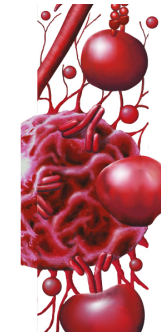
Short Communication

Immunotherapy



Development of a novel shared decision making aid for primary immunodeficiency diseases

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Aim: To describe development of a shared decision making (SDM) aid in treating primary immunodeficiency diseases (PID) with immunoglobulin replacement therapy (IGRT). **Materials & methods:** Expert engagement and qualitative formative research informed development. IGRT administration features were prioritized using object-case best–worst scaling (BWS) methodology. The aid was assessed by US adults self-reporting PID and revised following interviews/mock treatment-choice discussions with immunologists. **Results:** Patients participating in interviews (n = 19) and mock treatment-choice discussions (n = 5) deemed the aid useful/accessible and supported the utility of BWS, with content and BWS exercises refined following participant feedback. **Conclusion:** Formative research led to an improved SDM aid/BWS exercise, and illustrated how the aid may improve treatment decision making. The aid may help less-experienced patients and facilitate efficient SDM.

Plain language summary:

Shared decision making and developing a decision aid: Shared decision making happens when patients and doctors work together to choose treatment options based on a patient's concerns, preferences, goals and values, as well as medical information. The aim of this project was to develop a decision aid to help patients with primary immunodeficiency diseases (PID), in which part of the body's immune system is missing or doesn't function correctly. This will allow patients to better understand and communicate with the healthcare team on their preferences about immunoglobulin treatments, which fight infection by boosting antibody (protein) levels in the blood. The authors talked to experts and reviewed existing information to decide what treatment features the aid should consider. Patients with PID then tested the aid, and changes were made based on their feedback. Doctors specializing in treating PID also provided their feedback. The final aid was judged to be helpful and easy to use by the participants. With further research, this aid could be used to help inexperienced patients better understand what immunoglobulin treatment features are most important to them, and support shared decision-making between patients and their doctors.

Tweetable abstract: For patients with #primaryimmunodeficiency considering how to access immunoglobulin replacement therapy, a shared decision-making aid using best–worst scaling may improve treatment decision-making and help less-experienced patients.

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Future Medicine

Primary immunodeficiency diseases (PID) are a group of >450 genetic conditions affecting the immune system, causing chronic or recurrent infections and often requiring lifelong immunoglobulin replacement therapy (IGRT) [1–3]. Several IGRT modalities are available that effectively treat PID. These include formulations for intravenous (IV) and subcutaneous (SC) administration, home- or hospital-/clinic-based infusion, and varying frequencies of infusion, depending on the mode of administration. Given that the efficacies of these products are equivalent [4], choosing the most appropriate IGRT is primarily based on infusion parameters (e.g., route and site[s] of administration, volume and rate of infusion), tolerability, location of care and access to care. Thus, IGRT treatment choices should be chiefly informed by patient preferences [5].

Shared decision making (SDM) is a process by which healthcare providers (HCPs) and patients communicate to make informed decisions that align with the individual concerns, preferences, goals and values of patients [6]. SDM is considered particularly useful when clinical evidence does not show a clearly superior healthcare option [7] or when the healthcare option is intended to minimize the impact of treatment on daily life and functioning [8,9].

The use of decision support aids is recognized as an evidence-based way to facilitate SDM [10–13], particularly when making decisions on the management of chronic diseases requiring lifelong treatment [14]. One example is the severe asthma SDM aid that was created by the CHEST Foundation and the Allergy & Asthma Network in partnership with the American College of Allergy, Asthma and Immunology [15]. The SDM aid was intended to help adult patients with asthma and their HCPs work collaboratively to improve patient self-management skills, choose the most appropriate treatment option and improve adherence to treatment [15].

Decision support aids can also promote efficiency in medical practice, improve the quality of the time spent for both patients and physicians when discussing treatment choices that are informed by patient preferences, and encourage open discussion and communication between patients and HCPs. Decision support aids include educational content needed for patients to make informed decisions and encourage weighing harms and benefits of each treatment choice, and often employ exercises for clarification of patient values [7]. In the absence of decision support aids, complex treatment decisions, which are based on patient preference and values, might otherwise lead to decisional uncertainty and extensive iterative discussions between patients and HCPs.

