing

patients with RA and to identify potential barriers to effective risk communication in order to inform the development of predictive and preventive approaches.

Patients and Methods

All procedures were conducted in accordance with the Helsinki Declaration and approved by the South Yorkshire Research Ethics Committee (ref. 13/YH/0329). All participants gave written informed consent prior to participation.

Participants were 18 years of age or older, fulfilled the 2010 American College of Rheumatology/ European League Against Rheumatism classification criteria for RA,(38) had one or more first-degree relatives (biological offspring or full siblings, but not parents) and were able to participate in an interview conducted in English. Participants were recruited from secondary care clinics in Birmingham (United Kingdom) between January and July 2015. Recruitment continued until thematic saturation was achieved. Semi-structured interviews were conducted either face-to-face or by telephone for those participants who had difficulty attending in person. The interview schedule assessed perceptions about risk factors for RA, family susceptibility and communication about RA risk and potential risk modification strategies. Patients were also asked about different types of predictive tests (blood tests, genetic tests, ultrasound / MRI scanning, and synovial biopsy). The development of this schedule was informed by a review of qualitative literature exploring perceptions of risk and predictive testing for chronic inflammatory diseases,(39) and input from an international multi-disciplinary consortium of healthcare professionals, patient research partners and researchers (EuroTEAM;

www.team-arthritis.eu). Sample questions are available online (Supporting Information 1). Audio recordings of the interviews were transcribed verbatim.

Analysis

Data collection and analysis were carried out in parallel allowing assessment of when saturation of major themes had been achieved. The data were managed using NVivo software (40), coded by MF and analysed using a thematic approach.(41) A sample of 5 (25%) transcripts was independently coded by RJS. Coding categories that lacked consistency or concordance were discussed and absorbed into the coding framework. Initial codes were grouped into the most salient and frequently occurring categories. Continuous discussion and review of the coding framework took place between the researchers (MF, RJS, and KR) and in consultation with patient research partners in order to interpret the meaning and development of basic and higher order themes.

Results

Twenty-one patients participated in either face-to-face (n=13) or telephone (n=8) interviews. The mean number of codes resulting from each type of interview method (46 and 41 respectively) was not significantly different (t=-0.88, P=0.39). Participants were aged between 35 and 80 years (mean 64). Fifteen (71%) were female, 13 (62%) were retired and 19 (90%) identified their ethnicity as White British (See Table 1 for participant characteristics). Four organizing themes emerged: 1) Selective communication of risk information to relatives, 2) Lack of knowledge about RA, 3)

(Mis)perceptions about risk information and 4) Preference for behavioural, rather than pharmacological intervention.

These organizing themes are described in detail below, with supporting quotations presented in the text and supplemented in Table 2.

Selective communication of risk information to relatives

Participants expressed a willingness to communicate with relatives about their risk of developing RA. Communication of risk information was constructed as a positive process, which would benefit their relatives. Despite this willingness to pass on such information, participants described a process of choosing which relatives to communicate with and would not communicate with them all.

> "So it's about choosing who you speak with." (Participant 15 (P15)).

This selective process was often based on an assessment of which relatives would be receptive to risk information, or likely to act upon it.

> "I think it depends on the people themselves really. Some people want to know about it and some don't… I think you've got to know which person you can talk to about it." (P2)

Reasons suggested for a potential lack of receptivity included relatives being too busy (Quote 1; Q1); having too many other problems to cope with (Q2); being too young (Q3); being in denial about their susceptibility (Q4) and preferring to deal with things when they happened (Q5).

One participant stated that they would not communicate with relatives about their risk of developing RA as they felt that RA was not serious enough to warrant such

communication (Q6). Some participants were mindful of the potential for relatives to be anxious about their risk status, and wanted to prevent relatives from unnecessary anxiety.

