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# *I would never take preventive medication!* Perspectives and information needs of people who underwent predictive tests for rheumatoid arthritis

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**Competing interest**

JS has received grants for his institution from Abbvie, Lilly, MSD, Pfizer and Roche and has provided remunerated expert advice to and/or had speaking engagements for Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Boehringer-Ingelheim, Celgene, Celltrion, Chugai, Gilead, ILTOO, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB. TS has received speaker fees from AbbVie, Janssen, MSD, Novartis, and Roche and grant support from AbbVie. KR has received grants from Abbive and Pfizer and has provided remunerated expert advice to and/or had speaking engagements for Abbvie, BMS, Janssen, Lilly, Pfizer, Roche, Sanofi and UCB. The other authors declare that there is no conflict of interest with respect to the research, authorship, and publication of this article.

**Short Title:** Perspectives and information needs on predictive testing in rheumatoid arthritis

**Keywords**: Qualitative research, patient perspective, Rheumatoid Arthritis, Treatment, Autoantibodies

**Abstract**

**Objective:** Little is known about the experiences, values and needs of people without arthritis who undergo predictive biomarker testing for the development of rheumatoid arthritis (RA). Our study aimed to explore the perspectives of these individuals and describe their information needs.

**Methods:** A qualitative, multicenter interview study with a thematic analysis was conducted in Austria, Germany and the UK. Individuals who underwent predictive biomarker testing for RA and had a positive test result, but no diagnosis of any inflammatory joint disease, were interviewed. Participants included patients with arthralgia and asymptomatic individuals. Information and education needs were

developed from the qualitative codes and themes using the Arthritis Educational Needs Assessment Tool (ENAT) as a frame of reference.

**Results:** Thematic saturation was reached in 34 individuals (76% female; 24 [71%] with arthralgia and 10 [29%] asymptomatic individuals). Thirty-seven codes were summarized into four themes, namely (i) decision making around whether to undergo initial predictive testing, (ii) willingness to consider further predictive tests and/or (iii) preventive interventions, including medication and (iv) varying reactions after receiving a positive test result. Individuals with arthralgia were more likely to be willing to take preventive action, undergo further testing, and experience psychological distress than asymptomatic individuals. All participants expressed the need for tailored, lay-understandable information.

**Conclusion:** Individuals at risk of RA are currently the subjects of research aimed at developing better predictive strategies and preventive approaches. Their perceptions and needs should be addressed to inform the future development of interventions combined with education.

**Significance and Innovations**

- To our knowledge, our study explored for the first time experiences of being tested, as well as information and support needs of people with arthralgia and asymptomatic individuals who underwent predictive biomarker testing for RA and had a positive test result.
- All individuals expressed the need for tailored, lay-understandable information on predictive testing. Most of them emphasized the advantage of knowing that they were at risk for developing RA as early as possible.
- Individuals with arthralgia were more likely to be willing to take preventive action, undergo further testing, and experience psychological distress than asymptomatic individuals.
- As individuals at risk of RA are currently the subjects of research aimed at developing better predictive strategies and preventive approaches, their perceptions and needs should be addressed to inform the future development of interventions combined with education.

Rheumatoid arthritis (RA) is a chronic inflammatory rheumatic disease with an incompletely understood etiology. RA is characterized by polyarticular swelling leading to pain, stiffness and loss of joint function and affects between 0.3% and 1% of the population (1). Delays in diagnosis and treatment are still common and are associated with worse outcomes, including irreversible joint destruction, disability, limitations in functioning and reduced quality of life (2-5). Early identification of RA patients is thus essential to achieve an optimal clinical outcome (6) and has been the target of several research initiatives (7). Since RA is commonly preceded by a phase of immunological abnormalities including the presence of antibodies to citrullinated proteins (ACPA) and low grade inflammation (8-12), future interventions might start even earlier, by identifying and treating individuals who are at risk of developing RA (e.g those with a first degree relative with RA and patients with clinically suspect arthralgia or undifferentiated arthritis) before the development of clinically apparent polyarthritis (13, 14). Therefore, researchers have explored predictive testing methods involving blood based biomarkers, imaging (e.g. ultrasound and magnetic resonance imaging [MRI]), as well as more invasive methods like synovial biopsies (6, 8, 15-20) in the time preceding RA.