To gain a better understanding of key SDM concepts, the impact of SDM on patient outcomes and the current state and opportunity for SDM in PID, we performed a targeted literature search of the Embase and MEDLINE databases from 1 January 1999 to 25 February 2020 [16]. While the broader asthma, allergy and immunology community has developed decision support aids for SDM, our targeted literature search found no existing decision support aid for SDM in PID and only one study that directly addressed the topic of SDM in PID [17]. Furthermore, surveys of patients with PID and their HCPs identified discordance in perceptions about who makes treatment choices [18].

To address this need, we developed a decision support aid to facilitate SDM between HCPs and patients with PID who are considering IGRT for the first time or thinking about switching therapy modalities. This paper describes the process of designing and refining a prototype (called 'the prototype SDM aid' here) that will be used to generate the final decision support aid. In this qualitative formative research, semi-structured interviews were combined with observational data collection and analysis was used to guide development of the prototype SDM aid in an iterative process, to provide proof of concept for the use of best–worst scaling (BWS). Future research should focus on the impact of the SDM aid on patients' choices. The SDM aid incorporated object-case BWS methodology to quantify patient priorities with regard to different IGRT features.

Materials & methods

Prototype SDM aid development process

This qualitative formative research was designed to gather data useful for the development and implementation of an SDM aid, and was intended to provide proof of concept for BWS. Development of the prototype SDM aid was informed by the International Patient Decision Aid Standards (IPDAS) [10]. The study team, which included the investigators, expert immunologists, and the study sponsor, provided input throughout the development of the prototype SDM aid. Three immunologists, all with >15 years of experience treating pediatric and adult patients with PID, in both private practice and academic clinical practice settings, provided clinical expertise in the formative research; two of the immunologists conducted mock treatment-choice discussions as part of the formative research activities for the prototype SDM aid.

Table 1. Features of modalities of administration of immunoglobulin replacement therapy in the best–worst scaling preference assessment exercises used in the two rounds of interviews.

Features used in the first round of pretest interviews	Features used in the second round of pretest interviews
1. Given at home by you or a family member	1. Given at home by you or a family member
2. Given at home by a healthcare provider	2. Given at home by a healthcare provider
3. Given at a hospital, clinic or doctor's office by a healthcare provider	3. Given at a hospital, clinic or doctor's office by a healthcare provider
4. One needle used each time	4. One needle used each time
5. More than one needle used each time	5. More than one needle used each time
6. Given monthly for about 4 h or more each time	6. Given monthly
7. Given monthly for about 2–3 h each time	7. Given every other week
8. Given every other week for about 1–2 h each time	8. Given weekly
9. Given weekly for about 1 h each time	9. Given for about 4 h or more each time
	10. Given for about 2–3 h each time
	11. Given for about 1–2 h each time
	12. Given for about 1 h each time

I like this the most (please check one)	**Things you could choose about the treatment**	**I like this the least** (please check one)
	1 needle used each time	
	Given every other week for about 1–2 hours each time	
	Given monthly for about 2–3 hours each time	
	Given weekly for about 1 hour each time	
	Given at home by a healthcare provider	

Figure 1. Example best–worst scaling question from the prototype shared decision-making aid used in formative research activities.

BWS methodology was employed in the prototype SDM aid to elicit patient priorities with regard to key IGRT administration features. BWS is a stated preference method that elicits ranking and relative importance data by asking patients to choose the most and least desirable options [19–21]. This methodology was chosen because of the simple design and analysis that can yield personalized ranking data using results from a single respondent. The prototype SDM aid presented a series of BWS questions; each question comprised a list of five treatment features. Table 1 lists features used in the BWS questions; Figure 1 shows a sample BWS question. The prototype SDM aid used a simple, straightforward calculation to yield a personalized output with rankings of the importance of the administration features from the BWS questions. The rankings were calculated by rescaling the difference between the number of times a patient selected a feature as the best feature and the number of times the patient selected the feature as the worst feature such that the ranking lies between 0 (worst feature) and 10 (best feature).