> "But I don't think to worry people unduly is a good thing either. To say, 'Yes, you've got the factor but we don't know if you're going to get it or not,' I don't think that's right." (P21)

Feelings of guilt and responsibility were associated with an appreciation of relatives' increased risk. Participants reported feeling responsible for passing on a hereditary predisposition (Q7), and some felt it was their responsibility to encourage relatives to be aware of RA and to manage their increased susceptibility, though such communication was not necessarily seen as something that participants or relatives would feel comfortable with.

> "I knew, as her grandmother, and I knew about the subject, it was my responsibility to talk to her… I think, if you love your family, sometimes you've got to do the things you don't really like doing to them, haven't you?" (P3)

Many emphasised that if they were to communicate risk information to their relatives, it was the responsibility of their relatives to pay attention to, and to act upon such information (Q8).

Many participants identified one or more first degree relatives that they were not in regular contact with (Q9). Some mentioned that they would not pass on information to particular relatives who they did not have a good relationship with, even though they had previously reported being happy to communicate openly with their family members about their risk of developing RA in the future (Q10).

To summarize, participants' willingness to communicate risk information to relatives involved a complex, decision-making process about who should receive such information, based in part on an assessment of who would be receptive and/or equipped to deal with it. This process was influenced by participants' own conflicting feelings of guilt and responsibility.

Lack of knowledge about RA

Some participants felt that their own knowledge of the causes of RA was incomplete (Q11). Some described genetic risk factors for RA and many identified one or more relatives who they felt were at risk of developing RA in the future.

> "Yes, I fear for my girls, my daughters and my granddaughter. I'm concerned that they will get it." (P15)

However, others did not feel that RA was hereditable, and many reported having no family history of RA.

> "No, my mum never had it and my father didn't have it, and my sister hasn't got it. No, I don't think it does run in families." (P2)

Environmental risk factors for RA such as infection (Q12), diet (Q13), having a sedentary lifestyle (Q14), psychosocial stress (Q15) and 'wear and tear' (Q16) were suggested by many participants, though only 2 participants highlighted smoking as being a risk factor. Without accurate knowledge about risk factors for RA patients are unlikely to be able to communicate effectively with their relatives about risk.

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Participants described a lack of awareness of RA and its impact by both their relatives (Q17) and the general public (Q18). Participants also highlighted that RA is often confused with osteoarthritis or perceived to be a normal consequence of ageing (Q19). Experience and understanding of the severe negative impact of RA was identified by participants as an important driver of engagement with predictive/preventive strategies.

> "I honestly believe that if – you might have problems with people who've never seen, okay? … They think, 'Oh, I'll deal with that when I get it. It will be when I'm old'… but if their families are people like me, who have seen it first hand, I'm certain they'd take any kind of medicine to help it." (P3)

Participants identified a need for awareness raising initiatives (Q20), with some suggesting that informational resources should be 'hard-hitting' in order to graphically convey the potential severe negative impact of RA on quality of life (Q21).

In summary there was a lack of awareness about the causes of RA amongst patients and a perceived lack of awareness of its impact on quality of life amongst relatives, both of which should be addressed if predictive/preventive strategies are to be successful.

(Mis)perceptions about risk information

Most participants held positive views of testing to predict RA risk in their relatives. Information about RA risk was described as being inherently interesting (Q22) enabling individuals to prepare for their future (Q23) and to cope better if they were to develop symptoms of RA (Q24). Some suggested that predictive testing for their relatives could bring them (the interviewee) peace of mind (Q25). Participants were of the opinion that prediction would typically be associated with early diagnosis and treatment of RA (Q26)

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and with the possibility of preventive intervention (Q27). Predictive testing in the absence of preventive intervention was perceived negatively by some participants.

> "Are you going to give them an injection or a pill or whatever, that's going to stop it ever coming? Then, yeah, that's good … You need to know - if you're going to test my child, another person's child - why? What is going to be the benefit of them having that test?" (P20)

When asked about various kinds of predictive test, participants expressed preferences for non-invasive tests (Q28) that were easily and locally accessible (Q29). A small number of negative perspectives were mentioned, such as the impact of genetic risk information on future generations (Q30) and personal privacy (Q31). The majority of participants viewed predictive tests involving the sampling of synovial tissue as overly invasive and inappropriate for someone who had not yet developed symptoms (Q32). Participants felt that the results of predictive tests would be more meaningful if they gave an indication of the time of onset and/or likely severity of RA symptoms (Q33). Participants generally conceptualised the results of predictive tests as binary (definitely ruling in or ruling out future RA) or at least having a high (if not absolute) degree of accuracy.

