Technical Report

Harnessing the Voice of the Patient in Rheumatoid Arthritis

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Disclosures

Suepattra May - Slater holds the position of Senior Research Anthropologist and Associate Director at Precision Health Economics, a health economics consultancy providing services to the life science industry.

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About the Innovation and Value Initiative

The Innovation and Value Initiative (IVI) is a multi-stakeholder initiative that seeks to improve the way value is measured and rewarded in the healthcare system to promote the development and use of high value interventions that advance human health. To achieve this, IVI pursues the following goals:

- Establish best practices for measuring the real-world value of healthcare technologies using both existing and innovative scientific methods;
- Provide a range of marketplace stakeholders – including patients, consumers, providers, healthcare systems, and payers – with salient, accurate, and actionable information about value in healthcare;
- Develop and test innovative approaches to link healthcare spending to value.

The IVI is hosted by Precision Health Economics, a health economics consultancy. IVI's direction and research agenda are determined in collaboration with its Strategic Advisory Panel, which includes representatives from patient advocacy organizations, pharmaceutical firms, academia, insurers, and health systems. All funding supports IVI's overall activities, with no funding or funder tied to specific activities or research projects.

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List of Abbreviations

Abbreviation	Description
AAHRPP	Association for the Accreditation of Human Research Protection Programs
ACA	Affordable Care Act
DMARD	Disease modifying anti-rheumatic drug
ICER	Institute for Clinical and Economic Review
IRB	Institutional Review Board
NSAID	Nonsteroidal anti-inflammatory drug
OHRP	Office for Human Research Protections
RA	Rheumatoid arthritis

Executive Summary

Rationale and Background

Patient-centered care has been highlighted as one of the key criteria for delivering high quality, high value treatment, and was a key provision in several initiatives included in the Affordable Care Act legislation. Many studies have shown that placing patients at the center of care results in greater participation in clinical decision-making and higher patient satisfaction. Value frameworks have been developed to guide pricing and reimbursement decisions by key stakeholders in healthcare delivery, but have been criticized for not being sufficiently patient-centered. Value frameworks typically utilize data from randomized controlled trials to assess the value of different therapies. While these clinical endpoints are important, patients themselves value other aspects of treatment that are not captured in clinical trials.

Objectives

Identify the prioritization of treatment attributes among patients with rheumatoid arthritis.

Methods

This was a double-blind qualitative study utilizing focus group methodology. Patients were included in the study if they were ages 18 years and older, had been diagnosed with moderate or severe rheumatoid arthritis, (Stage 2, 3, or 4) and had received disease-modifying anti-rheumatic drugs (DMARDs) in the past 5 years.

Key Findings

Qualitative data analysis revealed three overarching themes related to treatment decision-making:

1) RA patients face significant challenges associated with assessing treatment effectiveness and disease progression. Specifically, many patients expressed frustration around how best to assess whether or not a treatment was still effective or if their disease was progressing;
2) RA patients value care that addresses their functional status and maintains their daily quality of life. Specifically, RA patients valued treatment that helped to continue to work, engage in activities, and retain independence;
3) RA patients avoid treatment if they find it too cumbersome or costly. For example, the mechanisms or frequency by which treatment was administered, or the out of pocket and ancillary costs associated with treatment impacted subsequent adherence to therapy.

These key findings, on what is most meaningful to patients at an individual level, is not well reflected in value frameworks that largely consider the societal or population perspective.

Conclusions

This study suggests that, aside from the clinical efficacy endpoints, many of the inputs utilized in value frameworks for RA treatments run counter to the circumstances and contextual considerations that are most meaningful to patients. While many frameworks are increasingly acknowledging the value of incorporating patient preferences, a continued focus on clinical endpoints alone is insufficient for the framework to be considered patient centered.

Introduction

1.1. Background

The Institute of Medicine defines patient-centered care as care that is respectful of patients' values and preferences.[1] Patient-centered care has been highlighted as one of the key criteria for delivering high quality, high value treatment, and was a key provision in several initiatives included in the Affordable Care Act legislation.[1, 2] Many studies have shown that placing patients at the center of care results in greater participation in clinical decision making and higher patient satisfaction.

Value frameworks have been developed to guide pricing and reimbursement decisions by key stakeholders in healthcare delivery (e.g. payers, policymakers, and providers), and to date, have been criticized for not being fully patient centric. Value frameworks typically utilize data from randomized controlled trials to assess the value of different therapies and to measure the health benefits and costs of treatment. While these clinical endpoints are important, patients themselves may value other aspects of treatment.[3, 4] One major gap is limited use of concepts that capture the patient's perspective of what should be valued and value frameworks have acknowledged the challenges and limitations in effectively incorporating patient values into their assessments.[5, 6] As an example of growing interest in the patient perspective, the Institute for Clinical and Economic Review (ICER), in its most recent update, acknowledged that patient preferences are often not captured in clinical trial data. In response, they have proposed strategies to include metrics in future assessments that are actually meaningful to patients.[6, 7]

These considerations are particularly salient for RA patients who can choose from many different types of treatment regimens. Further, patients with RA often respond very differently to the same treatment, also known as heterogeneity of treatment effect. In addition, patients bring their own values and preferences to medical decision-making. These three factors can have great impact on an RA patient's day-to-day life. Valuing and selecting therapy based only on clinical endpoints such as response to treatment may mischaracterize the benefits to patients and result in suboptimal valuation of treatments. How RA patients prioritize and assign value to different aspects of their treatment has broad implications for the meaningful incorporation of the patient perspective into evaluation of therapies.

