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ORIGINAL RESEARCH ARTICLE

Perspectives of Pediatric Rheumatologists on Initiating and Tapering Biologics in Patients with Juvenile Idiopathic Arthritis: A Formative Qualitative Study

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Abstract

Background Few studies have examined pediatric rheumatologists' approaches to treatment decision making for biologic therapy for patients with juvenile idiopathic arthritis (JIA). This study presents the qualitative research undertaken to support the development of a Best–Worst Scaling (BWS) survey for tapering in JIA. The study objectives were to (1) describe the treatment decision-making process of pediatric rheumatologists to initiate and taper biologics; and (2) select attributes for a BWS survey.

Methods Pediatric rheumatologists across Canada were recruited to participate in interviews using purposeful sampling. Interviews were conducted until saturation was achieved. Interview recordings were transcribed verbatim and transcripts were analyzed using deductive thematic analysis. Initial codes were organized into themes and subthemes using an iterative process. Attributes for the BWS survey were developed from these themes and a literature review was conducted in parallel to inform survey development. Further refinement of the attributes was done through consultation with the research team.

Results Five pediatric rheumatologists participated in the interviews. Shared decision making was part of the approach to initiating and tapering biologics in their practice. Tapering approaches differed; some pediatric rheumatologists preferred to stop biologics immediately, while others tapered by reducing dose and/or increasing the dose interval over time. A total of 14 attributes were developed for the BWS. Thirteen attributes were selected from the themes that emerged from the qualitative interviews and one attribute was included after review with the research team. Attributes related to patient characteristics included JIA subtype, time in remission, history or presence of joint damage or erosive disease, how challenging it was to achieve remission, and history of flares. Contextual attributes included accessibility of biologics and willingness to taper biologics.

Conclusion This study contributes to the limited literature on pediatric rheumatologists' approaches to treatment decision making for biologics in JIA and identifies attributes that affect the decision to both initiate and taper. Further research is planned to implement the BWS survey to understand the importance of the attributes identified. Additional investigation is required to determine if these characteristics align with patient and parent preferences.

1 Background

Juvenile idiopathic arthritis (JIA) is a chronic disease that starts before the age of 16 years and imposes a significant social and economic burden on patients and their caregivers [1]. The treatment and management of JIA has dramatically changed with the introduction of biologics and a paradigm shift towards early and aggressive treatment with treat-to-target strategies [2, 3]. Disease remission or low levels of disease activity are now attainable for children with JIA while limiting long-term structural damages, comorbid conditions, and optimizing quality of life [3]. Biologics have improved the lives of children with JIA but there are concerns about short-term risks, such as infections, and long-term safety and use. [4–6] In addition, these medications are extremely expensive [4–7]. The safe tapering or discontinuation of biologics in children who have achieved clinically inactive disease could potentially mitigate these risks and

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Key Points for Decision Makers

There is limited clinical guidance for how to taper biologics in children with juvenile idiopathic arthritis.

This study identified patient-specific and contextual factors that affect pediatric rheumatologists' decision to taper biologics.

The findings informed the development of attributes for a Best–Worst Scaling survey to examine the importance of factors in the decision to taper biologics.

reduce costs [8]. The American College of Rheumatology (ACR) has published guidelines to treat JIA but there is currently no consensus on when and how tapering could be safely performed [3].

In the absence of clear clinical guidance for tapering, studies have found variability in how pediatric rheumatologists make treatment decisions in JIA [9, 10].

The treatment decision-making process in JIA, from the perspective of patients, families and pediatric rheumatology clinicians, has been explored in prior qualitative research [11–15]. For patients and families, the decision-making process is iterative and changes over the disease course [13, 15]. In regard to clinician decision making in JIA, the literature is sparse. A study examining pediatric rheumatologist perspectives revealed a clinician-centered process [11]. Clinicians were more inclined to incorporate families' contributions in the decision to taper or stop treatment compared with the decision to initiate treatment. In the decision to initiate treatment, clinicians would typically present options to patients based on their assessment of the clinical situation, and their preferences [11]. However, where there is clinical equipoise, such as with tapering, clinicians described a more active role for patients and families. Clinical attributes in the course of JIA, such as medication adverse effects, pain and quality of life, were considered high priority by patients, families and pediatric rheumatologists [12].

