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Exploring preferences of at-risk individuals for preventive treatments for rheumatoid arthritis

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Objective: Some immunomodulatory drugs have been shown to delay the onset of, or lower the risk of developing, rheumatoid arthritis (RA), if given to individuals at risk. Several trials are ongoing in this area; however, little evidence is currently available about the views of those at risk of RA regarding preventive treatment.

Method: Three focus groups and three interviews explored factors that are relevant to first degree relatives (FDRs) of RA patients and members of the general public when considering taking preventive treatment for RA. The semi-structured qualitative interview prompts explored participant responses to hypothetical attributes of preventive RA medicines. Transcripts of focus group/interview proceedings were inductively coded and analysed using a framework approach.

Results: Twenty-one individuals (five FDRs, 16 members of the general public) took part in the study. Ten broad themes were identified describing factors that participants felt would influence their decisions about whether to take preventive treatment if they were at increased risk of RA. These related either directly to features of the specific treatment or to other factors, including personal characteristics, attitude towards taking medication, and an individual's actual risk of developing RA.

Conclusion: This research highlights the importance of non-treatment factors in the decision-making process around preventive treatments, and will inform recruitment to clinical trials as well as information to support shared decision making by those considering preventive treatment. Studies of treatment preferences in individuals with a confirmed high risk of RA would further inform clinical trial design.

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease, with articular (1, 2) and extra-articular manifestations (3). In the general population, the prevalence of RA is approximately 0.5–1% (4). Among first degree relatives (FDRs) of RA patients, the risk is four-fold at approximately 4% (5). The risk becomes progressively higher for groups with relevant environmental exposures, RA-related autoantibodies (including anti-citrullinated protein antibodies), and clinically suspect arthralgia (6).

Current management involves long-term treatment with conventional, biological, or targeted synthetic disease-modifying anti-rheumatic drugs. The prolonged use of these treatments is associated with risk, including infection and pulmonary, hepatic, and haematological toxicity (7). Early treatment of RA has been shown to improve patient outcomes (8, 9) and there is now considerable interest in the concept of treating 'at-risk' individuals (10, 11) to assess whether a relatively short course of therapy will prevent or delay RA. Several treatments approved for use in

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established RA are currently being assessed for their ability to delay or prevent RA onset (12), and novel therapeutic approaches are also being developed (13).

When developing new treatments or repurposing treatments for a novel indication, it is essential to understand the views of the intended recipients about potential benefits and risks (14). This information could help to inform the selection of treatment candidates that will be acceptable to them, inform the outcome and endpoint selection in clinical trials (14, 15), and inform the development of informational resources to support patient decision making.

Patient preferences for RA treatments have been studied; however, preventive treatment is an emerging field, and there is limited information on factors influencing decision making by the prospective recipients of preventive treatment (16, 17). The views of patients with established RA are likely to be different from those considering preventive treatment, as patients will have experience of the disease itself. Furthermore, in the context of preventive treatment there is uncertainty around the chance of developing RA and the perceived and actual potential for treatment benefit. This may be reflected by challenges to recruitment to RA prevention trials (18, 19).

The current study was conducted to provide insight into perceptions of preventive treatment and the factors affecting decision making about the acceptability of such treatments by FDRs of RA patients and members of the general public, both asked to assume an increased risk of developing RA. This work further directly informed attribute development for a quantitative preference study (20) in FDRs and members of the public as part of a case study conducted within the Patient Preferences in Benefit–Risk Assessments during the Drug Life Cycle (PREFER) project (21), and informed guidelines on how and when patient preference studies can be incorporated in decision-making processes during the medical product life cycle (22, 23).

Method

Study design

Focus groups, using the nominal group technique (NGT) (24, 25), were conducted following best practice guidelines (24). If participants were unable to attend a focus group in person, individual semi-structured interviews following the NGT procedure were conducted instead. The current paper focuses on the thematic analysis of the qualitative data. Rank-order exercises were also conducted but are not reported here. Further information can be found in the study protocol (20) and interview guidelines (supplementary Table S1). The COnsolidated criteria for REporting Qualitative research (COREQ) guidelines (26) were used to report the methods and results of this study.

For the coding and analysis of the transcripts, an inductive approach was taken using the framework method (27), a method particularly suitable for use by multidisciplinary teams, including patient research partners (PRPs) and non-specialists (28). Some of the researchers (GS, MF, and KR) and PRPs (ECJ) have been involved in previous studies on preventive approaches for RA. To limit any impact of this prior experience on focus group proceedings and interpretation, the interview schedule was developed with input from additional members of the international multidisciplinary research team (including experts in rheumatology, psychology, and preference research, and an international panel of eight PRPs, all with established RA) and was informed by the findings of previous research (29–32) and a literature review (17). The entire research team contributed to data analysis and interpretation.