To evaluate the elements of treatment found to be most meaningful to RA patients, we conducted focus groups with RA patients. The goal of the focus groups was to investigate how patients valued and prioritized various attributes associated with RA therapy across the treatment journey, including side effects, affordability, and cost, in their treatment decisions. Patient insights contributed to a list of treatment attributes found to be most salient and meaningful to patients and that can be used to inform future research studies and initiatives.

1.2. Objectives

Identify the prioritization of treatment attributes among patients with rheumatoid arthritis.

2. Methods

2.1. Methodology and Approach

Using qualitative data collection methods, we conducted focus groups among patients with RA. We sought input from patients diagnosed with RA in the form of interview questions and reports of and opinions about the patients' deliberations around treatment decisions and experience of clinical care for RA. Qualitative research methods are particularly appropriate for investigating subjective impressions and is also well-suited to the exploration of topics or issues that stimulate a variety of opinions based on personal experiences.[8, 9] The goal of the qualitative approach was to collect and aggregate data on a diverse set of patients' experiences with and opinions about what factors of treatment are most important in their treatment for RA. Focus groups enable the elicitation of individual opinions, such that the focus group facilitator can explore what is meaningful to patients about their RA treatment and care experiences.

2.2. Study Population

Patients 18 years or older with a self-reported diagnosis of moderate or severe rheumatoid arthritis (Stage 2, 3, or 4) were eligible to participate in the study. Participants were also required to speak, read, and write English fluently and to have received disease modifying anti-rheumatic drugs (DMARDs) or biologics within the past 5 years. We excluded patients from participation if they had been diagnosed with Stage 1 rheumatoid arthritis, had never received DMARDs or biologics, or it had been greater than five years since last received. Specific inclusion and exclusion criteria are as follows:

2.2.1. Inclusion Criteria

- Has been told by a doctor that they have moderate or severe rheumatoid arthritis (Stage 2, 3, or 4)
- English language proficient
- Age 18 years and older
- Has received disease-modifying anti-rheumatic drugs (DMARDs) or biologics within the last five years
- Completes informed consent

2.2.2. Exclusion Criteria

- Has been told by a doctor that they have Stage 1 rheumatoid arthritis
- Has NOT received disease-modifying anti-rheumatic drugs (DMARDs) or biologics at all or it has been greater than five years since last received
- Under the age of 18
- Does not complete informed consent

2.2.3. Sample Size

The study aimed to recruit up to 16 patients diagnosed with severe to moderate rheumatoid arthritis. Based on the research design and study objectives, we expected the sample size to be sufficient to provide the necessary diversity of opinion and experiences, as well as the ability to confirm and validate shared views in accordance with established qualitative research guidelines for sampling. [8, 10]

2.3. Discussion Guide Development

A semi-structured focus group discussion guide was developed. We designed the discussion guides to investigate patients' treatment decisions from the emergence of initial symptoms and the diagnostic experience through disease maintenance and monitoring. For the purposes of this study, we define RA treatment decision-making as a process that includes immediate decisions about medical, psychological, and alternative treatments to manage RA disease and its symptoms, as well as ongoing decisions and lifestyle choices to enhance physical and mental health and well-being. Table 1 provides an overview of the type of questions included in focus group discussion guide. The discussion guide is included as Appendix A.

Table 1. Sample Interview Guide Questions

Domain	Objective	Question
Diagnosis	Understand diagnosis experience	When you were first given the diagnosis, how well did you understand what was being said to you? Did you run into any challenges during the diagnosis process? Please explain
Initial Treatment Decision Making	Understand how treatment options were presented and prioritized	I want to ask you a bit about your initial treatment decision(s) focusing on medications that help to ease symptoms or stop the progression of disease. By these, I mean anti-inflammatories (NSAIDs), corticosteroids, disease-modifying therapies (DMARDS), and biologics. How soon after diagnosis did you speak with your care team about these therapies? How much did you think about the potential side effects of treatment?
Subsequent Treatment Decision Making	Explore how patients' treatment decisions changed over time	Can you briefly walk me through the different types of care/treatments you have been prescribed and what you were told about how successful your treatment(s) might be? When, if ever, have you switched treatments because your doctor thought something different would work better for you?
Care Team Collaboration	Explore patients' relationship with care team	How would you describe your involvement in treatment decisions? What are the most important things that doctors and patients should discuss about RA treatment?

Domain	Objective	Question
Values and Preferences	Understand what matters to patients	What would you say matters most to you, at this stage, about the care that you receive for your RA treatment?
Online Tool for Treatment Decision Making	Understand what elements of a tool would be important for patients	Imagine that there was an online tool; a website that you could visit and answer questions and that would show you the different options for treatment, and that could help you to make decisions about what treatment would be best for you. What types of information should be included in the tool that would be most helpful for you in making decisions about treatment?

2.4. Participant Recruitment

2.4.1. Institutional Review Board Approval

Chesapeake Institutional Review Board (IRB) reviewed the study protocol, informed consent documents, and discussion guide. Chesapeake IRB is an independent organization accredited by the Office for Human Research Protections (OHRP) and the Association for the Accreditation of Human Research Protection Programs (AAHRPP). The Chesapeake IRB determined that the study met the requirements for exemption from IRB oversight and granted a waiver of review.