Predictive and preventive approaches can lead to the early detection of certain diseases with benefits for the people themselves, the health system and its payers, and for society as a whole (21, 22). However, there is a risk of over treatment of those receiving a false positive test result (13). Although predictive tests have been carried out in a range of disease contexts, there is limited research on the perspectives of those who undergo such tests (23). Moreover, the tested individuals need to be informed by physicians and health professionals about the tests and their purpose, as well as test results, potential risk factors and preventive strategies relevant for them. Therefore, targeted, person-centered information and communication strategies should be developed alongside the predictive tests to explain what it means to be at risk of RA and the potential benefits and risks of early intervention as well as preventative strategies. This may improve the self-efficacy and health literacy of individuals who are at risk of developing RA, raise awareness of (future) preventive interventions, reduce potential delays in help-seeking for early symptoms, and facilitate improved clinical outcomes. In recent years, a great number of putative predictive tests in the context of RA have been carried out in numerous cohort studies and as part of extended preventive medical check-ups (24, 25). Nevertheless, little is known about the needs, values and beliefs of individuals who undergo predictive testing for RA, and are informed about a positive biomarker test result. In their recent work, Sparks et al. (14, 26) showed that individuals receiving personalized risk disclosure and education were more motivated to change their health behavior than individuals who received standard education about RA. However, the experiences of being tested, as well as information and support needs of individuals who undergo predictive testing for RA have not been described in detail yet.

The aims of this study were to (i) explore the perspectives of individuals who underwent predictive biomarker testing for RA and were informed about a positive test result regarding ACPA and/or rheumatoid factor, (ii) find similarities and differences in the views of individuals with arthralgia and asymptomatic individuals which might represent different levels of risk in the development of RA and (iii) describe the information and education needs in both groups.

## Participants and Methods

*Design*

A qualitative, multicenter interview study and thematic analysis were conducted, as part of the EuroTEAM (Towards Early diagnosis and biomarker validation in Arthritis Management) project (27). Information and education needs were developed from the codes and themes that emerged out of the qualitative analysis using the Arthritis Educational Needs Assessment Tool (ENAT) as a frame of reference (28-30).

*Participants and sample size consideration*

Individuals, ≥ 18 years attending rheumatology centers in Vienna (Austria), Erlangen (Germany) and Birmingham (UK) who had predictive biomarker tests for RA with a positive test result, but had not received a diagnosis of any inflammatory joint disease, were eligible for the present study. Individuals were either referred for testing because of symptoms or had a predictive test for RA as part of an extended medical check-up. ACPA and rheumatoid factor (RF) were considered positive according to the reference values in each center. Participants included both people with arthralgia in at least one peripheral joint and asymptomatic individuals. All participants were contacted by phone, and appointments for conducting the interview at the participating center were made with those wishing to participate. Recruitment continued until thematic saturation was reached. Saturation was defined as no new qualitative codes coming up in at least ten subsequent interviews (31, 32). In order to determine the number of new codes in each interview, data analysis started soon after the first interview and proceeded in parallel to data collection (33).

The study was approved by the Ethics Committee of the Medical University of Vienna (EK Number 2174/2013), the Ethics Committee of the University of Erlangen-Nuernberg (Re.No-87_14B), and the Humber Bridge National Research Ethics Committee of Birmingham (REC reference 13/YH/0329). Eligible people were informed about the purpose and procedures of the study and gave their oral and written informed consents.