> "So if there is a link with, well, mum having it and me having it, really if that flagged up they could have done that test right at the start and say yes it is or no it isn't." (P10)

A small number of participants were concerned about the uncertainty associated with risk information and this concern was associated with more negative perceptions of predictive/preventive approaches for RA.

> "That's really difficult because you know that the tests show that you're at a higher risk of getting it, but that's not saying that you are going to get it, and so are you taking medication unnecessarily?" (P20)

Generally positive viewpoints about predictive testing for RA may be based on unrealistic expectations about the information that would be provided by such tests and about the degree of certainty associated with such information.

Preference for behavioural, rather than pharmacological intervention

Participants were in favour of their relatives making changes to their lifestyle in order to reduce their risk of developing RA and most felt that this approach would be acceptable to their relatives.

> "I think they'd do it. They would, definitely. My daughter's already started because I said to her - there was one time I came into the clinic and I was told that, 'You need to keep healthy; you need to go swimming and do exercise.' I came home and told my daughter. She joined the gym almost immediately and she hasn't stopped...Once I relayed that information to her she was at the gym." (P15)

However, lifestyle change was thought to be unlikely and problematic for some relatives, (Q34) and some relatives were thought likely to become hostile at the suggestion of lifestyle change (Q35), or to find justification for not changing their present behaviour (Q36). Some described specific relatives who they felt were unlikely to modify their current lifestyle.

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> "I don't think she would change her lifestyle or anything, in any way… she smokes too much and she knows she could get cancer but she still smokes." (P16)

The concept of preventive medication was constructed as positive (Q37), however some noted that they and their relatives would prefer a lifestyle intervention.

> "Medicines are acceptable but I think if you could prevent it by just changing and by not smoking and eating better, cut certain food out then that would be a lot easier than maybe taking medication." (P10)

It was suggested by some that medication would only be considered after RA symptoms had developed.

> "I don't think I'd want to take medication if I don't have any of the symptoms… If it were life threatening I believe I would take something. Prevention is better than cure. But if it's not life threatening I wouldn't do it." (P15)

A general orientation away from the use of medicine was identified with participants describing their relatives' dislike of taking medicines, (Q38), or concern about adverse reactions (Q39), methods of administration or duration of therapy (Q40). Negative perceptions of preventive medication were sometimes associated with understanding of the uncertainty about the future development of RA for an individual considered to be 'at risk'.

> "But what if they took this medicine but they never ever got it? You couldn't prove that they were one that definitely would get it or wouldn't. So you could be dosing up with medicine that they didn't need in the first place." (P21)

For this participant, pharmacological intervention would be justified for their relative only where there was near absolute certainty that RA would otherwise develop.

Discussion

The findings of the present study have elucidated the perspectives of patients with a diagnosis of RA about the elevated risk of their relatives developing RA in the future, and about communicating with their relatives about risk and strategies for risk modulation. The themes identified will inform the design of materials to support family communication about RA risk and the delivery of predictive and preventive research studies and future clinical services.

This study confirms the findings of research in other disease contexts which show that the communication of disease risk information amongst family members is a complex, dynamic and selective process(42) and suggests that reliance on information delivery via existing patients alone is unlikely to support a comprehensive preventive campaign. More widespread or more direct approaches to the delivery of information to individuals who may be at risk of developing RA may also be necessary.