2.4.2. Participant Identification and Approach

The study team collaborated with Schlesinger Associates to identify and recruit study participants. Schlesinger Associates identified potential participants in their existing study database who met basic eligibility criteria and conducted direct recruitment with these potential participants. Potential participants received a study recruitment email. Due to the double-blind nature of the study, announcements did not identify the Innovation and Value Initiative as the sponsor of the study but did specify that researchers from PHE were conducting a study with RA patients. Potential participants were also referred to the study for eligibility screening from participant referrals through snowball sampling.

Schlesinger Associates also worked with trusted clinical partners (hospitals, clinics, and provider groups) to identify potential participants who may not have already been on their panels and utilized additional recruitment methods for these potential participants. This included approaching healthcare providers directly for participation as well as having healthcare providers talk with their own patients about the study and provide a flyer with Schlesinger Associates contact information. Healthcare providers were not told if any of their patients had contacted Schlesinger Associates about participation, and patients were assured their participation in the study was confidential and would not affect the care they were receiving from their provider.

For direct invitations to existing panel members, Schlesinger Associates minimized selection bias by utilizing probability sampling to select potential participants to receive a study invitation. For

the other types of recruitment through clinical partners, they used non-probability sampling techniques but attempted to minimize bias by establishing quotas by geographic region/zip code and participant demographic characteristics to ensure that potential participants in catchment areas had an equal chance of receiving an invitation to participate in the study. Interested participants contacted the Schlesinger Associates study coordinator to complete eligibility screening by telephone. Participants deemed eligible based upon the inclusion and exclusion criteria specified were scheduled for one of two focus groups.

2.5. Data Collection

2.5.1. Structure and Format

Eligible participants were invited to join one of two 90-minute focus groups at a specified time and date. Focus groups were double blind: neither the focus group participant nor the study sponsor were identified in this process. Schlesinger instructed participants to arrive 15-30 minutes prior to the start of the scheduled group to review enrollment paperwork and to ensure that the group started on time. Upon arrival at the focus group facility, a facility coordinator greeted participants and escorted them to a holding area for the focus group participants.

To protect anonymity, participants did not sign a consent form. Rather, participants were provided a copy of the Information Statement (included as Appendix B) to review. The Information Statement outlined the purpose of the study and the participant's obligations and protections. Participants received a copy of the Information Statement for their records. After any questions had been answered, the participants were invited into the focus group room for the group discussion. Participants provided consent by verbally agreeing to be audio recorded and participate in the focus group at the time of data collection.

The focus groups were held in a focus group facility in Atlanta, GA and moderated by Alisha Carti, a Senior Moderator and experienced focus group facilitator with Thinkpiece research. The moderator introduced participants to the 90-minute focus group format, which included time for introductions and topic discussions. Prior to the start of the discussion, the facilitator instructed the participants that the audio recording would begin, and then proceeded with the focus group discussion. At the end of the focus group discussion, participants received $150 in remuneration for their participation.

2.6. Data Analysis

The focus group audio recordings were transcribed verbatim into word documents ready for export to a qualitative data management software program. We applied a standardized layout to all content generated from the focus groups to facilitate the comparison of data at the analysis stage. [11] The transcription method reflected the interpretative approach utilized in qualitative research, which strives to convey as fully as possible the experiences of the participants. [12] This includes word-for-word transcription, including utterances and incomplete sentences [11] All transcribed text, handwritten notes, and observational field notes were then imported into a qualitative data software package (MAXQDA12; VERBI, GmbH). Qualitative data analysis software enables the manipulation, searching and retrieval of coded text data to facilitate analysis.

We analyzed the qualitative data in multiple stages using the constant comparative method. [13] First, the study team independently reviewed the transcripts to identify emergent themes. This review, along with topic areas and questions from the discussion guide, identified category labels representing the domains of interest and detailed in a coding dictionary. We then applied a final

confirmed coding structure to the focus group transcripts, enabling the identification of salient relationships within and among categories across both focus groups. The coders met to discuss themes identified in the data as well as any patterns in the data which emerged as a result of consensus or controversy among the participants or by the intensity with which a topic or issue is expressed. Through these steps, we identified central themes and attributes of interest.

3. Results

3.1. Study Sample

Fifteen participants attended the focus groups (Table 2). Nearly two-thirds of the sample were female and ages ranged from 44 years to 73 years. Most were employed either full time or retired. Most participants were White with a college education or technical/trade background and a high average annual household income. With respect to history of RA treatment, two thirds had received physical/occupational therapy, taken NSAIDs, or been prescribed Enbrel. Nearly two thirds of the sample had also received Methotrexate or Humira at some point in their treatment trajectory. Table 1 provides detail on patients demographic and treatments ever received.

Table 2. Socio-demographic Characteristics

Characteristics	N=15	%
Age (Mean 55.7, Range 44-73)		
Years since diagnosis (Mean 9.9, Range 2-30)		
Gender		
Male	6	40.0%
Female	9	60.0%
Race/Ethnicity		
Asian	1	6.7%
African American/Black	3	20.0%
White/Caucasian	11	73.3%
Employment		
Employed Full Time	6	40.0%
Employed Part Time	2	13.3%
Retired	6	40.0%
Full time homemaker	1	6.7%
Education		
College graduate	5	33.3%
Graduate Degree	3	20.0%
High school graduate/GED	3	20.0%
Some college or technical or vocational school	3	20.0%
Technical/Trade	8	53.3%
Income		
$10,000 - $19,999	1	6.7%
$20,000 - $39,999	1	6.7%
$40,000 - $59,999	2	13.3%
$60,000 - $74,999	5	33.3%