Participant recruitment

Participants were either the biological offspring or full siblings of a person with a confirmed diagnosis of RA (FDRs), or members of the public, aged 18 years or over, without a clinical diagnosis of RA. Recruitment took place between May 2019 and March 2020 and stopped when no new factors impacting treatment decisions were discussed. Data saturation (33) was determined on the basis of the lists of factors produced as part of the focus groups as well as an assessment of the transcripts. When face-to-face groups/interviews were no longer possible owing to the coronavirus disease 2019 (COVID-19) pandemic, interviews were conducted by telephone.

The FDRs were recruited indirectly through patients with confirmed RA identified at outpatient rheumatology clinics in the West Midlands, UK. Patients were introduced to the study either in person by their rheumatologist or a research nurse, or by mail, and asked to pass on the study invitation letter and participant information to their FDRs.

Members of the public were invited to take part through advertisements on message boards and online research recruitment platforms.

Having a relative with RA may impact an individual's perceptions of RA prevention, and therefore FDRs and members of the public took part in separate focus groups. All participants received a £20 shopping voucher for their participation. Because the sample was self-selected, it was not possible to assess the characteristics of non-participants.

Procedure focus groups and interviews

Focus groups/interviews took place at the University of Birmingham, UK, or, in the case of two interviews, over the telephone. Participants completed a brief demographic questionnaire, described any family history of RA (and how certain they were of such a history), and listed any current musculoskeletal symptoms. They rated their perceived risk of developing RA in the next

2 years and over their lifetime on a five-point Likert scale (very unlikely to very likely). Participants interviewed by telephone returned the questionnaire via post or e-mail.

This was followed by the focus group/interview itself. Figure 1 provides an overview of the structure of the focus groups/interviews (full guidelines are given in supplementary Table S1). The focus group/interviews were facilitated by two female researchers (GS and MF, both PhD) with expertise in qualitative methods.

Participants were asked to imagine that they had developed joint pain and stiffness, and that a blood test indicated a 40% risk of developing RA in the next 2 years. This profile represents the characteristics of participants included in current trials of preventive interventions for RA (34). They subsequently discussed the possibility of preventive treatment and treatment factors that may impact treatment choice.

Following this, two treatments currently under investigation as preventive treatments for RA [hydroxychloroquine (35) and abatacept (12)] were introduced as treatments A and B, and briefly described, followed by another discussion of factors that may affect treatment decisions. Finally, any treatment factors identified in a literature review of RA preference studies (17) that had not been mentioned were introduced, followed by further discussion.

Data analysis

The discussions and interviews were audio-recorded and transcribed verbatim by an independent transcription company. Transcripts were not returned to participants. The transcripts were read in depth by three researchers (KB, ME, and a research assistant) to familiarize themselves with the content, who subsequently independently coded three transcripts line by line, facilitated by NVivo (36). These codes were compared, and a coding framework was developed by GS and MF and discussed with KB and KR. Using this framework (see supplementary Table S2), all transcripts were fully coded by two independent research assistants, with two of the transcripts coded by both coders to assess