*Data collection*

A semi-structured one-to-one interview was conducted with each participant. Based on a review of the qualitative literature exploring public perceptions of predictive tests and experiences of being labelled as "at risk" for a chronic disease (34, 35), the research team co-developed an English interview guide together with biomarker experts and patient research partners (DS, MD). The initial structure of the interview schedule was revised and questions were modified as a result of feedback from both groups, to ensure that the descriptions of predictive tests were accurate and understandable by a lay audience. The interview questions are depicted in Table 1. Health professionals with experience in qualitative research data acquisition and/or experiences as principal investigators of qualitative studies performed the interviews: EM (female, MSc, background in occupational health and health science), MS (female, PhD, occupational health and health science), AH (male, MD, PhD, rheumatology), RS (female, PhD, psychology) and GS (female, PhD, psychology). All interviews were audio-recorded, transcribed verbatim and analysed centrally in Vienna, Austria, by EM with input from the local investigators from Erlangen and Birmingham and the patient research partners.

- Table 1

*Data analysis*

Qualitative data analysis followed a modified form of thematic analysis (36, 37) and was facilitated by using QSR International's NVivo 10 qualitative data analysis software [43-45]. The analysis comprised the following steps: firstly, the first author (EM) read through the transcripts to gain an overview of the collected data and to become familiar with the content. Secondly, the transcripts were divided into meaningful segments of data (defined as specific units of text, either a few words or a few sentences with a common meaning). In the third step, initial codes (descriptive or conceptual labels), such as *be shocked/be anxious*, *get worried* and *stay calm* were assigned to these segments. Codes could refer to the main topic of a meaningful segment, but one segment could also contain more than one code. In the fourth step, the initial codes were grouped into associated higher-level themes. The codes *be shocked/be anxious*, *get worried* and *stay calm* were grouped under the higher-level theme *varying reactions after receiving a positive test result*. Thereafter, we compared the codes and themes between individuals with arthralgia and asymptomatic individuals for similarities and differences regarding the qualitative meaning of a concept and its quantitative frequencies using descriptive statistics. Information and education needs were developed based on the qualitative codes using the ENAT as a frame of reference (28-30).

*Rigor and accuracy of the qualitative data analysis*

Several strategies were used to improve and verify the trustworthiness of the qualitative data: debriefing notes were recorded after each interview. All local investigators who conducted interviews, namely EM and MS in Austria, AH in Germany and RS and GS in the UK checked the transcripts against the audiotapes for accuracy. After analyzing all interviews, the results were discussed with researchers of all centres and reviewed by patient research partners (DS,MD) and a senior researcher (TS) who had not been involved in the analysis of the transcripts. Finally, the consolidated criteria for reporting qualitative research (COREQ) Checklist (38) was used to ensure the high quality of reporting the study results (supplemental table 1).

## Results

*Participant characteristics*

Thematic saturation (supplemental table 2) was reached after including 34 individuals (76% female; 24 [71%] individuals with arthralgia and 10 [29%] asymptomatic individuals). Of these, 15 (44%) participated in Austria, 15 (44%) in Germany and 4 (12%) in the UK (table 2).

- Table 2

*Codes and higher-level themes*

We extracted 37 codes that were grouped under four higher-level themes, namely (i) decision making around whether to undergo initial predictive testing, (ii) willingness to consider further predictive tests and/or (iii) preventive interventions, including medication and (iv) varying reactions after receiving a positive test result (tables 3 and 4).

- Table 3

*Similarities between individuals with arthralgia and asymptomatic individuals*

Asymptomatic participants and individuals with arthralgia indicated that being told about their risk of developing RA had both, positive aspects (knowing the risk; knowing whom to contact if symptoms progressed), as well as negative consequences (having to deal with the uncertainty associated with risk information) for them. Regarding positive aspects, the majority of participants in this study (32; 94%) were convinced that they benefited from knowing their risk status as early as possible. They felt this knowledge would enable them to react appropriately if RA related symptoms developed or

extended in the future. Furthermore, getting to know the people whom one should approach in case of symptom onset or progression, was described as positive:

> *If I develop RA, I know that I will get the best possible care here. I know I'll get very quick access to care; and I know the people whom to approach; this will improve my outcome.* (No. 13, female, age 40, arthralgia, UK)

> *After the test I knew, if I develop it I have to react quickly, so that something will be done.* (No. 4, male, age 52, asymptomatic, Austria)