Research to elicit clinician preferences in treatment decisions has been done in JIA and rheumatoid arthritis [16, 17]. These preference elicitation methods can include discrete choice experiments (DCEs) and Best–Worst Scaling (BWS) surveys [18–20]. Both methods involve the development of attributes or characteristics that influence a decision of interest which are used to develop a set of choice scenarios that participants respond to. Good research practice guidelines have been published to guide and standardize health preferences research, and involve a qualitative component to develop study attributes [21]. Further guidelines have been introduced for the reporting of formative qualitative research in preferences research [22]. Although fundamental to the attributes development process, qualitative research is underreported in the literature and the quality of reporting is inadequate [22].

The purpose of this study was to report on the treatment decision process of pediatric rheumatologists, using qualitative interviews, and to use these results to inform the development of a BWS (type 1) survey to understand what attributes are important in the decision to taper biologics. The study objectives were to (1) describe pediatric rheumatologist approaches to treatment decision making for initiating and tapering biologics; and (2) use the qualitative results to select attributes for a BWS survey.

2 Methods

Individual interviews were conducted with Canadian pediatric rheumatologists who were identified as part of the Understanding Childhood Arthritis Network (UCAN), and who were invited by email to participate. We identified participants with some diversity in terms of province, sex and experience, and participants were consecutively recruited until saturation was reached, as assessed by whether new data were being generated in interviews. Participants did not receive any reimbursement for their time participating in the study. The interviews were completed by two researchers (TP and GC), either in-person or through videoconference. The semi-structured interview guide was developed by the research team and was in part based on a similar study in adult rheumatoid arthritis [23]. No additional piloting was completed for this study, although the guide was updated by the research team, which included pediatric rheumatologists, to include prompts related to the pediatric population (e.g. patient age, patient and parent views on tapering, family concerns). The interview guide is available in Online Resource 1. With each interview conducted, the semi-structured interview guide was applied in a manner responsive to the discussion and informed by the previous interviews. The interviews ranged from 30 to 60 min, and were audio recorded and transcribed verbatim by a researcher (TP). In addition to the audio recording, detailed notes were taken during the interviews. Data were anonymized prior to analysis.

Deductive thematic analysis was used to analyze the qualitative data using NVivo 12 software [24]. This methodology was chosen because of the flexibility it offers to identify patterns or themes within the data. Interviews were analyzed independently by two researchers (TP and PMH). Each researcher reviewed the transcripts and created preliminary codes from the data. Using an iterative process, the preliminary codes were refined and collated into subthemes and themes that were then used to fully code the data. After three transcripts were coded, the researchers discussed and agreed upon the emerging

themes together. Once all the transcripts were coded, the researchers met again to further refine and finalize the themes. The subthemes were grouped within the themes. The themes and subtheme structure were generated from the preliminary codes. During the process, the themes were also reviewed and finalized with other team members (GC, DM). Quotes presented in this study were edited for readability. We did not perform participant checking.

A similar iterative process was followed to refine the themes to develop the attributes for the BWS survey. Two sources of information were used: (1) the themes identified from the interviews, and (2) the themes corroborated from published literature. Using these two sources of information, a preliminary list of potential attributes was created. The list was refined further through a series of meetings with the research team (DM, GC, TP) and reviewed with a clinician team member with expertise in JIA (MT).

In terms of reflexivity, the researchers acknowledge that the qualitative research process and analysis were influenced in part by the characteristics of the researchers who conducted the interviews (GC, TP) and completed the analysis (TP, PMH). The researchers (GC, TP, PMH) are all female and have experience in arthritis research. Through their experience in arthritis research, the researchers have some understanding of the patient and clinician experience in regard to treatment decisions. GC and TP had no existing relationships with the participants at the time of the interviews, and TP and PMH have prior experience in qualitative thematic analysis.

The manuscript and the results are reported per the consolidated criteria for reporting qualitative research (COREQ) [25].