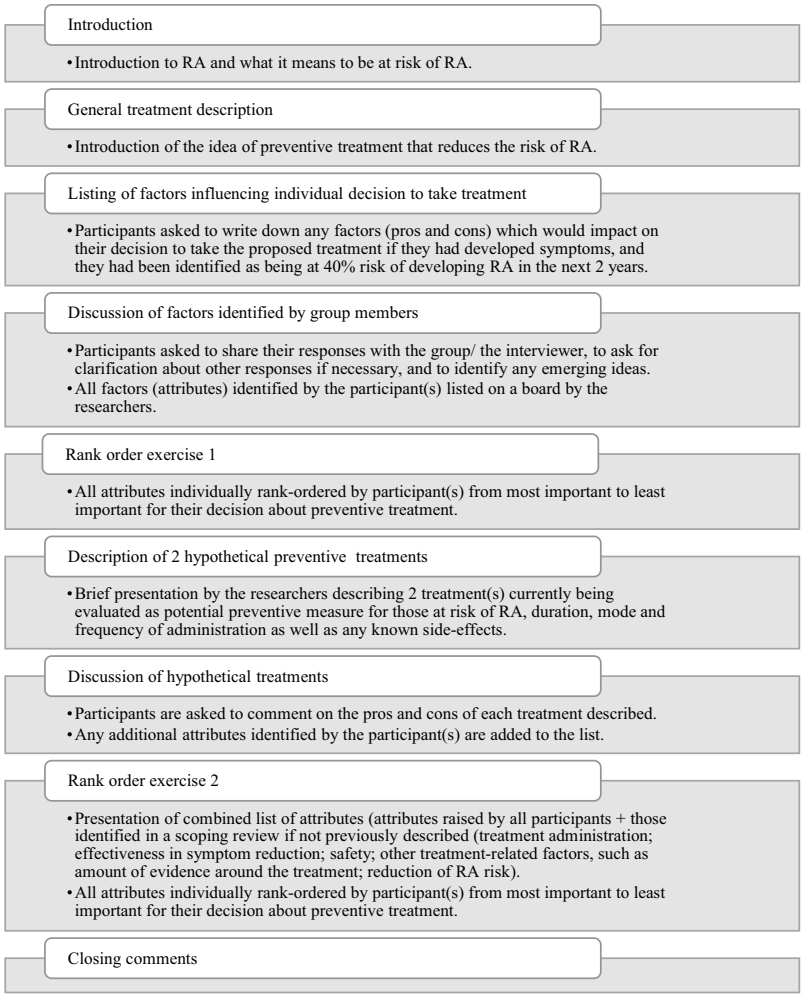

Figure 1. Overview of focus group structure. RA, rheumatoid arthritis.

consistency. Where necessary, additional codes were added and the framework was adapted. Any disagreements between coders were discussed and resolved by a third coder (GS or KB). The thematic framework and coding were validated by ECJ. Codes were organized into themes by GS and discussed with ECJ, MF, and KR. The themes were refined and discussed to achieve consensus.

Results

Participants

Twenty-one individuals took part in one of three focus groups (two with members of the public) or in individual interviews (three FDRs), which lasted for 1.5–2 h. For one interview, only interviewer field notes, rank orders, and demographic data were available because of technical problems.

Participants included five female FDRs and 16 members of the public (12 female). Four individuals from the general population sample reported a definite family history of RA. The median perceived risk of RA during the next 2 years was 3 ('neither likely nor unlikely'; interquartile range = 2–3) for both samples. Further participant characteristics are summarized in supplementary Table S3.

Framework analysis

The analyses resulted in seven themes pertaining to treatment-related factors and three themes pertaining to personal characteristics and circumstances that participants mentioned would impact on their treatment decision (see also supplementary Table S4).

Treatment-related factors. Treatment-related factors refer to aspects of the treatments themselves that would influence the decision about preventive treatment. These factors are: (i) effectiveness; (ii) treatment administration; (iii) side-effects; (iv) costs; (v) uncertainty around the treatment benefits and side-effects; (vi) unwanted effects of treatment other than side-effects; and (vii) information needs and (medical) opinion. These themes are discussed below, with illustrative quotations in Tables 1–3.

Effectiveness: Effectiveness encompasses improving existing symptoms, preventing future symptoms [Table 1, quotations 1–3 (T1Q1–3)], and preventing or delaying the development of RA. Participants often quoted a specific level of reduction in their chance of developing RA (between 20% and 35%) that they deemed significant enough to merit taking the preventive treatment (T1Q4–5). Effectiveness also covers the risk–benefit assessments in which participants spontaneously engaged (T1Q6–8).

Treatment administration: Certain aspects of treatment administration may impact treatment preferences. Although many participants preferred tablets (T1Q9), some preferred a subcutaneous injection (T1Q10). Preference for a particular mode of administration was associated with factors such as concern about forgetting tablets (T1Q11) and perceived invasiveness of injectable treatments (T1Q12). Frequency and dosage of treatment were discussed (T1Q13), and while some indicated that daily tablets would be acceptable (T1Q14), others preferred less frequent treatment administration (T1Q15).

Treatment convenience was also discussed, with treatments needing refrigeration considered inconvenient (T1Q16). Perceptions around treatment duration varied, and whereas some assumed that long-term treatment would be needed (T1Q17), others thought that treatment would only be taken for 1 or 2 years and described the benefit of short-term preventive treatment over long-term treatment for established disease (T1Q18).

Side-effects: Participants discussed the perceived seriousness of some side-effects compared to others (e.g. nausea was considered less serious than cancer; T2Q1–3), and the severity of the side-effect (T2Q4–5). Concerns related to the long-term effects of the treatments and reversibility of side-effects were also described (T2Q6–7).

Participants further discussed how the perceived likelihood of side-effects might influence their choice (T2Q8), although they recognized that individual side-effects would only affect a proportion of patients (T2Q9–10) and that individuals have varied views on the impact of side-effects on quality of life (T2Q11).