The formative, iterative process of designing and evaluating the prototype SDM aid is summarized in Figure 2. To start the development of the prototype SDM aid, an outline of the structure and content of the prototype SDM aid was created by the study team. In addition, an advisory panel of nine immunologists from the USA and 10 immunologists from Europe provided perspectives from differing practice types and settings early in development, and their perspectives were integrated into the construction of the prototype SDM aid. Two immunologists from the study team engaged in mock treatment-choice discussions without the use of an SDM aid with patient-volunteers. The immunologists and research team attempted to make the discussions as realistic as possible to provide the entire team with context about a typical treatment consultation between HCP and patient. These were observed by the study team to increase understanding of the content of and approach to SDM about IGRT. After these expert engagement activities were completed, a prototype SDM aid was developed to contain the following sections:

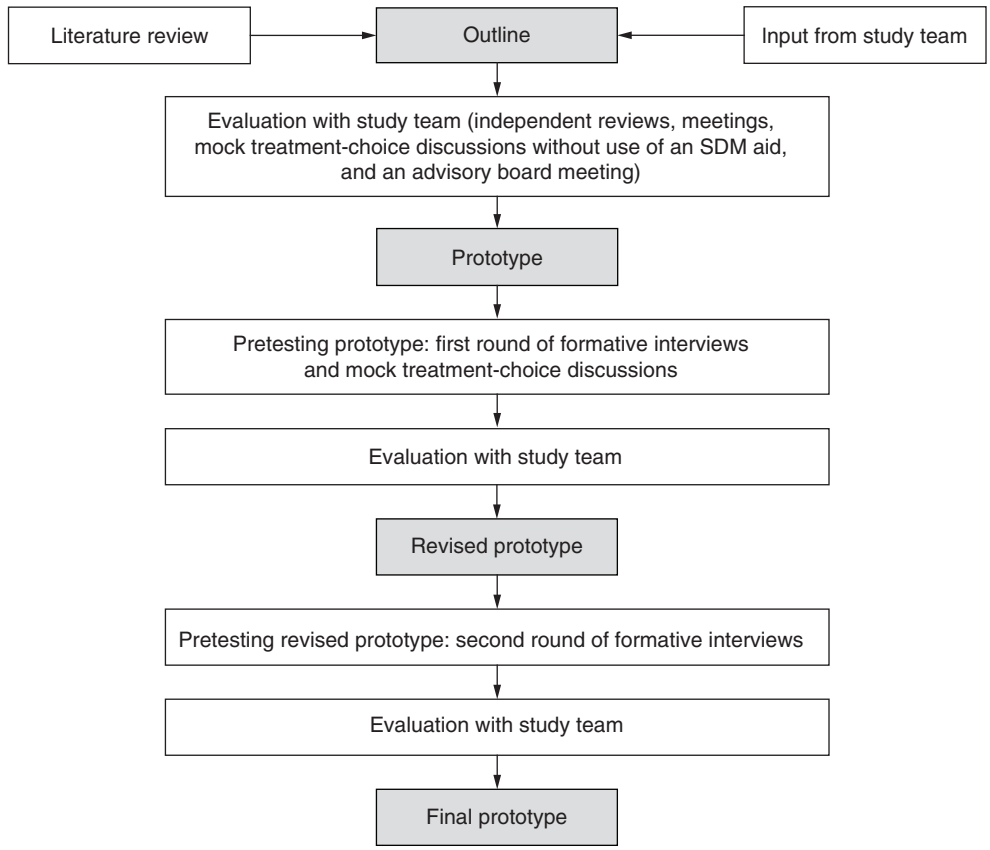

Figure 2. Summary of formative research and shared decision-making prototype aid development activities.
SDM: Shared decision making.