3 Results

Interviews with five pediatric rheumatologists from four different Canadian provinces were conducted (four female, one male). No participants declined participation but one was invited and did not respond. As we had reached saturation, we did not further follow-up. Saturation was considered achieved when no further data were arising from the last interview. In addition, the published literature was used to corroborate this conclusion. Although it was a small sample, the total population of pediatric rheumatologists in Canada is also quite small (approximately 60) and we deliberately invited participants who represented some variation in terms of province, sex and years in practice. The themes and subthemes from the analysis, for initiating and tapering of biologics, are presented in Tables 1 and 2, respectively. The following sections summarize the themes and subthemes into two categories: (1) pediatric rheumatologist attitudes and approaches to treatment decision making; and (2) patient and contextual characteristics in the decision to initiate and taper biologics. A preliminary list of attributes is shown in Table 3 and the final list of attributes for the BWS survey is shown in Table 4.

3.1 Pediatric Rheumatologist Attitudes and Approaches to Treatment Decision Making

Biologics were considered an effective treatment for JIA among pediatric rheumatologists, who also acknowledged there are long-term risks associated with the use of biologics.

> "I think there are a lot of patients who benefit greatly from biologics, so we are certainly using them more and more frequently." [Participant 3]
> "I think you know they are the new kid on the block, so you know, not having been around as long and not having as much experience with these agents as some of the other drugs we have been using for children with polyarthritis for many, many years now does raise concerns regarding side effects both short term, medium and long term." [Participant 1]

With regard to biologic tapering, all pediatric rheumatologists acknowledged that there is a lack of evidence to optimally reduce biologics in JIA, and more research is required to understand when and how tapering can be safely performed. Tapering approaches varied among participants, with some pediatric rheumatologists preferring to stop biologics immediately, while others tapered by increasing the dose interval and/or reducing the dose over time. Frequent monitoring outside of routine care was noted as a necessary factor in the decision to taper. There were some concerns about clinic capacity to manage additional appointments for patients who may flare during tapering. Approaches to monitoring varied; some pediatric rheumatologists would set up additional appointments, while most had a prediscussed plan with patients in the event of a flare. In the absence of clinic monitoring, adjustments would be made to the tapering strategy. In most cases, patients were instructed to restart their medication or return to the previous dose that was effective before tapering.

> "And generally what I tell families; if there is any evidence you see they are starting to get stiff in the morning, they are starting to have more joint pain, or there is a swollen joint, I would right away go back to the last dose where they were perfect." [Participant 5]