Treatment cost and funding: Some participants discussed treatment-related cost, especially the cost to the National Health Service (NHS) or to society at large (T2Q12). Cost-effectiveness (T2Q13) and the potential for reduced costs for the treatment of RA with effective prevention were discussed by some (T2Q14), whereas others worried that preventive treatment may be too expensive for the NHS and thus unavailable to at-risk individuals (T2Q15). Possible personal costs, such as prescription charges (T2Q16) or increased travel insurance costs for at-risk individuals (T2Q17), were also discussed.

Uncertainty around treatments and side-effects: Uncertainty around side-effects, treatment duration (T3Q1–2), and the potential for treatment benefit were seen as potential barriers to treatment uptake (T3Q3–4). Participants further indicated a need for confidence in information on risks and benefits, scientific experience, and evidence (T3Q5).

Unwanted effects of the treatment apart from side-effects: Participants discussed potential unwanted effects of treatment beyond side-effects, including the treatment affecting their ability to get vaccinated (T3Q6) or interacting with regular medication (T3Q7). Participants were also concerned about the effect of the

Table 1. Quotations illustrating the themes 'Effectiveness' and 'Treatment administration'.

Effectiveness	
1	'If you take this tablet you're going to feel so much better in an hour's time … and it's been proved, then you'll take the tablet.' (General public)
2	'… but I think for me, the effectiveness, in terms of, you know, preventing pain, or reducing pain, or issues with mobility, is my main thing … .' (FDR)
3	'Influence to take it … it's the peace of mind it would give me of having that risk reduced and being pain-free or at least, reduced pain in future, that would influence me to take it.' (General public)
4	'I think because it's starting under 50% already so, if you are going to go to the trouble of taking it, you want it to be really effective.' (General public)
5	'I suppose if it [the risk] may be reduced it to 20 then I would consider it … .' (FDR)
6	'… and you take your chances, but you go with what would have the least side-effects, with perhaps the most benefits, again.' (FDR)
7	'I just think that saying that you could develop cancer from taking this preventative medicine … would not necessarily just be side-effects, it's whether it's worth … .' (General public)
8	'… if you are going to try it and the impact of coming off it is quite severe so, it's not that easy to stop it if you do get fairly radical side-effects, then it would again, deter you from going on it unless you were very, very, high-risk … .' (General public)
Treatment administration	
9	'Whereas you do get used to sort of, if you are taking tablets just to take one, it's another one to take isn't it, just as long as you don't mix them.' (FDR)
10	'Yeah I think rather than taking a tablet, I don't know if it is a psychological thing, it's just injecting yourself or being injected with something and it is that … Yeah, that's quite a positive thing that's it's just a, it's small, you're not constantly taking pills.' (FDR)
11	'Because if it is like to take three times a day, every single day and if I forget there are some implications of that … .' (General public)
12	'I'm not scared of injections I'm not scared about that but with a tablet I think you can take it and then if it doesn't agree with you it's out of your system fairly quick but with an injection I don't know, I don't know what it is I don't know if it's just a personal thing I just feel as if it's, I don't know poisoning your body but it's there you know what I mean straight away. I know the drugs do the same job, they travel round but I don't know just I'm not keen on an injection.' (FDR)
13	'I think as well, how it's administered as well as dosage because if you've got to have four injections a day to get any result, that's not going to be … and then again, it depends on what the result is.' (General public)
14	'That's quite positive though that it's only one or two pills a day.' (FDR)
15	'Yeah, that's quite a positive thing that's it's just a, it's small, you're not constantly taking pills.' (FDR)
16	'I just think with administration it's convenience as well because like … with treatment B, if you're going away for two or three weeks, you've got to make sure you're going to have a fridge in your hotel and how do you get your delivery … if it's short and it's come late or something, it's inconvenient.' (General public)
17	'And also the duration, how long you have to take the drug for because if one of the side-effects is eye problems, it's as though you have to take it for at least five years. So, if I take it for four [years], it's okay, if I'm not potentially running the risk of having eye problems but if I know it's a treatment for ten years or life-long and that's an additional risk that could in the future also affect my decision.' (General public)
18	'But then it's only a year treatment isn't it, so in theory once you have done treatment everything, it's going to be alright. It might be better than being on tablets all the time.' (FDR)

General public or FDR after the quotation denotes that it is from a participant of the general public focus groups or from a first degree relative (focus group or interview), respectively.

treatment on their lifestyle, quality of life, and life choices (e.g. reproductive options; T3Q8).

Information needs and (medical) opinion: Participants described how they would research proposed treatments and their need for treatment-related information, including risks and benefits (T3Q9–11), as well as treatment alternatives (T3Q12). The importance of expert knowledge and medical opinion of the person prescribing the treatment (T3Q13) and the need for further support while on the treatment (T3Q14) were also discussed. Participants further valued the opinion of family, friends, and those with relevant experience of the treatment (T3Q15).