Characteristics	N=15	%
$75,000 - $99,999	2	13.3%
$100,000 - $119,999	1	6.7%
$120,000 or more	3	20.0%
Insurance		
Medicare/Medicaid	3	20.0%
Private Health Plan + Medicare	3	20.0%
Private Health Plan	7	46.7%
None	1	6.7%
Other	1	6.7%
Treatments Ever Received		
Surgery	2	13.3%
Physical/Occupational Therapy	10	66.7%
NSAIDS	10	66.7%
Methotrexate	9	60.0%
Hydroxychloriquine (Plaquenil)	5	33.3%
Leflunomide (Arava)	2	13.3%
Sulfasalazine (Azulfidine)	2	13.3%
Tofacitinib (Xeljanz)	2	13.3%
Abatacept (Orencia)	1	6.7%
Adalimumab (Humira)	8	53.3%
Adalimumab-atto (Amjevita), a biosimilar to Humira	0	0.0%
Anakinra (Kineret)	0	0.0%
Certolizumab (Cimzia)	0	0.0%
Etanercept (Enbrel)	10	66.7%
Etanercept-szzs (Ereizi), a biosimilar to Enbrel	0	0.0%
Golimumab (Simponi, Simponi Aria)	1	6.7%
Infliximab (Remicade)	1	6.7%
Infliximab-dyyb (Inflectra), a biosimilar to Remicade	2	13.3%
Rituximab (Rituxan)	0	0.0%
Tocilizumab (Actemra)	1	6.7%

3.2. Overarching Themes and Key Findings

Thematic analysis revealed three overarching themes: (1) RA patients face significant challenges associated with assessing treatment effectiveness throughout the course of disease (2) RA patients value treatment and care that addresses their functional status and daily quality of life, and (3) patients avoid treatment if they find it to be too cumbersome or costly.

3.2.1. Assessing Disease Progression and Treatment Effectiveness

In both focus groups, the moderator asked participants to describe the circumstances that led to their diagnosis and the factors they considered in their treatment decision-making. In providing the context and background of their diagnostic experience, participants repeatedly described the difficulties they encountered during their diagnostic workup. For many, the initial workup is a

period where patients engage repeatedly with the healthcare system, seeing different primary care physicians and specialists, misdiagnosis and/or undergoing multiple procedures and tests before finally being diagnosed with RA and coming to terms with the diagnosis and its implications. One patient describes her experience as follows:

> *"My doctor called me to tell me the results of the bloodwork and he said I had a significant [number]…I was off the charts. I was like, how could that be possible?...at first I was in shock…I was in denial because I was thinking, you know, it's hereditary. No one in my family…t's almost like I had to convince my family I did have it…it started with the hands…and I thought it was carpal tunnel. And that's where the flare-ups started. I thought, well, I'm overusing it with teaching. And so I went on that for a while…then I came in and he [the doctor] set me up with methotrexate…"*

After the initial diagnosis experience, patients moved into a stage that required continual and constant monitoring to determine disease progression and treatment effectiveness. Participants were well aware that RA progression manifests differently in patients, at different rates and with varying symptoms and impacts as the disease progresses or treatment becomes less effective. While patient experiences and situations varied, the experience of having to frequently assess and re-calibrate a treatment regimen resonated with all participants. In discussing treatment effectiveness, participants emphasized the critical need to calibrate treatment to what would work for the patient at any given time in the disease course, and depending upon the individual patient's circumstances and health, treatment effectiveness eventually waned. In the following excerpt, one patient describes her experience:

> *"The recommendation was methotrexate. I started with five tablets. And then they recommended Humira injections…and had a Humira nurse come out to the house and teach me how to do the injections. And I gave them to myself every two weeks. After six months…the Humira stopped working…and then I went on Actemra as an infusion…and in October of 2016, same kind of thing…the medicine wasn't working, so they bumped me to a full dose. So I've had three doses of a full dose of Actemra as an infusion. And I'm up to eight methotrexate once a week; eight tablets. I have taken prednisone at various times throughout the process as needed. And when I was at the doctor last…she did prescribe diclofenac just for pain as needed kind of thing."*

More generally, "switching" treatments was extremely common among the focus group participants. In the following excerpt, another patient describes his experience with switching and the subsequent administrative hurdles and other medications he was instructed to go through before obtaining a new, potentially more effective medication advised by his doctor:

> *"I know for me when medication wasn't working the way that they wanted it to. They would have a variety of medications that we could try next and it would depend on the insurance and what my insurance would approve. My insurance made me go through specific biologics before [certain drugs], so I couldn't even though they would work… I had to kind of go with others…"*

3.2.2. Living with RA

RA greatly impacted participants' independence and activities and participants characterized living with RA as trying to find a "new normal" while also navigating potential disease progression, treatment, and side effects. In the following excerpt, one patient describes how having RA has changed his life and his outlook and valuing of quality over quantity of life:

"Quality of life, for me, it becomes everything. Philosophically speaking, I know exactly where I'm going after this life is over, so I get to live with no fear. Once you can operate from that position, you really can have a little victory in your life to where it's like whatever happens is going to happen, I'm still going to be okay. As long as I can move, I'm good and then if I don't make it through this life, I know where I'm going in the next one. I just do what I do and risk, reward, toleration of the medications. I'd rather have two good years than ten bad ones."

In addition to quality of life, participants cited navigating the specialty care system, insurance approvals, and out-of-pocket costs as significant barriers to living with RA. The weight of navigating coverage and out-of-pocket cost greatly affected participants. In the following excerpt, an insured participant describes the importance of affordable medication even if it meant having to navigate a confusing and complex insurance approval process to obtain an affordable and effective treatment:

"And that the medicine is affordable because like methotrexate is more expensive than the Enbrel. And having to pay $50…I think there's so much [variation], with everybody's different insurance plans. So, too, the affordability of the medicine is important to me, too."