Table 1 Themes and subthemes in the decision to initiate a biologic

Themes/subthemes	Description
Theme 1: Attitude and approach to initiating biologics	
1.1 Discussion with patients and families	How physicians approach the subject of initiating biologics with their patients. Also includes references to patients' need for information or to be fully informed (e.g., benefits, risks, adverse effects, duration of medication, administration) before deciding to start biologics. Also includes descriptions of families feeling overwhelmed with information (e.g., regarding diagnosis, medications)
1.1.2 Shared decision making	Shared decision making between physicians and patients and/or parents when initiating biologics and patient. Also includes references to patient and/or parent preferences
1.2 Management approach to initiating biologics	Physician management plans when initiating treatment (including what, when, why and how their approach is managed in clinic)
1.2.1 Mode of medication administration	Physician considerations or preferences for mode of DMARD or biologic administration (e.g., subcutaneous injections, intravenous injections). Also includes references to medication injection training and needle phobia
1.2.2 Support strategies	Physicians consulting other health professionals in their decision to initiate biologics
1.3 Research evidence and guidelines	The use of research evidence and guidelines in the decision to initiate biologics, and the lack of research evidence for biologics
1.4 Physician thoughts and/or concerns towards biologics	Physician thoughts and/or concerns towards initiating biologics (e.g. risk of malignancy)
Theme 2: Patient characteristics	
2.1 Disease activity	The presence of active disease (e.g., joint damage or active joints) was an indication not to taper, while low disease activity was a criterion for tapering
2.1.1 Active joints	The number of affected joints or active joints
2.1.2 Joint damage or erosion	Joint damage or erosion
2.2 JIA subtypes	JIA subtypes in the decision to initiate biologics
2.3 Comorbidities	The consideration of existing comorbidities and other health conditions in the decision to initiate biologics
2.4 Patient age	Physicians expressed concerns around making medication changes (e.g., tapering) when a patient is close to the age of transition to adult care
Theme 3: Contextual considerations	
3.1 Patient experience with current medications	A patient's past and current experiences with their medications prior to initiating biologics (e.g., medication adverse effects, toxicity, adherence issues)
3.1.1 Medication adherence	Medication adherence in the decision to initiate biologics and how it influences the type of biologic used
3.1.2 Medication effectiveness	Medication effectiveness of DMARDs and its influence on the decision to initiating biologics
3.1.3 Medication intolerance to DMARDs or NSAIDs	Patient inability to tolerate DMARDs or NSAIDs as a factor in initiating biologics
3.1.4 Medication adverse effects from DMARDs	Medication adverse effects (e.g., DMARDs) as a factor in initiating biologics
3.2 Accessibility of biologics	The process of and challenges with obtaining public funding and/or private insurance for restarting biologics after tapering and discontinuation
3.3 Access to follow-up and monitoring	The clinic capacity for follow-up appointments or physician ability to follow-up with their patients who are initiating biologics
3.4 Patient family history	A patient's family history and familial risk factors that may be a contraindication for a biologic (e.g., for multiple sclerosis)
3.5 Patient willingness to start biologics	A patient's attitude towards medication/biologics and willingness to initiate biologics
3.6 Parent willingness to start biologics	Family attitude towards medications (e.g., biologics) and general receptiveness to initiating biologics
3.7 Patient social situation	The social situation of patients (e.g., family structure) influences the type of biologic prescribed (e.g., injections vs. other)
3.8 Family members or social media influence	Other family members or social media influence on decision to initiate biologics

DMARD disease-modifying antirheumatic drug, *NSAIDS* nonsteroidal anti-inflammatory drugs, *JIA* juvenile idiopathic arthritis

Table 2 Themes and subthemes in the decision to taper a biologic

Themes/subthemes	Description
Theme 1: Attitude and approach to tapering	
1.1 Management approach to tapering	Physician management plans when tapering treatment (including what, when, why and how their approach is managed in clinic)
1.1.1 Managing flares	Physician plans for patients (e.g., pre-discussed plan) in the event of a flare
1.1.2 Monitoring	Physician plans to monitor patients while tapering
1.1.3 Tapering strategy	Tapering vs. stopping (i.e., changes in biologic frequency or dose, decreasing interval between injections, etc.)
1.2 Research evidence and guidelines	The use of research evidence and guidelines in the approach to tapering biologics
1.3 Shared decision making	Shared decision making between physicians and patients and/or parents when reducing biologics. Also includes references to patient and parent preferences
1.4 Patient self-tapering	Examples of patient self-tapering and overall adherence to medication and how it influences the decision to taper
Theme 2: Patient characteristics	
2.1 Disease activity	The presence of active disease (e.g. joint damage or active joints) was an indication to not taper, while low disease activity was a criterion for tapering
2.1.1 Active joints	The number of affected joints or active joints
2.1.2 Joint damage or erosion	Joint damage or erosion
2.2 Disease remission	Disease remission and difficulty achieving remission as factors in tapering
2.2.1 Achieving remission	The amount of time or challenges in obtaining disease remission (e.g., failing multiple medications, number of medications needed to get the patient into remission)
2.2.2 Duration of remission	The duration of remission before the decision to taper
2.3 JIA subtype	Physicians were hesitant to taper in patients with certain JIA subtypes (e.g., systemic, spinal involvement) and serological phenotype (e.g., Rheumatoid Factor (RF) positive) that indicated more severe disease
2.4 Comorbidities	The consideration of the history and/or presence of comorbidities that the biologic is currently used for (e.g., IBD)
2.5 Patient age	Physicians expressed concerns around making medication changes when a patient is close to the age of transition to adult care
2.6 Risk of flares	The risk and fear of patients flaring during the tapering process
2.7 Spine involvement	Spine involvement in the decision to taper
2.8 Ability to recapture	The ability to recapture disease (regain disease remission) in the event of a flare during tapering
2.9 Medication effectiveness	Medication effectiveness or efficacy as a consideration for tapering biologics
2.10 Medication adverse effects	The inability to tolerate a biologic (e.g., due to adverse effects, toxicity) was a consideration in tapering or stopping a biologic
2.11 Uveitis	The presence of uveitis was a consideration to not taper
Theme 3: Contextual characteristics	
3.1 Accessibility of biologics	The process of and challenges with obtaining public funding and/or private insurance for re-initiating biologics after tapering and discontinuation
3.2 Access to follow-up and monitoring	The clinic capacity for follow-up appointments or physician ability to follow-up with their patients who are tapering biologics
3.3 Parent willingness to taper	A parent's attitude towards medications/biologics and willingness to taper a biologic for their child
3.4 Patient willingness to taper	A patient's attitude towards medication/biologics and willingness to taper biologics