Themes related to treatment context and personal circumstances. Participants also mentioned other, non-treatment-related factors that would affect on their treatment choice, which relate to personal circumstances, perceptions, and experiences, as well as the treatment context. The overarching themes are: (i) personal characteristics or circumstances (e.g. family history, age); (ii) attitude towards taking medicine in general; and (iii) their personal risk of developing RA. These themes are discussed below, with illustrative quotations in Tables 4 and 5.

Effect of personal characteristics or circumstances: Previous health-related experiences may impact treatment preferences. One participant described being wary of the risk of cancer as a side-effect of preventive treatment for RA in light of their family history of cancer (T4Q1). Another described how they felt that

Table 2. Quotations illustrating the themes 'Side-effects' and 'Treatment funding and cost'.

Side-effects	
1	'It's a bit like you know when you get some medication and you look at the side-effects, it could be just a little bit of nausea but then further on down there is all sorts of things.' (FDR)
2	'I think the first word that I would think about is cancer … do I want cancer more than I want RA? It's quite a … interesting choice.' (General public)
3	'In reading this, I would be a lot more hesitant in taking this treatment, than I would A, because of some of the side-effects, if I were to have been diagnosed with rheumatoid arthritis, then I'd be more inclined to consider a treatment like this, than as a preventative, because I think in this, some of the known side-effects seem a lot more severe and perhaps a lot more long lasting than the potential for drug A.' (FDR)
4	'I think it's more the severity of some of the side-effects for B seem perhaps wrongly, I don't know, more severe than the side-effects to treatment A.' (FDR)
5	'Looking at the side-effects, feeling sick, nauseas, stomach pain, it would depend on the severity.' (FDR)
6	'Depending on whatever the long-term consequences are because I see this as an immediate result from treatment B, the way it's displayed.' (General public)
7	'I suppose whether it's reversible once you stop taking it.' (General public)
8	'And when these aren't the extreme ones, these are the very common side-effects so chances are you probably are going to feel those.' (FDR)
9	'You get side-effects with every single drug that you put into your body, everyone can react differently, some of these things, to be honest, at this precise moment, don't bother me at all … .' (FDR)
10	'I think it's what you say … it's a personal … how you judge the risks of what can happen against … how you're living now.' (General public)
11	'Cos obviously you don't know or … or even it sounds really vain if it made me put on weight you know what I mean something that would change me really do you know what I mean like. It's not really, well it's kind of life changing.' (FDR)
Treatment funding and cost	
12	'Yeah, cost obviously if it is on the NHS then that is another strain on the NHS for something that I've said before possibly won't make any difference but then … .' (FDR)
13	'Or even cost-effectiveness because if something is amazing but it's expensive … is it worth it? Then those drugs are worth it … .' (General public)
14	'And if it works like fantastic and that will stop people like my relative, they are using a lot of resources.' (FDR)
15	'I suppose that would be the other thing if the drug was developed and they say it's too expensive to administer.' (FDR)
16	'If it's not proven to … not develop it and it's only an idea of prevention, would you want to pay prescription for a drug you don't know is going to actually help you.' (General public)
17	'If you're going abroad … I know if I go abroad I'm the high instance … it's no less than seven hundred to insure me, so, what is that cost going to be added?' (General public)

General public or FDR after the quotation denotes that it is from a participant of the general public focus groups or from a first degree relative (focus group or interview), respectively.

a significant previous health problem would impact their decisions around preventive treatment for RA (T4Q2).

Having a (suspected) family history of RA was an important consideration for some participants (T4Q3), as was knowing someone with RA. People further discussed the severity of any pre-RA symptoms as a factor influencing their choice (T4Q4). In contrast, the absence of a family history of RA and absence of musculoskeletal symptoms might cause preventive treatment to be declined (T4Q5). Participants further suggested that personal characteristics such as age and occupation (T4Q6) may affect treatment choice.

Finally, emotions such as fear and worry were elicited by discussions of RA, the risk of developing RA, the preventive treatment itself, and any risks associated with preventive treatment (e.g. T4Q7). One participant spoke of their fear of losing independence if they were to develop RA and feelings of embarrassment if someone had to care for them (T4Q8).

Attitude towards medicine in general: Some participants indicated that they did not like taking medication and would not consider doing so to prevent a disease (T5Q1–2). Some preferred lifestyle changes such as diet and exercise over pharmacological therapy as a preventive intervention (T5Q3). Others felt that drug treatments were only appropriate after someone had developed symptoms (T5Q4–5), and made a clear distinction between treating RA-related symptoms and prevention of future disease (T5Q6–7).