In the next excerpt, another participant described the significant financial impact moving from private insurance to Medicare had on his out of pocket costs to treat his RA:

"My corporate insurance covered it. No problem. Just like any other drug, they paid just about all of it and I didn't know how good I had it till I turned 65 and went on Medicare. I went on Medicare supplement and you know then my bills went up $50-60,000".

Although these passages illustrate the experiences of patients with health insurance, most participants at one point or another in their RA treatment journey reported avoiding care and treatment if they found the process to be too cumbersome or costly.

While being productive (through employment or socially), access to care, and maintaining independence free of pain and treatment side effects were all considered critical factors for maintaining as normal of a life as possible, participants also highly valued and desired good interpersonal communication with their healthcare providers. In particular, they valued positive interactions with providers who made themselves available to patients: be that primary care doctors, specialists, and support staff – and perceived such experiences as ensuring the best care possible for RA treatment, as exemplified in the following excerpt:

"I'm very fortunate that I can get online and email my physician every day as I need to and they will respond. Either the PA [physician assistant] or the nurse or sometimes even the doctor will respond and/or call me to talk me. But I've been very good about, you know, when the pain starts and the medicine is not working I will immediately say, okay, I'm having some problems. This is what I'm feeling. And they needed me to come off the Humira for about four to six weeks so they could gauge where I was pain-wise, and then determine what the next step was; what to put me on."

Participants also valued providers who were attuned to their specific needs, i.e., knowing when to offer new suggestions or connect the patient to a social worker, a counselor, or financial or support resources. In the following excerpt a participant describes how his relationship with his doctor is very positive, such that he was receptive to a suggestion to exercise regularly, which he has deemed to be very beneficial:

"Now, I'm so comfortable with them. I'll just send out emails saying, "Hey, I'm having

this problem" and they'll respond back and say, "Hey, why don't you do this? Why don't you do that?" And, one good advice they gave me is start to exercise. Let me tell you I love it. I feel so much better. I have more energy in me. Before I was like very fatigued. I was always tired."

3.2.3. Additional Factors in Treatment Decision Making

Participants described the many factors they took into consideration as they deliberated treatment options. In addition to cost considerations, patients weighed the anticipated side effects or perceived toxicity of treatment against anticipated benefits and impact on their lives. In the following excerpts, participants described their deliberations and experiences:

"What are the side effects? Steroids, if anybody has taken those, they can turn you into the meanest person in the valley and do I really want to live with that. Who wants to live with me while I'm being the meanest person in the valley?"

"I will tolerate the pain, not the side effects, but the pain versus the side effects, because I've learned like I said I had some major side effects from medications. I thought about and I said, "Okay, the benefits outweigh you know…"

"I got lucky. I was on the methotrexate and I had taken a long time before. Side effects and started getting like a sinus infection and then I couldn't breathe. I couldn't walk. I was short of breath. Then I went to the hospital. Both of my kidneys were shutting down. I mean I had gotten there early enough that it didn't get that bad. I was to the point where it could have gotten a lot worse."

Another important consideration in treatment deliberations was around the mode and frequency of treatment administration. In the following excerpt, one patient describes his how he deliberated the frequency and mode of administration of the suggested drug:

"I kind of went through that and it was one of the common things to take at that time and then I went to a biologic and I really wanted to study it just to make sure. I'm also diabetic. I'm a human pincushion, so I'm injecting myself all the time. I talked with him and he's like "if you take this, you have to take it once a week. If you take this, it's 26 times a year and if you take this, it's 12 times a year." I'm like "let's go with the 12 times a year. I kind of like that."

Finally, the presence of co-morbidities was a very important consideration in treatment decision-making. While some participants felt that their providers were attentive to the existence of co-morbidities, others reported having to bear the burden of responsibility of knowing how treatment and side effects may impact their other conditions as described by the following participants:

"*Number one first and for most is quality of life, but a sub-factor of that is I mentioned I got multiple issues – things going on – and I worry that one of the doctors is treating one of those things may not take into consideration that I got another problem and give me a medicine that's going to cause me other issues. I take that on myself to be sure that…"*

I talked to a doctor about going with biologicals and I of course got several doctors. I talked with primary care that I'd been with a long time. He knows how scary the side effects are just from the television. He said, "Don't go on it until you want to. When you're ready, we'll put you on it." But, I also had severe psoriasis and I have sporadic arthritis as well rheumatoid. I have more to gain when my risk level is a little greater. I eventually made the decision.

3.2.4. Utility of a web based decision tool

In addition to questions on care and treatment experiences for RA, we also queried participants about the utility of a tool to help with decision making about treatment. Participants identified three key considerations in the utility of such a tool for them. Firstly, who is recommending the treatment and why that matters, that is, what makes this tool credible? Participants also felt that the evidence base for the recommendation mattered as well as an ability to determine how a drug will benefit or harm the patient:

> *"I would probably want evidence-based…I've seen so many new drugs that have been miracle drugs that have been two-ten years later they figured out no that's actually killing you. Also in my mind, it takes so much to get through FDA and all that so really it shouldn't be a new trendy thing. There should be some evidential basis to it".*

> *"What would drive the tool is credible sourcing…with institutions like Cleveland or Mayo putting their stamp of approval on there…I'm going to read it"*

Second, patients valued easy to understand information about study results (i.e. clinical trial data) and what real world data/use shows about a particular treatment. Participants suggested that such a tool take into consideration where the patient is currently at (age, stage/severity of disease, existing co-morbidities, previous treatment) and couch that in terms of not only anticipated benefits and side effects but why the patient should consider a particular treatment relative to other options, i.e. what does this treatment provide that others do not:

> *"I think it should show what is different or why they made a new drug. It either has a less side effect or it doesn't have this side effect. They should show some kind of difference in what we already have and what they're creating."*

Finally, a tool that helps to provide data on cost was considered most useful. Specifically, how expensive the treatment was relative to perceived benefits, information on the existence of assistance programs or support cards to help with costs, what the patient will have to pay out of pocket and how frequently, and the extent to which insurance will cover a treatment and for how long.