JIA juvenile idiopathic arthritis, *IBD* inflammatory bowel disease

Shared decision making was stated to be a part of the decision-making process by pediatric rheumatologists. The decision to initiate or taper biologics was made in agreement with patients and their families, and with consideration of patient preferences for initiating and tapering biologics.

"And if necessary, sometimes I would offer them another opinion if that would be helpful to them, but basically you know the families are obviously key players in making any decisions, and I do always try to have them ensure that they understand as best as possible the risks and benefits. Really, emphasizing the

Table 3 Preliminary list of attributes for Best–Worst Scaling survey

Attribute (from qualitative analysis)	References from literature
1. Ability to recapture	Horton et al., 2017; Kuijper et al., 2017 [9, 16]
2. Access to biologics	Lipstein et al., 2013; Horton et al., 2017 [9, 11]
3. History of joint damage or erosion	Horton et al., 2017; Kuijper et al., 2017; Shenoi et al., 2019 [9, 16, 30]
4. Difficult to accomplish remission/easy to accomplish remission	Kuijper et al., 2017; Shenoi et al., 2019 [16, 30]
5. Time in remission	Horton et al., 2017; Kuijper et al., 2017; Vavricka et al., 2014; Broughton et al., 2012; Shenoi et al., 2019 [9, 10, 16, 27, 30]
6. JIA subtype	Horton et al., 2017; Broughton et al., 2012; Shenoi et al., 2019 [9, 10, 30]
7. Uveitis	Horton et al., 2017; Tymm et al., 2014; Shenoi et al., 2019 [9, 26, 30]
8. Spine involvement (associated with certain types of JIA, i.e. polyarticular or systemic JIA)	Shenoi et al., 2019 [30]
9. IBD	Horton et al., 2017; Tymm et al., 2014 [9, 26]
10. Presence of adverse effects	Broughton et al., 2012; Shenoi et al., 2019 [10, 30]
11. Patient age (transition of care)	Horton et al., 2017; Broughton et al., 2012; Shenoi et al., 2019 [9, 10, 30]
12. Child willingness to taper	Horton et al., 2017; Broughton et al., 2012; Kuijper et al., 2017; Tymm et al., 2014; Shenoi et al., 2019 [9, 10, 16, 26, 30]
13. Parent willingness to taper	Horton et al., 2017; Lipstein et al., 2013; Shenoi et al., 2019 [9, 13, 30]
14. Risk of flares	Horton et al., 2017; Broughton et al., 2012; Shenoi et al., 2019 [9, 10, 30]
15. Geographic location/access to care	Lipstein et al., 2013; Shenoi et al., 2019 [11, 30]

JIA juvenile idiopathic arthritis, *IBD* inflammatory bowel disease

Table 4 Final list of patient and contextual attributes for a Best–Worst Scaling survey