Chances of developing RA: For many participants, the 40% chance of developing RA that they were asked to assume was insufficiently high to consider taking any form of preventive medication (T5Q8–11), whereas for others it was sufficient (T5Q12–13). Some participants focused on the risk of salient side-effects, particularly cancer, and indicated that unless their risk of RA was extremely high, they would not accept any risk of getting cancer as a side-effect of preventive treatment (T5Q14).

Table 3. Quotations illustrating the themes 'Uncertainty around treatment and side-effects', 'Unwanted effects of the treatment', and 'Information needs and (medical) opinion'.

Uncertainty around treatment and side-effects	
1	'This treatment B has a lot of unknown things that you're not very sure if you take it what might happen to you. So, I feel it is more risky than the first one.' (General public)
2	'But to prevent it could you stop it because obviously it's an auto immune thing so you're doing something to stop that immunity occurring would that mean that these drugs you would be on them all of your life.' (FDR)
3	'Nobody can give 100% promise that it will be effective.' (FDR)
4	'Say, for example before you take the drugs, this is what it will say … after you take the drugs you will reduce 20%. I think people want to see something like that to be assured about its effectiveness. I think it's a measurement.' (General public)
5	'Well you would hope that whoever, if you did need to take it, whoever is telling you that you should be taking these drugs has done their research, that the research has been done, that you are not just a guinea pig.' (FDR)
Unwanted effects of the treatment other than side-effects	
6	'I have a flu injection every year … and I'm not sure how effective that is but however, I wouldn't be able to have vaccinations … .' (General public)
7	'I read this … I would be thinking how it fits in with my current medication regime. So, I would be more likely to take it. So, it fits in with … yeah … if it fits in with my lifestyle.' (General public)
8	'I think one of the other things is lifestyle because if you take this treatment and it affects the food or alcohol or whatever and you're quite young and you know you can't have alcohol three days a week or something … And you're quite a social being and you want to go out and so on, it can be quite off-putting so, there are factors you would have to weigh up … what is more important to you.' (General public)
Information needs and (medical) opinion	
9	'I research, and read, and ask the questions and find out, and make the informed decision, that would be my argument, make the informed decision of what's best for me, for my wellbeing.' (FDR)
10	'Some knowledge, yes, I wouldn't want to take something blindly, I wouldn't take it, just because they've got 40% chance, I wouldn't just take a drug, but I would be more interested, more invested, in finding out more about it, and making an informed choice.' (FDR)
11	'Side-effects. So, I would want to find out what is the risk element and the probability of limiting the risk.' (General public)
12	'If I did do my research I would maybe, anything that I could do diet wise or exercise wise first before you take it but if I did take it then I would take it and just go for it rather than worrying about the side-effects.' (FDR)
13	'I think if I was to consider anything like this, I would want to talk to somebody who is involved who knows, so yes, I would talk to the specialist, or the doctor.' (FDR)
14	'I think for treatment B, definitely … you could do treatment B, but you would want someone around you to help support it.' (General public)
15	'Well before I would ever go on that I would certainly be talking to a lot of people who was on that treatment to see whether, what sort of side-effects and problems they've had.' (FDR)

General public or FDR after the quotation denotes that it is from a participant of the general public focus groups or from a first degree relative (focus group or interview), respectively.

Discussion

The current study identified and explored factors likely to influence treatment decisions for RA prevention. It incorporated the views of FDRs of RA patients and members of the public, both asked to assume that they were symptomatic, autoantibody positive, and had a 40% risk of developing RA within 2 years.

Two distinct groups of factors were identified that would influence participants' decisions to take preventive treatment: (i) those related directly to the treatment itself and (ii) circumstantial factors or personal characteristics.

The seven broad themes directly related to the treatment were: effectiveness, side-effects, treatment administration, cost of the treatment, uncertainty around the treatment benefits and risks, unwanted effects of treatment, and information needs.

Effectiveness in the current study encompassed not only preventing or delaying RA and preventing future symptoms, but also improving current symptoms, which to date has not been included as a factor in quantitative preference studies related to preventive treatment of RA. Participants discussed treatment duration as part of the treatment administration theme, with some worrying that they would be on the preventive treatment indefinitely. For most, an acceptable preventive intervention for RA should be of short-term duration. Side-effects have been mentioned as a concern by FDRs in previous explorations of preventive RA treatment (29, 30, 37) as well as by FDRs in other disease areas such as axial spondyloarthritis (axSpA) (38). In the current study, the risk of cancer in particular was seen as a serious side-effect that people would not be willing to accept. Previous quantitative preference studies (39, 40) have assessed the importance of issues relating to the amount/quality of evidence regarding treatment effectiveness and safety, which was echoed in the current study. This highlights the need for further clinical trials to establish a robust evidence base for both pharmacological and non-pharmacological preventive interventions. Similarly, the need for information about the treatment and expert opinion/endorsement aligns with

Table 4. Quotations illustrating the theme 'Effect of personal characteristics or circumstances'.