Regarding the negative experiences, some participants of our study reported that dealing with an imprecise risk without further information, such as information about when RA is likely to develop had a negative connotation for them and posed a substantial challenge. One male participant described this as follows:

> *For me, the best would be to describe the risk in numbers and to know when the onset will be. How much will the disease impact on my life? What can I do? How can I prevent the onset of the disease? And so on. (...) just to say that it will come anytime, is not enough for me.* (No. 14, male, age 38, arthralgia, Germany)

> *One would have to learn in what way that* [test result] *is significant. But you hear, you have 10 percent risk for something, or 90 percent and the question is, whether something can be done.* (No. 4, male, age 52, asymptomatic, Austria)

*Differences between individuals with arthralgia and asymptomatic individuals*

Within all four higher-level themes, we found differences between individuals with arthralgia and asymptomatic individuals. Regarding the first higher-level theme *decision making around whether to undergo initial predictive testing*, people already suffering from pain or stiffness aimed to obtain assurance about causes for their symptoms and to receive confirmation that something was wrong with their body, whereas asymptomatic individuals were more likely to undergo predictive testing in order to contribute to research only.

Regarding the second higher-level theme *willingness to consider further predictive tests,* individuals with arthralgia were more likely to agree to further predictive tests than asymptomatic individuals. Invasive methods such as synovial or lymph node biopsies were the areas with the largest difference between both groups: 12 individuals with arthralgia (50%) would agree to synovial biopsy compared to only one asymptomatic participant (10%).

> *I would take it* [synovial biopsy] *and I would not mind but rather be interested in it. I am also not very sensitive to pain so it is no problem at all.* (No. 21, female, age 76, arthralgia, Austria)

Regarding the third higher-level theme *willingness to consider preventive interventions, including medication,* nine (38%) individuals with arthralgia would agree to take future preventive medication under certain conditions, if available, compared to none of the asymptomatic individuals. One participants with arthralgia described the circumstances

and conditions under which he would be willing to take preventive medication as follows:

> *Fundamentally positively, whereby you have to consider the side effects. There is almost no medicine without any side effect. Nonetheless, when I envision a future damage of the body, an early investigation is very useful.* (No. 14, male, age 38, arthralgia, Germany)

One asymptomatic participant who would refuse to take any future preventive medication articulated the following:

> *I would only take medication, if I am sick. In my opinion, chemicals and drugs always have side effects and you have to weigh the pros and cons, especially if you overdo it and take a whole cocktail of medicine then you are experimenting without knowing the outcome. So, medication is for treating already existing disease, not for prevention.* (No. 25, male, age 57, asymptomatic, Austria)

Regarding potential non-pharmacological interventions, the majority of the individuals with arthralgia (20/24 [83%]) reported that they were willing to consider life-style-changes to reduce their risk of developing RA compared to only 2/10 (20%) of the asymptomatic participants.

Regarding the fourth higher-level theme *varying reactions after receiving a positive test result*, asymptomatic partcipants in our study described that they had been able to *stay calm* (8/10 80%] compared to only 4/24 [17%] individuals with arthralgia). In contrast, 10/24 (42%) individuals with arthralgia reported *anxiety* and *were shocked* when they were told about the positive test result compared to none of the asymptomatic individuals.

Furthermore, some individuals with arthralgia experienced difficulties in talking about being a person at risk and informing their families and friends. One woman talked about avoiding unnecessary burden for her loved ones. She said:

> *[…] my last question when I left the clinic was how to tell people […]. So that was one of my concerns […], the communication of it all and I didn't want to, even though I was feeling overwhelmed, I didn't particularly want other people to panic and then panic me.* (No. 13, female, 40, arthralgia, UK)

We aimed to assess whether there were differences in views between participants with and without a positive family history of RA. Only one asymptomatic participant had a family history of RA. Despite the fact that her mother and grandmother had RA, this person was not concerned about the positive test result and reported that she was unlikely to modify her lifestyle or take future preventive medication. In contrast, people with arthralgia and a positive family history in RA reported higher levels of anxiety when being informed about the positive test and would modify their life to a greater extent.