1. History of joint damage or erosive disease
2. How challenging it was to achieve remission (e.g., number of medications or time needed to achieve remission)
3. Time spent in remission
4. JIA subtype
5. History of uveitis
6. History of spine/sacroiliac joint involvement
7. History of temporomandibular joint involvement
8. History of comorbidities (e.g., IBD, psoriasis)
9. Patient age
10. Patient willingness to taper/stop
11. Parent willingness to taper/stop
12. History of flares
13. Continuity of care and ability to access follow-up care (e.g., geographical limitations)
14. Accessibility of biologics

JIA juvenile idiopathic arthritis, *IBD* inflammatory bowel disease

benefits as well as making sure that they understand that nothing is without risks." [Participant 3]

"It is always a discussion with the family, this is shared decision making." [Participant 4]

"The other thing obviously, is patient preferences. Some parents are really wanting them off those daily injections and if they came under control quickly and they have no active disease, for a year even, rather than switch them to another biologic if the family feels they really can't do it anymore, I would usually taper them. And if they don't flare, taper them off and stop." [Participant 3]

3.2 Patient and Contextual Considerations in the Decision to Initiate and Taper Biologics

Initial disease presentation and specific JIA subtypes, which indicated a more severe disease course (e.g. polyarticular JIA) and high disease activity (e.g. number of active joints or joint damage), were cited as reasons to initiate a biologic.

Pediatric rheumatologists indicated that if their patients were not responding to first-line treatments (i.e. methotrexate) and had active disease, this would be another reason to reassess whether to add a biologic. The presence of existing comorbidities (e.g. inflammatory bowel disease [IBD], uveitis) was another reason to move more quickly to a biologic. Several considerations were noted by pediatric rheumatologists regarding a patient's prior medication experience, as reasons to reassess and add a biologic. These included inadequate effectiveness of first-line treatments and the inability to tolerate medication due to adverse effects. Lastly, patient age was a factor in the type of biologic prescribed (e.g. multiple injections), with clinicians wanting/aiming to minimize medication change/burden for children transitioning to adult care and very young patients.

> Regarding side effects: "So, … that moves us into a biologic if they've been on, for example, methotrexate and the child is no longer tolerating it or it loses it efficacy because of the dose reduction required, side-effects or just intolerance or refusal. And we see that with various age groups that they just can't stand the side-effects, which is generally horrible nausea, and they just don't want to take the methotrexate anymore. In fact, when we move them to a biologic that is by injection, for example, their number one fear is that they are going to have nausea again." [Participant 1].

A patient's social situation and the availability of family members to administer medication influenced the decision to move to a biologic and also the type of biologic prescribed. Furthermore, contraindications for biologics, such as familial risk factors for certain conditions (e.g. multiple sclerosis), were reasons not to start a biologic.

> "How reliable would the family be to give an injection at home? You do have some families where the psychosocial situation is suspect, and I'm not so sure that is a particular patient I would want the family to have access to needles. So, we have to think about that too, and some of those patients are more inclined to be treated in an infusion center and nobody is accessing anything, you know. So, we do have to think about that as well, and those particular situations are often the most challenging." [Participant 1].

Pediatric rheumatologists were hesitant to taper in patients with certain JIA subtypes that indicated a long and more severe disease course (e.g. systemic JIA). Patients with active disease, existing joint damage or erosion were not suitable candidates for tapering, however patients with low disease activity were considered for tapering. If a patient had an existing comorbidity where a biologic was indicated, then this would be a consideration to stay on the biologic (e.g. IBD). There was agreement among pediatric rheumatologists that the time a patient spent in remission was important in the decision to taper, but there was variability in the length of remission needed to consider tapering, which varied from 6 months to 2 years. Some pediatric rheumatologists stated that a longer remission period of at least 2 years was required for patients whose biologic was used to treat their uveitis. How challenging it was to achieve remission (e.g. medication effectiveness and the number of medications needed to get a patient into remission) was another consideration to stay on a biologic. Medication intolerance, due to adverse effects for example, was a reason to taper biologics. Furthermore, pediatric rheumatologists were concerned about their patients flaring while tapering and the possibility of not being able to regain disease control with the same medication.