Participants' knowledge of risk factors for RA was often either incorrect or incomplete. For example, some cited 'wear and tear' on joints as a contributory factor, some were unaware of genetic risk factors or that cigarette smoking was a risk factor. Causal beliefs about RA are likely to be related to beliefs about the need for risk communication, and are also likely to affect patients' ability to communicate effectively with relatives about their risk of developing RA. Participants also reported a general lack

of public awareness about RA. This resonates with previous findings that members of the public often do not perceive the symptoms of RA to be serious or to warrant urgent medical attention.(43, 44) Awareness and experience of the serious nature of this condition was identified by participants in the present study as an important driver for engagement with predictive and preventive strategies, and participants identified a need for awareness raising initiatives and informational resources. Therefore addressing this information gap will be an important antecedent to preventive approaches to RA. Participants also highlighted concerns about the potential for negative emotional consequences associated with the delivery of information relating to RA susceptibility, both for existing patients who may feel guilty about their relatives' susceptibility to RA, and for their relatives who may be anxious about their risk status. This is consistent with previous findings on the perceptions of relatives.(34) Informational resources designed to facilitate family communication about RA to 'at risk' relatives and to educate individuals who may be at risk about the availability of predictive and preventive approaches should therefore provide appropriate and sensitive support for all family members.

Predictive testing for RA was viewed positively by most participants, and was associated with increased opportunities for early diagnosis and effective treatment, and with the possibility of preventive interventions. Many of these positive viewpoints were based on a conceptualisation of the outcome of predictive tests and preventive interventions for RA as having a high degree of certainty. This preference for certainty is in broad agreement with previous research on lay models of genetic risk which suggests that responses to disease risk information are guided more by personal theories of risk

than by numerical probabilities communicated by healthcare professionals.(45) Conceptualising personal outcomes in terms of certainty may serve as an effective coping mechanism for individuals faced with complex probabilistic information with potentially distressing consequences for themselves and for other family members. This presents a particular challenge for the communication of risk information for diseases of multifactorial polygenic aetiology such as RA(46) and suggests that patients' support for and subsequent uptake of preventive therapeutic interventions by their relatives may be limited until a high degree of confidence in the effectiveness of predictive testing and preventive interventions can be offered.

In order to consolidate and extend this qualitative investigation, and assess cognitive and demographic predictors of the perceptual variations identified here, large scale quantitative research is necessary. A limitation of the present study is that the sample of participants interviewed is mostly comprised of retired patients of white British origin whose views may not fully represent those of other groups. The issues raised by this research may have particular sociocultural significance for some communities, and further work is needed to capture diverse perspectives.

An interesting finding of this study was that some participants did not consider RA to be a hereditable condition, and yet continued to respond to interview questions about communicating with relatives about risk prediction and reduction. Such participants may have responded differently to the interview questions if they did consider their relatives to be at risk. Future quantitative investigations are needed to further elucidate the relationships between illness perceptions about RA and attitudes towards predictive/preventive strategies and risk communication.

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In summary, this research identifies a need for widely disseminated, accurate information about risk factors for RA, risk reduction possibilities and the potential severe negative impact of RA, in order to facilitate the implementation of preventive approaches to this disease and to support family communication about disease susceptibility. Awareness raising of this kind is also likely to improve outcomes for patients who do develop RA by facilitating timely help-seeking and early treatment. Management of expectations in relation to the probabilistic nature of risk information about RA may be necessary, as well as the provision of appropriate support for any negative psychosocial impact of such information for all family members, including patients who have already received a diagnosis of RA, and who may be concerned about their relatives' risk status.

Acknowledgement

The authors would like to thank the EuroTEAM patient research partners for their contribution to this research.