Effect of personal characteristics or circumstances	
1	'We have got more of a family history of that [cancer] then RA, so in your mind you would have to really think about that one I think, wouldn't you?' (FDR)
2	'I've had a health scare recently and having to evaluate that risk is quite interesting, isn't it? In the way that they thought my condition was something more serious and actually, it wasn't but … in the end, after lots of tests and investigations.' (General public)
3	'I think in seeing the good and bad [of RA in relative], there is a lot of, for me, interest in seeing what I can do, if there is a chance that I might get rheumatoid arthritis, I would prefer to be on the preventative, or let's restrict the development of it, rather than waiting for it to happen, and then needing care and support, to – because I can't manage it myself.' (FDR)
4	'I think it entirely depends on your circumstances because if you are in so much pain, you've just not got anything to reduce but if you can tolerate it then you just think … you think about all the other options.' (General public)
5	'Coming from a relatively healthy background at the moment … touch wood … then I don't have to personally think about things like other drugs and medications or family history is not that important. So, yeah, I guess I'm thinking more of what my healthy status might lose, were I to take a preventative drug.' (General public)
6	'I would be much more likely, as an older person, just … I'd be much more likely perhaps to take this. Whereas, perhaps as a young person that thinks I'm invincible … you might actually … you might not consider that to be a risk worth taking or need to address yet.' (General public)
7	'It's [biological therapy] just got like a scary sound to it, it sounds more imposing as well you know what I mean it's, because of it, you know it interfering with your own cells.' (FDR)
8	'I would be very, very embarrassed if somebody had to do that [take care of personal needs] for me, or I would feel, it's almost a loss of liberty.' (FDR)

General public or FDR after the quotation denotes that it is from a participant of the general public focus groups or from a first degree relative (focus group or interview), respectively.

Table 5. Quotations illustrating the themes 'Attitude towards drug treatment' and 'Chance of developing RA'.

Attitude towards taking (preventive) treatment in general	
1	'Why not leave things to happen, I am of the opinion that nobody should really be taking stuff that they don't really need to take unless there is a very, very good reason.' (FDR)
2	'Yes I am very wary of taking anything myself anyway but also why would you take stuff that you really don't need to take?' (FDR)
3	'I would say … like natural alternatives, like therapies, low exercise, movement therapy, and a more holistic approach … Yeah, it could potentially reduce the development of the condition in the long-term and also managing it effectively, even if you were diagnosed with it, it could help and support your recovery.' (General public)
4	'I think so because unless I was told that that is definitely what it was, I would need a definite diagnosis and maybe, I don't know, a certain time that it's harder to manage your life.' (FDR)
5	'I would take this drug if I had been diagnosed with it, possibly … .' (General public)
6	'If we're assuming that … in my personal opinion, if we assume that I haven't got the condition yet means that preventative treatment, then I would probably prefer not to have these … because enough of these contraindications that perhaps I wouldn't go with it.' (General public)
7	'But that's a treatment rather than a preventative … because I think if it's a treatment, I'd take it but actually, if it's preventing something, I'm not sure I would take that.' (General public)
Chance of developing RA	
8	'But as a preventative thing, my risk [of developing RA], I think, would have to be really high … 80 or 90% … You are almost definitely going to get rheumatoid arthritis then I might take it.' (General public)
9	'It has to be a higher risk than that (40%). To take something like treatment A.' (FDR)
10	'The risk level would have to be a lot higher to take something like this as a preventative rather than a curative.' (General public)
11	'I think the only reason it puts me off is it's saying that there is a 60% chance you won't get it, even if you don't take the medication. So, if you don't do anything at all, there is still a 60% chance you won't get it.' (General public)
12	'I think 40% or higher is something that I would have to investigate more, I've always been more of a preventative rather than a cure kind of person, in my life generally anyway, I would definitely consider it, I think, 40% is – it's such a high percentage – it might never happen – but if I can perhaps consider, and then take something that's going to potentially restrict that development of the disease, it may still develop, who knows, but it would perhaps limit the extent to which it affects me, my mobility.' (FDR)
13	'Yeah, 40% I think is quite high as I say if it just went to 50% that's the game changer because that's half and half isn't it so it's like yeah, it's like being in a lucky dip at 50%.' (FDR)
14	'If I was going to get the risk of cancer, it would have to be 90%, I think. If I was going to have to swap RA for cancer.' (General public)