> "Well recapture, let's say they were on remission on Enbrel and they have been on Enbrel for 2 years and we stop it and they flare, and sometimes you can't get them back on remission on Enbrel and you have to try to pick another agent." [Participant 1]

Several of the contextual characteristics that were identified in the decision to initiate biologics were also important in the decision to taper. Pediatric rheumatologists voiced challenges navigating both public and private insurance for starting biologics, and this contributed to their hesitance to taper; although most were able to obtain treatment for their patients despite concerns.

> "And it also depends on, unfortunately in Canada, how we get [biologics] funded because sometimes it's really hard to get funding. Then you have to work in the constraints you have. Sometimes that prolongs you to not stop [biologics], because you are too worried that you won't get the funding for the medication again." [Participant 2]

Another consideration was the ability to follow-up and monitor patients who transitioned to a biologic. In addition, geographic limitations were recognized as a barrier to tapering as it limited the opportunities for follow-up due to patients having to travel for care.

Patient and/or parent attitudes and receptiveness to initiate or taper a biologic was another consideration. According to some pediatric rheumatologists, some parents were hesitant to start a biologic due to the lack of information, and/or misinformation from friends or social media, and the general fear surrounding the use of biologics. Regarding tapering, some parents were more open to tapering and initiated the conversation, while others were more cautious due to fears of their child's disease flaring. Similarly, some patients were more willing to taper (e.g. older patients), whereas others were more cautious and had fears of flaring.

> "So, most of the time, if it's teenagers, they start to talk about it every time you see them. As soon as

you start it, three months later they ask when we can stop, especially if they feel well. Of course if they still have active [disease] it's different. This decision also depends on families because some families are very strict." [Participant 2]

"There are some patients that don't want to stop; they are afraid of what is going to happen. And for the most part I wouldn't push them to stop, because I don't think we have good enough data that shows that patients do really well with stopping." [Participant 5]

3.3 Selection of Attributes for a Best–Worst Scaling Survey

A preliminary list of 15 attributes from the qualitative analysis is shown in Table 3 and the final 14 attributes for the BWS survey are shown in Table 4. There was strong agreement between the final list and the characteristics identified from prior research (Table 3) [9, 16, 26, 27]. Two decisions were made to refine the themes for the survey: (1) the attributes were framed to be observable characteristics or describe the health system context of a patient at the time of the decision to taper; (2) the wording of the attributes, where applicable, was refined to indicate 'the history of', to be consistent with this decision. Themes such as medication adverse effects (alone) were deemed unrelated to tapering as the reasons were not about tapering in a child in remission but rather stopping for other reasons. The ability to recapture disease after a flare was not considered for the survey as these are not patient or contextual factors that are observable at the time of tapering. Themes that were closely related were consolidated into one attribute. For example, themes such as medication effectiveness and time in remission were combined into one attribute, 'Time spent in remission'. Characteristics from the literature that were not identified in the qualitative analysis were reviewed [9]. Some characteristics (e.g. presence of asymptomatic imaging abnormalities) were deemed not relevant for the purposes of the survey, and others (e.g. number of medications needed to achieve remission) were already captured in other attributes (i.e., how challenging it was to achieve remission). Temporomandibular joint involvement was not identified in the qualitative analysis but was included as an attribute after consultation with the research team.

4 Discussion

This study presents pediatric rheumatologists' approaches to treatment decision making in JIA, and the process of selecting attributes for a BWS survey. In the interviews, shared decision making was identified as an important element to initiate or taper biologics by pediatric rheumatologists. As expected, in the absence of clear guidelines and biomarkers, there was variability in how and when tapering should be performed. The final list of attributes that influence pediatric rheumatologist choices about tapering included both patient characteristics and contextual characteristics that were important in the treatment decision process.