References

1. Symmons D, Turner G, Webb R, Asten P, Barrett E, Lunt M, et al. The prevalence of rheumatoid arthritis in the United Kingdom: new estimates for a new century. Rheumatology. 2002;41(7):793-800.
2. Nell VPK, Machold KP, Eberl G, Stamm TA, Uffmann M, Smolen JS. Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. Rheumatology. 2004;43(7):906-14.
3. Raza K, Buckley CE, Salmon M, Buckley CD. Treating very early rheumatoid arthritis. Best Pract Res Cl Rh. 2006;20(5):849-63.
4. van der Linden MP, le Cessie S, Raza K, van der Woude D, Knevel R, Huizinga TW, et al. Long-term impact of delay in assessment of patients with early arthritis. Arthritis Rheum. 2010;62(12):3537-46.
5. National Rheumatoid Arthritis Society. Economic Burden of RA Report. 2010.
6. Birnbaum H, Pike C, Kaufman R, Marynchenko M, Kidolezi Y, Cifaldi M. Societal cost of rheumatoid arthritis patients in the US. Current Medical Research and Opinion. 2010;26(1):77-90.
7. Smolen JS, Landewé R, Breedveld FC, Dougados M, Emery P, Gaujoux-Viala C, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. Ann Rheum Dis. 2010;69(6):964-75.
8. Karlson EW, van Schaardenburg D, van der Helm-van Mil AH. Strategies to predict rheumatoid arthritis development in at-risk populations. Rheumatology. 2014.
9. Gerlag DM, Norris JM, Tak PP. Towards prevention of autoantibody-positive rheumatoid arthritis: from lifestyle modification to preventive treatment. Rheumatology. 2016;55(4):607-14.
10. Prevention of clinically manifest rheumatoid arthritis by B cell directed therapy in the earliest phase of the disease (PRAIRI). http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=2442.
11. Arthritis Prevention In the Pre-clinical Phase of Rheumatoid Arthritis with Abatacept (APPIPRA) http://www.isrctn.com/ISRCTN46017566.
12. Statins to Prevent Rheumatoid Arthritis (STAPRA) Prevention of Rheumatoid Arthritis by Atorvastatin in Seropositive Arthralgia Patients: a Multicenter Double-Blind Randomized Placebo-Controlled Trial. http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=5265.
13. Gerlag D, Safy M, Maijer K, de Hair M, Tas S, Starmans-Kool M, et al. Prevention of rheumatoid arthritis by B Cell directed therapy in the earliest phase of the disease: The PRAIRI study. Ann Rheum Dis. 2016;75(Suppl2):125.
14. de Vries R. Genetics of rheumatoid arthritis: time for a change! Curr Opin Rheumatol. 2011;23(3):227-32.
15. Turesson C, Matteson EL. Genetics of rheumatoid arthritis. Mayo Clin Proc. 2006;81(1):94-101.
16. Frisell T, Holmqvist M, Källberg H, Klareskog L, Alfredsson L, Askling J. Familial Risks and Heritability of Rheumatoid Arthritis: Role of Rheumatoid Factor/Anti–Citrullinated Protein Antibody Status, Number and Type of Affected Relatives, Sex, and Age. Arthritis & Rheumatism. 2013;65(11):2773-82.
17. Aho K, Koskenvuo M, Tuominen J, Kaprio J. Occurrence of rheumatoid arthritis in a nationwide series of twins. J Rheumatol. 1986;13(5):899-902.
18. Karlson EW, Deane K. Environmental and gene-environment interactions and risk of rheumatoid arthritis. Rheumatic Disease Clinics of North America. 2012;38(2):405-26.
19. Lahiri M, Morgan C, Symmons DPM, Bruce IN. Modifiable risk factors for RA: prevention, better than cure? Rheumatology. 2012;51(3):499-512.
20. Kallberg H, Ding B, Padyukov L, Bengtsson C, Ronnelid J, Klareskog L, et al. Smoking is a major preventable risk factor for rheumatoid arthritis: estimations of risks after various exposures to cigarette smoke. Ann Rheum Dis. 2011;70(3):508-11.
21. Costenbader KH, Feskanich D, Mandl LA, Karlson EW. Smoking intensity, duration, and cessation, and the risk of rheumatoid arthritis in women. American Journal of Medicine. 2006;119(6):503 e1-9.
22. Aho K, Palosuo T, Raunio V, Puska P, Aromaa A, Salonen JT. When does rheumatoid disease start? Arthritis Rheum. 1985;28(5):485-9.