General public or FDR after the quotation denotes that it is from a participant of the general public focus groups or from a first degree relative (focus group or interview), respectively.

previous research (40, 41) highlighting the need for the development of effective tools to communicate risk and benefits. Given the importance that participants placed on the impact of personal characteristics, as discussed below, these tools should also be sensitive to personal considerations. Finally, the restrictions that may come with taking certain types of treatment, such as the restriction on certain vaccines and the effects of the treatment on current lifestyle and quality of life, could also act as barriers to taking the preventive treatment, but have not been previously explored in great depth.

Non-treatment-related factors, such as individuals' attitudes towards taking medication in general and the corresponding effect on their decisions around preventive treatment, are important factors to consider when developing participant information for clinical trials and to support shared decision making between healthcare professionals and patients. In line with previous research (29) and prevention research in other disease areas, such as cardiovascular disease (42), some participants indicated that they would prefer lifestyle changes over drugs as a preventive intervention. Although research has shown that personalized information about the risk of RA has a positive impact on risk-related health behaviours (43), clinical trials of the impact of non-pharmacological and lifestyle interventions to prevent or delay RA are currently lacking.

A 40% chance of developing RA was often not perceived to be high enough for someone to consider taking any form of preventive medication. Indeed, research has shown that some individuals with RA-related autoantibodies are hesitant to consider taking preventive medicine (32). Similarly, for axSpA FDRs, both their perceived risk of developing axSpA and perceived disease severity negatively influenced their willingness to consider preventive treatment (38). Further studies are needed to quantify the minimum acceptable benefit needed for participants to accept varying levels of treatment risks, and the degree of treatment risks that are acceptable for an acceptable level of treatment benefit.

Quantitative studies of treatment preferences (e.g. choice-based survey studies) often focus on treatment-related factors (attributes) only. However, contextual considerations are clearly also important for the intended recipients of the treatment, and decision making by stakeholders in the development and approval of new medical products should be informed by both.

Strengths of this study include extensive input from PRPs and a multidisciplinary team of researchers with expertise in qualitative research, clinical rheumatology, and preference research. A further strength is the inclusion of FDRs recruited through patients with a confirmed diagnosis of RA, rather than self-declared FDRs. This is advantageous as RA is often confused with other musculoskeletal conditions (44, 45) and people may mistakenly believe that their relative has RA.

Limitations include the potential for a response bias owing to the sample being self-selected, with participants either responding to advertisements or being invited through their relative. Furthermore, the sample size of FDRs was rather small compared to the general public sample, which may have led to an imbalance of discussed views and perceptions. However, although FDRs of confirmed RA patients and members of the public took part separately, the current analyses did not suggest major differences between the two groups, and findings are largely in line with previous qualitative research using FDRs (37). Furthermore, four members of the public reported a family history of RA, and although their FDR status could not be confirmed independently, it is likely that the current research captured a balanced mix of views from both individuals with and those without a family history of RA.

Although this qualitative study was not designed to quantify differences between FDRs and the general public, our findings are informative for the development of quantitative studies [e.g. (20)]. Furthermore, understanding the impact of the many personal characteristics that could be associated with perceptual variations in this context (e.g. reproductive status, severity of relatives' RA, personal knowledge about chronic diseases) is an important area for future research.

Participants were provided with background information about RA, developed with input from PRPs. This is a recommended approach (23, 46) in treatment preference studies, in order to standardize participants' background knowledge and facilitate informed choice. While it is possible that this information influenced the perceptions of participants in this study, at-risk individuals being asked to consider a preventive treatment in a clinical context would receive similar information to support shared decision making. The views that we have elicited are thus likely to be similar to those of people considering participating in a preventive trial or taking a preventive medication.

A final limitation is that participants were asked to assume a hypothetical scenario where they have symptoms and laboratory data indicating an elevated risk of RA. Further investigation is needed to explore the preferences of symptomatic/autoantibody-positive individuals whose actual risk of developing RA is high.

Conclusion

The treatment-related themes identified in this study add to those identified in previous preference research and confirm which treatment features are especially relevant for individuals considering preventive RA treatment. The non-treatment themes highlight the importance of additional personal and contextual factors that should be addressed in the development of tools to support shared decision making about participation in RA prevention trials.

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Ethical approval

This study was approved by the London–Hampstead Research Ethics Committee (19/LO/0407), and participants gave their written informed consent before starting a focus group or interview. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Declaration of Helsinki.

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Supplementary material

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