*Information and education needs*

All participants in both groups described the need for tailored, lay-understandable information to be delivered by health professionals together with the positive test result (second-last column of table 3). One participant expressed her experience in the following statement:

> *It's important that they don't use these medical terms when explaining something, but trying to explain it by using examples. For them, this is a standard vocabulary, but for me this is a foreign word.* (No. 6, female, age 52, asymptomatic, Austria)

Furthermore, the majority of participants in this study missed clear and precise statements concerning different possibilities to prevent the onset of the disease. In that sense, they were especially interested if and what they could do themselves to reduce the risk of RA development. As an example, participant No. 15 (female, age 52, arthralgia, Germany) argued:

> *The one thing I would be curious about to find out, would be what I can do to stay healthy. And there is not much I found out so far. Specific information would help a lot.*

The qualitative codes and themes could be linked to all seven sections of the ENAT; however, predictive testing has not been part of the ENAT so far (last column of table 3).

- Table 4

## Discussion

To our knowledge, this is the first study that provides insights about the experiences, values and needs of people with arthralgia and asymptomatic individuals who underwent predictive testing for RA and had a positive test result. The results from the study show that predictive testing raises several ethical issues. All participants were informed about their risk of developing RA when receiving the test results. They also heard about RA related symptoms that might occur in future and whom to contact if such symptoms developed or their current symtoms extended in the future. Nevertheless, and in accordance with Cornelis et al. (39), participants of our study pointed out that they experienced a negative impact on their emotional well-being and that they were not well prepared for a possible positive test result. Participants with arthralgia in particular reported that they were frightened and worried. Although they had developed strategies to cope with this situation, they indicated that they would have preferred additional tailored information and support at the time when they were told that they had an elevated risk of developing RA. Clinicians should address the information and support needs identified in the current study by further developing effective, tailored education to support decision making about whether to take a

predictive test and provide guidance and support for understanding and coping with test results (14, 40).

Interestingly, insurance implications were only mentioned by two participants in this study; both were critical of the fact that preventive stategies were not paid by their health insurances. Moreover, ethical issues, such as confidentiality of the given risk information, were not explicitly mentioned by any of the participants. Participants might have assumed that these tests fall under the legal requirements of data protection regarding health data and as such are strictly confidential. In contrast to that, some people with arthralgia had chosen not to talk about their risk for developing RA with their families and friends in order not to frighten them. They decided to wait for tests with a higher degree of predictive accuracy before informing their loved ones. In two recent studies, researchers found that "at risk" individuals had a strong preference for a predictive test that would rule future RA in/out with absolute certainty (23, 41).

Despite the negative issues raised by the participants, very few (two) of them regretted they had been tested. However, arthralgia patients did not take an active decision to engage in predictive testing, but rather a decision to seek medical help for their arthralgia and the testing was a consequence of that. This knowledge might be of great importance when testing on a large scale and developing personalized, innovative preventive strategies in the next few years. Even if there is currently limited evidence to support both population-based screening programmes and personalized individual predictive tests, the scenario may change significantly in the future (22, 42). The desire to ensure that testing programmes do not cause more harm than good, has led to a considerable body of research on the psychosocial impact of predictive testing in adults, for a range of conditions including hereditary breast and ovarian cancer and Huntington's disease (43). In this sense, predictive testing for RA can also be seen as an important public health issue with benefits for at-risk individuals themselves, clinicians, researchers and the health system, if it were to be introduced into clinical practice and public health in a responsible manner combined with a tailored information for all the persons concerned.

As the aim of our qualitative study was to explore a wide range of experiences, differences regarding the time between tests and the interviews were considered to be an advantage. Even if the time between being informed about the personal risk and being interviewed differed among the participants, the majority emphasized the advantage of knowing about their risk for developing RA. Being aware of their risk status would allow them to react appropriately and rapidly, if symptoms such as synovial joint swelling occurred. In accordance with the study results of Stack and colleagues [23], exploring the perceptions of risk and predictive testing held by the first-degree relatives of patients with RA, some participants suggested that ongoing support by health professionals should be offered for those who have additional questions regarding their personal risk.