23. Rantapaa-Dahlqvist S, de Jong BAW, Berglin E, Hallmans G, Wadell G, Stenlund H, et al. Antibodies against cyclic citrullinated peptide and IgA rheumatoid factor predict the development of rheumatoid arthritis. Arthritis Rheum. 2003;48(10):2741-9.
24. Shi J, van de Stadt LA, Levarht EW, Huizinga TW, Hamann D, van Schaardenburg D, et al. Anti-carbamylated protein (anti-CarP) antibodies precede the onset of rheumatoid arthritis. Ann Rheum Dis. 2014;73(4):780-3.
25. Sparks JA, Chen CY, Jiang X, Askling J, Hiraki LT, Malspeis S, et al. Improved performance of epidemiologic and genetic risk models for rheumatoid arthritis serologic phenotypes using family history. Ann Rheum Dis. 2015;74(8):1522-9.
26. Sparks JA, Chang SC, Liao KP, Lu B, Solomon DH, Costenbader KH, et al. Incident Rheumatoid Arthritis and Risk of Mortality Among Women Followed Prospectively from 1976 to 2010 in the Nurses' Health Study. Arthritis Rheumatol. 2014;66:S359-S60.
27. Minnock P, Kirwan J, Bresnihan B. Fatigue is a reliable, sensitive and unique outcome measure in rheumatoid arthritis. Rheumatology. 2009;48(12):1533-6.
28. Nicklin J, Cramp F, Kirwan J, Urban M, Hewlett S. Collaboration With Patients in the Design of Patient-Reported Outcome Measures: Capturing the Experience of Fatigue in Rheumatoid Arthritis. Arthrit Care Res. 2010;62(11):1552-8.
29. Studenic P, Radner H, Smolen JS, Aletaha D. Discrepancies Between Patients and Physicians in Their Perceptions of Rheumatoid Arthritis Disease Activity. Arthritis Rheum. 2012;64(9):2814-23.
30. www.arthritis-checkup.ch.
31. Pre-clinical Evaluation of Novel Targets in RA (Prevent-RA). http://www.preventra.net/.
32. Sparks JA, Iversen MD, Miller Kroouze R, Mahmoud TG, Triedman NA, Kalia SS, et al. Personalized Risk Estimator for Rheumatoid Arthritis (PRE-RA) Family Study: rationale and design for a randomized controlled trial evaluating rheumatoid arthritis risk education to first-degree relatives. Contemp Clin Trials. 2014;39(1):145-57.
33. Kolfenbach JR, Deane KD, Derber LA, O'Donnell C, Weisman MH, Buckner JH, 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(12):1735-42.
34. Stack R, Stoffer M, Englbrecht M, Mosor E, Falahee M, Simons G, et al. Perceptions of first degree relatives of patients with rheumatoid arthritis about their personal risk of, and predictive testing for, rheumatoid arthritis: a cross-European qualitative study. BMJ Open. 2016;6(6):e010555.
35. Novotny F, Haeny S, Hudelson P, Escher M, Finckh A. Primary prevention of rheumatoid arthritis: A qualitative study in a high-risk population. Joint Bone Spine. 2013;80(6):673-4.
36. Seymour KC, Addington-Hall J, Lucassen AM, Foster CL. What Facilitates or Impedes Family Communication Following Genetic Testing for Cancer Risk? A Systematic Review and Meta-Synthesis of Primary Qualitative Research. Journal of Genetic Counseling. 2010;19(4):330-42.
37. Wiseman M, Dancyger C, Michie S. Communicating genetic risk information within families: a review. Fam Cancer. 2010;9(4):691-703.
38. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2010;69(9):1580-8.
39. Bayliss K, Raza K, Simons G, Falahee M, Hansson M, Starling B, et al. Perceptions of predictive testing for those at risk of developing a chronic inflammatory disease: a meta-synthesis of qualitative studies. Journal of Risk Research. 2016:1-23.
40. NVivo qualitative data analysis software (Version 10). QSR International Pty Ltd.
41. Guest GS, MacQueen KM, Namey EE. Applied Thematic Analysis. Thousand Oaks, California: Sage Publications. 2012.
42. Atkinson P, Featherstone K, Gregory M. Kinscapes, timescapes and genescapes: families living with genetic risk. Sociology of Health and Illness.35(8):1227-41.
43. Simons G, Belcher J, Morton C, Kumar K, Falahee M, Mallen CD, et al. Symptom recognition and perceived urgency of help-seeking for rheumatoid arthritis and other diseases in the general public: a mixed method approach. Arthritis Care & Research 2016: July 7. doi: 10.1002/acr.22979
44. Simons G, Mason A, Falahee M, Kumar K, Mallen CD, Raza K, et al. Qualitative Exploration of Illness Perceptions of Rheumatoid Arthritis in the General Public. Musculoskeletal Care. 2016: Feb 1. doi: 10.1002/msc.1135