> *"…an even better idea is to have it all calculated honestly and then be able to put it through another algorithm to see how your insurance fits. Then you know it's not being recommended strictly because that's all your crappy insurance will cover."*

4. Conclusions

The focus groups identified multiple factors as both facilitators of and barriers to value in RA treatment. Cost and insurance coverage were critically important for participants. However, when making decisions about care and treatment, our findings revealed that improvements in RA diagnosis as well as accurate methods to assess and respond to disease progression were considered critical components of quality care. Further, a good relationship with the physician, as well as a care team attentive to quality of life issues were considered very important to patients. These elements are needed to enhance and improve the RA patient experience while also helping patients achieve and maintain an independent, reasonable quality of life.

4.1.1. Strengths and Limitations

A primary strength of this study is that it sought to elicit input from patients about different aspects of RA therapy in general and to begin to identify and document attributes of care most salient to RA patients, including the factors that patients consider as they deliberate treatment options and what is most meaningful to them about treatment. Further, by using a focus group methodology, this approach was able to solicit more detailed and nuanced information regarding why patients preferred specific treatment attributes.

There are limitations related to sampling to consider before interpreting the study and its implications. The study included a convenience sample of individuals who may be more vocal than other RA patients. Similarly, as the sample was self-selected, patients in this study may not be representative of the broader RA patient population, limiting the generalizability of the results. RA patients are diverse and these results may not extrapolate to all patients diagnosed with RA. However, this study provides preliminary data on attributes of treatment that could be tested with a larger, more diverse cohort of patients with respect to socioeconomics, race/ethnicity, and geography.

While this study cannot reasonably obtain population-representative views from a sample of this size, the purpose of the focus groups was to obtain insights from patients about their RA treatment decision making and care experiences, and to better understand how these insights can help to identify salient attributes most meaningful to patients.

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Appendix A Focus Group Discussion Guide

Introduction

Thank you for meeting with us today. We very much appreciate your time and insights. My name is [name] and I will be moderating the focus group today. We are joined by [names] from the study team. They will be here to observe our discussion.

Before diving into the session, I would like to go around the room and introduce ourselves to one another.

- Your name
- Is this your first time in a focus group?
- Diagnosis history
- Ice breaker – If you could go away to anywhere, where would you go?

Background

Overview of study

We have invited you here today to speak with us about your rheumatoid arthritis diagnosis, your treatment decisions, and your treatment experiences. We are developing a survey for patients diagnosed with rheumatoid arthritis (RA). The purpose of the survey is to ask patients about their treatment decisions, their treatment experiences, and their satisfaction with their rheumatoid arthritis treatment. Speaking to you today will help us to better understand the range of experiences patients with rheumatoid arthritis have, what they look for in treatment and those elements of care that they find valuable.

Purpose

The primary purpose of today's meeting is to gather information that will help us design a patient survey that will capture rheumatoid arthritis patients' experiences with treatment. This includes, but is not limited to the various elements, attributes, and experiences around treatment that you find valuable or meaningful. We are interested in learning about your own experiences and how best to ask these questions of others. The results of both this group and the survey will be used to understand what patients with RA value most when deciding between treatment options.

Ground Rules

Confidentiality

Before we begin, we want to emphasize that whatever is talked about here today is confidential and should not be shared with anyone outside of this setting.

It is important that we respect one another's privacy so I ask you to not reveal the identities of those who are present, or disclose what was discussed during our session to others outside of this group. If you inadvertently refer to anyone by their name, please be assured that any such identifying information will be removed once today's audio recording is transcribed.

Discussion

So that we may be fully engaged with one another during the discussion, we would like to ask that you please turn off your phones or place them on silent.

Before we start with the questions, I want to emphasize that while we recognize that there may be some commonalities between your rheumatoid arthritis journeys, we also recognize that everyone's rheumatoid arthritis journey is unique, as is every patient living with rheumatoid arthritis.

As we ask questions, please share your perspective based on your personal experiences

Please also let us know if you think the questions or discussion topics we bring up today are relevant or important to RA patients. These are the topic areas that we think may be important, but our goal is to find out what is most meaningful for patients when making treatment decisions.

Lastly, we are not looking for consensus and we don't expect you to always agree with each other. We want to hear about a range of thoughts and experiences. If you tend to be more openly communicative, I hope you won't mind if I moderate so that we can hear from everyone. If you are shy, I hope you'll try stepping out of your comfort zone to participate in the discussion.