Another frequent topic was the question of effective preventive strategies which would be important to prevent the onset of RA. While some risk factors for RA related to lifestyle have already been identified (e.g. smoking), it has not yet been fully clarified how most of the identified risk factors influence RA-related autoimmunity. Furthermore, risk factors may differ between individuals or groups of individuals, and be influenced by gender and other personal and environmental factors (44). Participants in our study asked for activities which they could implement in daily life to reduce the risk of RA onset. Therefore, they need to be provided with more information about these present uncertainties. Individuals at risk need to know that there is still more data needed before detailed environmental risk factor modification and lifestyle changes, other than smoking cessation, can be recommended. Meanwhile, we could at least ensure that people at risk recognize the symptoms of disease development/progression and know where to go if such symptoms were to occur (4). European guidelines for the management of RA (45, 46) highlight the importance of early treatment.

The strength of this study is that it represents a comprehensive exploration of the experiences, values and needs of people who underwent predictive testing for RA and had a positive test result by reaching data saturation in three centers/countries. However, one limitation of our study was the difficulty to recruit asymptomatic individuals with a positive test result. A selection bias might have occurred since people who take part in an extended preventive health exam might be more interested in additional data about their own health, than the average population. Furthermore, women were over-represented in our study, as women were found to be more likely to sign up for health check-ups than men (47).

To conclude, participants showed large differences in views about predictive testing in the context of RA risk and offered specific suggestions that should be incorporated into service design and delivery in the context of future predictive testing programmes. These findings may also be relevant to prediction and prevention in the context of other diseases where multiple genetic risk factors interact with environmental risk factors to drive disease development.

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## Tables

**Table 1.** Interview questions for individuals who underwent biomarker testing for RA and had a positive test result, but no diagnosis of any inflammatory joint disease.

| |
|---|
| **Can you please tell me what you already know about RA? About which other issues would you like to be informed?** |
| Promts: |
| What do you think the causes of RA could be? |
| What do you think the risks factors for RA are? |
| Tell me about how serious you think RA is? |
| How would you know you had RA, for example, what symptoms would you expect? |
| What would be the impact of RA on your life? |
| Do you think you would be able to control RA yourself? |
| Do you think there are treatments available that would effectively treat RA? |
| **Do you ever worry about the possibility of developing RA in the future?** |
| **What would you think if you were told that you could have a test that would tell you how likely you were to develop RA?** |
| Promts: |
| What sort of information should this test give you? |
| When do you think would be the right time to get this information? |
| How would you feel about a test telling you that you could develop RA in the future? |
| In what ways do you think it would be helpful to know your chances of developing RA? |

**What would your concerns be if you knew what your risk of developing RA was?**

**What kind of tests do you think people might be able to do to work out whether or not you might develop RA (test that are available now and tests that might become available in the future)?**

**Various tests can currently be done, and various tests are currently being developed to predict the development of RA. What are your thoughts about:**

1. Blood tests looking at biomarkers, molecules in the blood
2. Blood tests looking at genes
3. Tests involving scanning the joints with either an ultrasound or MRI
4. Tests involving taking tissue out of a joint (synovial biopsy) or elsewhere (e.g. lymph nodes)

**What are your thoughts about taking medicines to reduce the risk of RA developing in the future?**

**What are your thoughts about changing your lifestyle (e.g. stop smoking, more exercise, change diet) to reduce the risk of developing RA in the future?**

*Note. For using the questions in Austria and Germany, the interview questions were translated from English into German and translated back to English, blinded for the original wording of the questions, by a member of the Austrian research team using a forward-backward approach (33).*