45. 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(3):179-89.
46. Lautenbach DM, Christensen KD, Sparks JA, Green RC. Communicating genetic risk information for common disorders in the era of genomic medicine. Annu Rev Genomics Hum Genet. 2013;14:491-513.

Table 1. Description of participants

Participant number	Gender	Age (years)	Occupational status	Ethnic background
1	Female	73	Retired	White British
2	Female	62	Homemaker	White British
3	Female	62	Part time self-employed	White British
4	Male	76	Retired	White British
5	Female	78	Retired	White British
6	Female	44	Unemployed due to ill health	Black Caribbean
7	Female	65	Retired	White British
8	Male	70	Retired	White British
9	Female	80	Retired	White British
10	Male	35	Full-time employed	White British
11	Male	70	Retired	White British
12	Female	68	Retired	White British
13	Female	55	Carer	White British
14	Female	63	Retired	White British
15	Female	50	Student/part-time employed	Undisclosed
16	Female	57	Unemployed due to ill health	White British
17	Male	56	Unemployed due to ill health	White British
18	Female	68	Retired	White British
19	Male	75	Retired	White British
20	Female	62	Retired	White British
21	Female	70	Retired	White British

Table 2. Supplementary Quotations

Code	Quotation Number
Q1	"Oh, they're busy women in their forties and they can't be bothered to take the time out to do things like that." (Participant 1)
Q2	"She's just had cancer... and lost her grandson a year in June, her first grandson… I think she just thinks, 'I've got enough to be going on with.' So I don't like to go on and on…." (Participant 13)
Q3	"I think that it all depends on age... When you're, say, any age under the age of 25 you think you're indestructible anyway, unless something bad happens you don't think anything bad is going to happen." (Participant 9)
Q4	"You're obviously going to get some people that wouldn't want to know and would want to just push it under the carpet." (Participant 7)
Q5	"I don't know about my oldest one… She's a bit more, you know, wait till it happens sort of thing." (Participant 16)
Q6	"If it was, let's say, something like cancer... But because RA is not life threatening I wouldn't do it." (Participant 15)
Q7	"Oh gosh I'd feel as if I'd passed that... I mean I feel awful with the lad with his allergies. I feel as if I've given him that because my immune system is…. When he was born I had a lot of problems. Yes, I'd feel terribly guilty." (Participant 2)
Q8	"But I would tell her… and as much as she doesn't want to listen she's heard it. So what she does with that information is up to her." (Participant 15)
Q9	"But when our mother died he didn't want to remain in contact with the family. So neither I nor my other brother see him." (Participant 11)
Q10	"Well, I've spoken to… I don't have anything to do with my other sister, my youngest, but my other sister; I've spoken to her… I talk openly with all my family about it. They're aware. No, I've got no qualms about that. I don't think it's anything to be ashamed of. It's just unfortunate, isn't it, if you've got it." *[Interviewer: There are some members that you wouldn't talk to about it?]* "Well, just my sister." (Participant 13)
Q11	"I suppose I don't know anything about why it happens" (Participant 20)
Q12	"It could be something as simple as maybe getting a type of flu that could trigger it because your immune system could go haywire after something like that." (Participant 21)
Q13	"I would probably say looking after yourself properly – eating ways, the way you live, and my eating habits were never very good." (Participant 14)
Q14	"But other things may be your work pattern, what you do. If you're in an office, sedentary perhaps, and you're sitting down all the time." (Participant 8)
Q15	"I think I had a very stressful episode and it affected my immune system and then the results