Discussion Questions

Diagnosis

Objective: Understand patient diagnosis experience

- During our discussion today, I would like to focus on your personal experience living with rheumatoid arthritis, knowing that each of your experiences are likely to differ.
- To start, I'd like you to think back to when you were first diagnosed.
- Tell me a little about what was happening at that time and what led you to seek out a doctor (PROBE for symptoms, family history, etc.)?
    - How long ago was this?
    - IF EXPERIENCED SYMPTOMS: For how long had you been experiencing symptoms before seeking medical attention?
- When you were first given the diagnosis, how well did you understand what was being said to you?
    - AS NEEDED, PROBE ON: What type of information did you wish you had been given about the diagnosis?
- What, if any, questions did you have for your care team? Do you think that you got the answers you needed?
    - AS NEEDED, PROBE ON: What type of information did you look for?

      Where, if anywhere else, did you go for information? How helpful was it?

- Did you run into any challenges during the diagnosis process? Please explain.
    - What do you wish would have gone differently? Why?
- What were your expectations for treatment?
- Looking back, what would you have liked to have known about your diagnosis and treatment that you did not know then?

    Probe: What questions would you have liked to ask at the time, but didn't?

    Probe: What questions would you ask now?

Treatment Decision-Making at Diagnosis

Objective: Understand how treatment options were initially presented and prioritized

- I want to ask you a bit about your initial treatment decision(s) focusing on medications that help to ease symptoms or stop the progression of disease. By these I mean anti-inflammatories (NSAIDs), corticosteroids, disease modifying therapies (DMARDS) and biologics. These are treatments that are taken as a pill, injected, or infused into your body. We can leave any decisions or discussion about surgery or other therapies out of the conversation.
- How soon after diagnosis did you speak with your care team about these therapies? PROBE to understand if same visit or if patient came back later.
- I would like to understand the things you thought about (or felt you needed to know) in order to make your initial treatment decision. Before we discuss this as a group, I want you to jot down on the paper in front of you, as best as you can remember, the first three questions or things that came to your mind when your care team mentioned needing to go medication for your RA
- Now, let's go around the room and I would like each of you to read off your list. I will capture them on this flip chart.

Moderator: Write down questions/topics patients mention on easel pad/flip chart, noting where there is overlap (if any)

What other questions or factors did you think about that we have not captured on this list? Feel free to call them out and I will continue to build on our list.

- LISTEN FOR AND PROMPT AS NEEDED FOR:

  - Significant others/caregiver burden
  - Impact on relationships
  - Impact on everyday life
  - Co-morbid conditions
  - Doctors/nurses/caregiver opinions
  - Finances/insurance coverage
  - Relief from pain and fatigue
  - Treatment regimen (dosing, schedule, mode or route of administration, frequency, switching)
  - Chance of side effects/adverse reactions to treatment
  - QOL/Impact on ADLs
  - Chance of benefit/stemming progression
  - Strength of evidence/effectiveness
  - Experience of other patients
  - Out of pocket costs
  - Doctor recommendation
- Besides your care team, did you talk to anyone else about your treatment options and what to do?
  - Probe: What was their role in helping you make a decision?
- How much did you think about the potential side effects of treatment?
  - Probe: Were there any treatment side effects that you particularly want[ed] to avoid?
- Overall, what were your goals for treatment? Probes:
  - Reaching life milestones (e.g., graduation, wedding)
  - Overall quality-of-life
  - Minimal disruption to normal life
  - Maintaining emotional well-being and ADLs
  - Stemming progression of disease or secondary conditions
  - Timely and convenient care

- To what extent do you feel like your physician/care team listened to you and your needs when choosing your initial systemic treatment?
- Was the treatment decision a shared decision between you and your doctor?

Treatment Decision-Making Post Diagnosis

Objective: Explore how patients' treatment decisions changed over time

- Now let's talk about the types of treatment (again, not thinking about surgery or other therapies) you have received since that initial diagnosis. Can you briefly walk me through the different types of care/treatments you have been prescribed and what you were told about how successful your treatment(s) might be?
- How has your rheumatologist/provider assessed your response to treatment?
    - What test results, if any, does your doctor share with you?
    - How do you, personally, assess your own response to treatment?
    - PROBE for clinical endpoints, how you feel (physically), treatment milestones or other measures
- When, if ever, have you switched treatments because your doctor thought something different would work better for you?
    - IF HAS HAPPENED PROBE:
        - How many times has this happened?
        - What prompted the switch?
        - What was the most important thing for you to know about the treatment as you decided whether to switch?
        - How did switching impact your everyday life?
        - If you would have known you'd eventually have to switch treatments because the treatment you were originally prescribed wasn't working, would you have preferred a different treatment to begin with?
    - Are you currently on the RA drug that you prefer to be on?
        - Probe: If yes, why do you prefer this drug?
        - Probe: If not, why not?
    - If you aren't currently or haven't been on your preferred drug or treatment, what has prevented you from being on your preferred drug?
        - Probes: Costs, insurance restrictions, doctor/health care provider, access issues, mode of administration
    - Earlier we had talked about your initial questions/the factors that were most important to you when starting therapy. Looking back across your RA treatment journey, how have your decisions about treatment or your approach to decisions about treatment changed?
    - I would like you to take a minute and write down the top 3 factors that are most important to your treatment decisions today. [ONCE RESPONDENTS ARE FINISHED] What are they?
        - IF DIFFERENT: What, if anything, has prompted this change?
        - PROBE: Do you value certain types of treatments differently now compared to when you were first diagnosed? In what way? What do these other treatments offer/what features do you find more valuable now?
    - If a friend of yours was diagnosed with RA, and keeping in mind the experiences you have had, what would you tell him/her about what questions to ask or what factors to consider in making their treatment decision(s)?