**Table 2.** Demographic data of the participants

| Demographic data | Asymptomatic participants (n=10) | Symptomatic participants (n=24) | Total |
|---|---|---|---|
| Number of participants/percent (%) | 10 (29) | 24 (71) | 34 (100) |
| Number of women (%) | 7 (70) | 19 (79) | 26 (76) |
| Mean age in years (±SD) | 61.7 (±9.6) | 48.6 (±14.4) | 52.4 (±14.4) |
| Age in years min/max | 51 to 81 | 18 to 76 | 18 to 81 |
| Positive family history of RA (%) | 1 (10) | 9 (37.5) | 10 (29.4) |
| Number of participants who did not smoke at the time of the interview (%) | 9 (90) | 19 (79) | 28 (82) |

**Table 3.** Qualitative coding scheme, corresponding information and education needs, and the related sections of the Arthritis Educational Needs Assessment Tool (ENAT). The ENAT was used as a frame of reference for identifying information and education needs.

| Higher-level themes | Codes | Information and education needs of individuals who undergo predictive testing and have a positive test result | Related section of the ENAT |
|---|---|---|---|
| **4** | **37** | | |
| **Decision making around whether to undergo initial predictive testing** | ▪ Gain information about the own health<br>▪ Assurance about causes for symptoms<br>▪ Receive confirmation that something is wrong<br>▪ For research purposes only | Information on different reasons for undergoing predictive testing<br>Reasons for repeating the biomarker testing: future options might include regular (annual) tests/assessments for research purposes, but also to improve future prediction. Otherwise individuals should be advised to come once synovial swellings develop, telephone helplines might also be an option. | Predictive testing is so far not part of the ENAT Section related to *support from other people* |
| **Willingness to consider further predictive tests** | ▪ Positive attitude towards the previous test<br>▪ Negative attitude towards the previous test<br>▪ Right time point - as early as possible<br>▪ Not the right time point<br>▪ Agree to biomarker test<br>▪ Refuse biomarker test<br>▪ Agree to genetic testing<br>▪ Refuse genetic testing<br>▪ Agree to ultrasound or MRI<br>▪ Agree to ultrasound or MRI only with symptoms<br>▪ Refuse ultrasound or MRI<br>▪ Agree to synovial biopsy<br>▪ Agree to synovial biopsy only with symptoms<br>▪ Refuse synovial biopsy | Information on evidence and availability of potential additional predictive tests methods<br>Additional information about advantages and potential side effects, as well as validity of the various tests (statement to which extend a test method is diagnostically conclusive) | Predictive testing is so far not part of the ENAT Section related to *support from other people* |
| **Willingness to consider preventive interventions, including medication** | ▪ Agree to preventive medication<br>▪ Strictly reject preventive medication<br>▪ Fear of side effects<br>▪ Critical view on preventive medication<br>▪ More information needed to make a decision<br>▪ Modify one's life/changing lifestyle | Information about the lack of current availability of preventive medication for RA and potential future options | Section on *treatments one may be receive from health professionals* (including medication) |

| Higher-level themes | Codes | Information and education needs of individuals who undergo predictive testing and have a positive test result | Related section of the ENAT |
|---|---|---|---|
| **Varying reactions after receiving a positive test result** | ▪ Be shocked/be anxious<br>▪ Be surprised<br>▪ Feel vindicated<br>▪ Feel weak and powerless<br>▪ Get worried<br>▪ Stay calm<br>▪ Reconsider one's life<br>▪ Ignore the positive test result<br>▪ Uncertainty due to lack of information<br>▪ Difficulties in talking about being at risk with others, including family and friends<br>▪ Criticism on unspecific test results<br>▪ Agree on monitoring<br>▪ See monitoring critical | Knowledge about RA<br>Probability of risk to develop RA based on the test results<br>How and where to receive support to minimize psychological stress<br>Information about healthy life-styles in relation to the onset of RA<br>When to see a rheumatologist based on symptoms<br>Whom to contact when synovial joint swelling occurs<br>Monitoring on a regular basis<br>How to inform family members and significant others in easy words about being a person at risk of developing RA | Section related to *disease processes of arthritis*<br>Section related to *feelings*<br>Sections related to *treatments one may be doing for oneself, movement and managing pain*<br>Sections related to *treatments one may be receiving from health professionals and support from other people* |