The patient and contextual characteristics identified in the decision to initiate a biologic were consistent with the literature and clinical practice guidelines [3, 11, 28, 29]. Patient JIA subtype and initial disease presentation were important in the decision to start a biologic in the present study. A study in the UK examining treatment patterns in patients with JIA had similar results, with disease subtype, particularly in children with systemic JIA and history of uveitis, being the most important factor in starting biologics and the type of biologic prescribed [29]. Likewise, history of uveitis and JIA subtypes were also identified as factors when considering a biologic for patients in a study examining Dutch clinician treatment decisions [28]. Patient and parent preferences, as well as medication adverse effects, were other identified factors similar to what was reported in the present study [11, 28]. A patient's sociocultural context influenced the decision to start a medication and, subsequently, the type of medication prescribed [11]. Pediatric rheumatologists in the present study considered the ability or availability of family members to administer biologics safely and were hesitant to initiate a biologic if these conditions were not met. The logistical aspects of treatment, such as administration, including travel for clinic and infusions, were other considerations.

Factors that influenced the decision to taper were similar to those reported previously [9–11, 30]. Time spent in remission was identified as the most influential factor in the tapering decision in a study of pediatric rheumatologists from Canada and the US [9]. The majority of clinicians would wait a minimum of 6–12 months before deciding to taper, compared with 6 months to 2 years in the present study. However in a UK study, only 52% of pediatric rheumatologists required a minimum of 1 year in remission and a few (10%) required just 6 months [10]. Like prior studies, tapering strategies varied among clinicians [9, 11, 30]. One-third of clinicians from Canada and the US preferred to taper biologics over a 2- to 6-month period and only 17% of clinicians preferred to stop immediately [9]. While half of UK pediatric rheumatologists preferred to taper from full-dose to once weekly before stopping completely, 39% preferred stopping from a full dose twice weekly [10]. A study conducted by the Childhood Arthritis Rheumatology Research Alliance (CARRA) found that for patients with systemic JIA on combination therapy, a large proportion of North American pediatric rheumatologists preferred to taper methotrexate first [30]. The differences observed in tapering strategies may be influenced by practice patterns and

policies in respective jurisdictions. Additional factors that contributed to the tapering decision included failure of multiple medications before biologics, history of drug toxicity, JIA subtype, history of joint damage, and prior flares [9, 30].

Pediatric rheumatologists identified accessibility of biologics as a factor in the decision to initiate or taper a biologic due to concerns regarding funding. In Canada, biologics are funded, in part, through the provincial health authorities and through private insurance. A study examining access to biologics in Canada found limitations in access to these treatments and large discrepancies in the access criteria and coverage provided by provinces [31]. Concerns regarding the availability of medications were echoed by participants in the present study and in prior research [9, 11, 29]. Although most clinicians in the present study indicated that they were able to obtain funding required for biologic treatments, these treatments may not always align with what they would prefer for their patients, due to limited availability of biologics approved for JIA treatment.

This study adds to the current literature by reporting on Canadian pediatric rheumatologists' approaches to treatment decision making for initiating and tapering biologics in JIA. Specifically, common patient and contextual characteristics were identified that influence the decision to both initiate and taper a biologic, such as patient and parent buy-in. However, there are limitations to the present study that warrant discussion. Although we aimed to recruit pediatric rheumatologists with a range of experiences and from different provinces in Canada, approaches and considerations for initiating and tapering may vary by practice and location. In addition, an understanding of the patient/parent perspective is critical to designing patient-oriented approaches for the tapering of biologics.

5 Conclusion

The present study provides insights into how Canadian pediatric rheumatologists make treatment decisions about initiating and tapering biologic therapy in patients with JIA. Fourteen attributes were developed from the qualitative results, which were subsequently used to determine the importance of each patient and contextual attribute in a BWS survey. These attributes were used to design a series of choices each presenting a subset of the attributes to which survey respondents identify the most and least important attribute, and the responses to the series of choices enables a quantitative ranking of the full set of attributes. Until additional clinical evidence is available about which children can be safely tapered off biologic therapy, our findings can inform emerging guidelines for tapering biologics in children with JIA. This is part of a program of research that will further explore the variations in tapering practices by pediatric rheumatologists in both Canada and The Netherlands, and also examine, using both qualitative and quantitative methods, whether approaches to treatment decision making align with patient and family preferences.

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Ethical approval Ethics approval was obtained from the Conjoint Health Research Ethics Board at the University of Calgary (REB19-0360).

Availability of data and material The ethics approval and consent for this study preclude the sharing of the raw data.

Code availability Not applicable.

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