- How, if at all, have your treatment goals changed? Explain.
- Finally, when a patient is undergoing treatment for RA, doctors develop a treatment plan by reviewing many factors that contribute to a patient's response including clinical evidence that helps support a given treatment plan. This "evidence base" can consist of drugs that have a long history of use among patients and from a lot of clinical trials. Other drugs may be newer or more novel, without as much data from clinical trials or from patient experiences. Which do you prefer and why?

Care Team Collaboration

Objective: Explore how patients interact with their physician and the relationship they have

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- Now let's talk about how involved you are in treatment decisions. How would you describe your involvement in treatment decisions?
    - How active do you tend to be?
- How much would you say you and your doctor are on the same page when it comes to your treatment goals?
    - How frequently does your doctor ask you about your goals and preferences? To what extent do you feel like you volunteer this information more than it is asked for?
    - What would you prefer?
- In an ideal world, how much involvement would you have in your treatment decisions?
    - PROBE to understand whether this would be consistent or evolve with time
- What are the most important things that doctors and patients should discuss about RA treatment?

Values and Preferences

Objective: Understand what matters to patients

- We've talked a lot today about the decision you have made and what you value when making treatment decisions. What would you say matters most to you, at this stage, about the care that you receive for your RA treatment? PROBE FOR:
    - Doctors being up-to-date about available treatment options
    - Care team experience
    - Care team openness/candor
    - Care team coordination
    - Being informed about treatment options/alternatives
    - Being involved in decisions
    - Being asked about own preferences
    - Effectiveness of treatment

- Finances/cost/insurance coverage
- Minimal impact on daily life
- Returning “back to normal”
- Other

Online Tool for Treatment Decision-Making

Objective: Understand what elements of a tool would be important to patients

- Imagine that there was an online tool, a website that you could visit and answer questions and that would show you the different options for treatment, and that could help you to make decisions about what treatment would be best for you.
- What types of information should be included in this tool that would be most helpful for you in making decisions about treatment?
- Would an online tool be helpful for you in making some of your treatment decisions?
- What type of information would you like for this online tool have? Probes:
  - Usability
  - Interface
  - Presentation of treatment choices
  - Predictions of outcomes
  - Costs
  - Insurance coverage
  - Customization

Closing

- Based on your experiences and all that you have shared, is there anything that we didn’t ask about, that you’d like to share or think is important to address about this topic?
- Thank you all for your time. We really appreciate the experiences and insights you have shared with us today.
- Ask about feedback for the session

Appendix B: Information Statement

INFORMATION STATEMENT

Study Title:	Harnessing the Voice of the Patient in Rheumatoid Arthritis Treatment Decisions
Principal Investigator Name:	**Suepattra G. May-Slater**
Research Site Address(es):	Precision Health Economics 11100 Santa Monica Blvd. Ste 500 Los Angeles, CA 90025
Daytime Telephone Number(s):	310-984-7741

SUMMARY

You are invited to participate in a study about the elements of rheumatoid arthritis (RA) treatment that patients diagnosed with moderate or severe rheumatoid arthritis find most valuable. The purpose of the study is to learn about what patients with rheumatoid arthritis find most meaningful about their treatment. You were selected as a possible participant in this study because you have been diagnosed with rheumatoid arthritis.

You are being asked to be in a research study. The purpose of this consent form is to help you decide if you want to be in the research study. Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- You are free to choose whether or not you want to take part.

PURPOSE OF THE STUDY

The purpose of this study is to assess the elements of rheumatoid arthritis treatment that patients define as most valuable.

PROCEDURES

If you decide to participate, you will be asked to take part in the following study procedures:

You will be asked to participate in a focus group and complete a brief survey. The focus group discussion will last approximately 90 minutes. Questions will be asked about your background, your experience with your RA treatment and what things you considered as you made decisions about different treatment options. You are free not to answer any questions you do not wish to answer.

RISKS AND DISCOMFORT

No physical risks are anticipated, however there is the possibility that the study procedures may introduce anxiety or other uncomfortable emotions when responding to some of the questions. However, you may skip any question at any time or stop participating in the research at any time.

BENEFITS

There will be no direct benefit to you for participating in this study. However, it is hoped that advances in our understanding of rheumatoid arthritis patients' treatment preferences will benefit future patients. Information gained from this research could lead to improved understanding about how patients decide what treatments to pursue and how their choices are related to individual preferences. It cannot be promised that you will receive any benefits from being in this study.

COSTS AND COMPENSATION

There are no costs to you for being in this study. You will receive $150 for participating in the focus group discussion.

CONFIDENTIALITY

Participation in research may involve a loss of privacy. The researchers will keep information about you as confidential as possible, but complete confidentiality cannot be guaranteed. Privacy will be protected through several procedures. The only people who will know that you are a research subject are members of the company who invited you to participate in the study, unless research records are inspected by a regulatory agency. The results of this research study may be presented at meetings or in publications. When the results of the research are published or discussed in conferences or publications, your identity will not be disclosed in those presentations.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is completely voluntary. If you decide to participate, you are free to withdraw your consent and discontinue participation at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

SOURCE OF FUNDING FOR THE STUDY

The sponsor Precision Health Economics is paying for this research study.

QUESTIONS

Contact the study lead, Dr. Suepattra May-Slater at 310.984.7741 for any of the following reasons:

- if you have any questions about your participation in this study,
- if you have questions, concerns or complaints about the research

CONTACT INFORMATION

If you have any questions regarding the group or this study in general, please contact the study principal investigator Suepattra May-Slater at 310-984-7741 or via email at suepattra.mayslater@precisionhealtheconomics.com. You should contact the study principal investigator first if you have questions, complaints or concerns about the study.