**Table 4.** Additional quotes related to the four higher-level themes of the qualitative data analysis

| **Higher-level theme 1: Decision making around whether to undergo initial predictive testing** | **Corresponding codes** |
|---|---|
| *That was during a preventive health check-up and I thought, it's good to do research in this field and it's definitely something useful and then I took part.* (No. 3, female age 67, asymptomatic, Austria) | For research purposes only |
| *I thought, maybe this will help other people. Even if I am not affected, it might help somebody else.* (No.22, female, age 69, asymptomatic, Vienna) | For research purposes only<br>Assurance about causes for symptoms |
| *Yes, I have pain in the joints regularly and that's why it was interesting to me to find out the results. I think it was just confirmation that my feeling wasn't just made up of thin air.* (No. 24, female, age 47, arthralgia, Austria) | Assurance about causes for symptoms |
| *You're never happy about a disease, but I consider clarification as important. Every person thinks about it differently but I always would like to have the facts because I can then adapt myself more easily. I find it much more reassuring than the lack of knowledge.* (No. 19, female, age 49, arthralgia, Germany) | |
| **Higher-level theme 2: Willingness to consider further predictive tests** | **Corresponding codes** |
| *It's not one of my hobbies, that's not harmless, invasive and probably painful, extracting tissue is more substantial and I would only have that done if I really had problems.* (No. 25, male, age 57, asymptomatic, Austria – about synovial biopsy) | Refuse synovial biopsy |
| *I don't want that! It is going into too much detail - in my genes - I cannot imagine that I would like this at the moment.* (No. 31, female, age 52, arthralgia, Germany – about genetic testing) | Refuse genetic testing |
| **Higher-level theme 3: Willingness to consider preventive interventions, including medication** | **Corresponding codes** |
| *I would not do that, simply from my point of view. I would try other possibilities first, as I've mentioned life style. Not even a 100 percent chance of developing rheumatoid arthritis within the next 5 years, would lead me to take prophylactic medicine. Then I'd have to put preventive pills, against everything, in my cereal bowl in the morning already instead of breakfast; no, I would never agree to take preventive medication. (...) It's easy for me to say so, as I'm not in any pain. Maybe, if I will have any pain in three years, I would then think, if I only had taken preventive medication earlier! But you can't insure yourself against everything and you can't eat pills against everything!* (No. 2, female, age 66, asymptomatic, Austria) | Strictly reject preventive medication |
| *Only under the condition that a person would receive the necessary information to be able to decide whether to take a preventive medicine.* (No. 26, female, age 43, arthralgia, UK) | More information needed to make a decision |
| **Higher-level theme 4: Varying reactions after receiving a positive test result** | **Corresponding codes** |
| *It's like looking into a crystal ball [of a fortune teller] and saying to you, 'Oh, (…) you could potentially get rheumatoid arthritis.' And then, always, I have images of people in my mind who have deformities and disabilities.* (No. 26, female, age 43, arthralgia, UK) | Uncertainty due to lack of information |
| *I was quite shocked to find out that I had these cells [patient's interpretation after having been told they had a positive autoantibody test] , to tell you the truth. How am I gonna, you know, carry on with work, you know, things like that and, you know, my future.* (No. 11, male, age 50, arthralgia, UK). | Be shocked/be anxious |
| *I know that I have those positive factors. That was a coincidence but it doesn't worry me at all. I cannot change it anyway.* (No. 3, female, age 67, asymptomatic, Austria) | Stay calm |

| Higher-level theme 1: Decision making around whether to undergo initial predictive testing | Corresponding codes |
|---|---|
| *Well, changing life style means changing diet, difficult, because changing your diet, abstaining from certain food that you like to eat, means reducing your quality of life. I personally don't agree with that, I'm definitely not going on a diet because of a disease I don't have at the moment! But I certainly would if I had any symptoms*. (No. 25, male, age 57, asymptomatic, Austria) | Ignore the positive test result |

*Note. While themes two and three were strongly related to the interview questions, the first and last higher-level theme was brought up by the participants in addition to already raised topics by the researchers.*