	of that was RA." (Participant 15)
Q16	"I think it's probably wear and tear." (Participant 6)
Q17	"I don't think they understand that, you know, you can't do what you did before you had it, like, you know. And they, kind of, don't understand. They think you're being funny." (Participant 19)
Q18	"People don't realise how painful it is until they've got it. I just think we need to be made more aware." (Participant 14)
Q19	"Arthritis… everybody gets it…I tell people I've got rheumatoid arthritis - "I've got a bit of arthritis in my back." Of course you have, you're 93!" (Participant 8)
Q20	"There's very little out there in the open world about rheumatoid arthritis or the risks of it or what could add to your risks of it and what could help you not get it… what actually is rheumatoid arthritis? What is it? It's an illness; I understand that much, but what causes it?" (Participant 17)
Q21	"It's probably hard hitting but if you put a picture of somebody's hands on the front of the leaflets, with swollen fingers and bent and whatever… I think you need something hard hitting, to show some of the effects of RA." (Participant 7)
Q22	"Well, I mean personally, if somebody asked me, I would be interested in wanting to know, really." (Participant 4)
Q23	"Well, it'd prepare them wouldn't it, to, you know. It's, the sooner you're prepared for it the better it is." (Participant 19)
Q24	"I think I would like to have known because I'm one of those people who would have liked to have known everything and then I can cope with it then." (Participant 18)
Q25	"That would give me a bit of a peace of mind really." (Participant 6)
Q26	"I suppose if I had known, I could have gone to the doctor's even that bit sooner." (Participant 20)
Q27	"If there was something to say that they were going to get it but there was a drug to stop them having RA, then I'd be happy." (Participant 2)
Q28	"That [biopsy] could cause a problem because it's invasive, isn't it? So that could be a problem." (Participant 15)
Q29	"That's easy enough for both my daughters to go and have done, isn't it? ... Because they can have it done at our own centre, wouldn't they?" (Participant 1)
Q30	"Yes, but then that might throw up other things, mightn't it?... If it threw up any other indications of problems with themselves or with future generations then would they want to know that?... I think I would've been happy enough with just the blood test. I think I would've had to really think in depth about the genetic blood test." (Participant 7)
Q31	"But then there are people that, oh, you know, 'You're invading my privacy, and my body… I just think there would be people out there that wouldn't want to go for it." (Participant 20)
Q32	"I think if there wasn't any other symptom apart from I was feeling, you know, one of my

	joints was a bit achy, then it'd be a bit of a big thing to get done…I think it might be a bit too much for people." (Participant 10)
Q33	"It would have been nice to have some knowledge about it, or knowing that I was in some kind of risk to it and when it would strike me…Well, I don't know because would that test tell you how bad it's going to be for you?" (Participant 17)
Q34	"People do stop smoking but it's difficult, I believe, for them." (Participant 5)
Q35	"If I said anything to my wife about losing weight… she'd go ballistic!" Participant 8)
Q36	"I do think, in the case of if you're saying to them, that 'smoking is one of the things that will start it' – I mean I've never smoked, so even my family might say, 'Yeah, but mum' or 'Yeah, but Nan, you never smoked' because I've never put a cigarette into my mouth in my life." (Participant 3)
Q37	"I would be grateful for him to take the medication to prevent him going through all this pain that I'm going through." (Participant 6)
Q38	"Well, there are always people who say 'I don't believe in taking tablets'. How do you cope with those people?" (Participant 9)
Q39	"Yeah, because there are a lot of side effects with different medications and I think they're to be considered." (Participant 12)
Q40	"I suppose it would depend on whether it was a daily thing, or a weekly thing, or a monthly thing and how it was taken and, you know, whether you had to go somewhere to have it done or whether you could just do it yourself at home." (Participant 16)