- Brief description of the treatment choice, key features of IGRT modalities of administration and instructions on how to answer BWS questions;
- A series of BWS questions (the BWS exercise) to elicit patient rankings of the importance of the key IGRT administration features;
- Several rating questions using Likert scales to further elicit patient preference on aspects of IGRT, such as flexibility in dosing schedule and level of comfort being responsible for dosing and supplies, and;
- Personalized output showing the patient's individual results (both the ranking and the relative importance of the treatment features) in a bar graph, additional topics to discuss with his/her treating physician and a field for patients to record open-ended comments for discussion with a HCP.

Interviews

Adult patients (aged ≥18 years) living in the USA with a self-reported medical diagnosis of PID were identified by Rare Patient Voice (MD, USA) to participate in the interviews. To the best of the investigators' knowledge, there was no prior relationship between patients and the study sponsor. The goal of the interviews was to assess the prototype SDM aid for content relevance. Interviewers also explored the perceived utility of the aid in supporting an informed treatment choice.

Two rounds of semi-structured, web-based interviews were conducted by experienced interviewers from RTI Health Solutions and RTI International using the BlueJeans videoconferencing platform (CA, USA). Supplementary Figure 1 shows the prototype SDM aid used in the first round of interviews. The prototype SDM aid contained brief introductions to key features of IGRT modalities of administration used in the BWS exercise, 18 BWS questions using nine treatment features characterizing the modality of administration (Table 1), two non-BWS questions and a personalized output (Figure 3). An interview guide was developed that followed the structure of the prototype SDM aid, with specific pause points and structured questioning of the patients at prespecified places in the content.

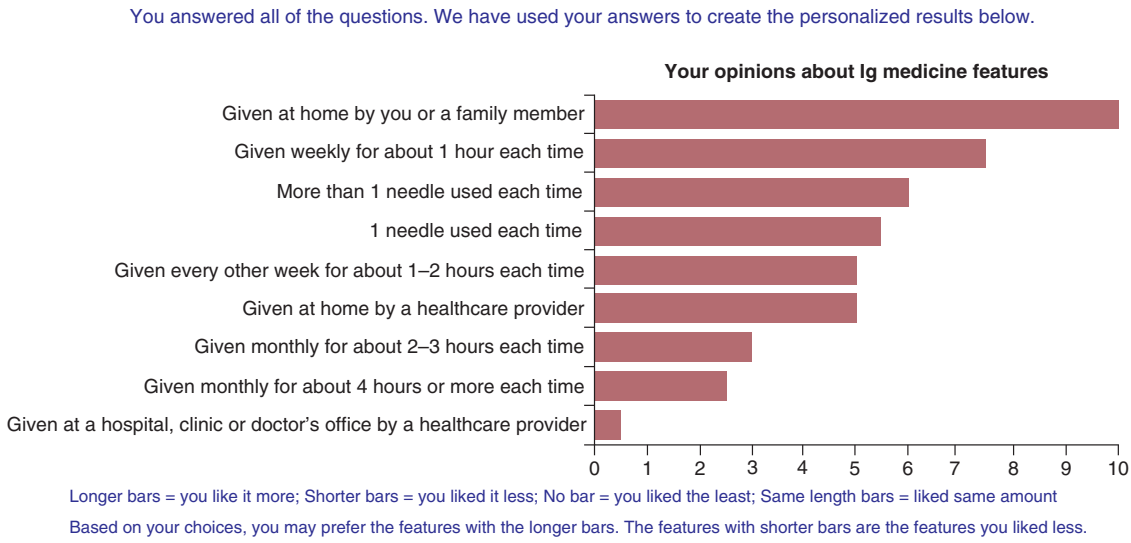

Figure 3. Example personalized output from the prototype shared decision-making aid used in formative research activities.
Ig: Immunoglobulin.

Patients were asked to think aloud, a method commonly used across many disciplines [22], as they completed the prototype SDM aid during the interviews. The study team recorded the interviews and developed summaries of each interview. Information from the interviews was entered into a response matrix.

The study team reviewed the prototype SDM aid after the completion of each interview round to determine if changes to the content and structure of the prototype SDM aid were needed, based on insights from the interviews.

Mock treatment-choice discussions

After completion of the first round of interviews, five of the patients were invited to engage in a web-based, mock treatment-choice discussion with one of two participating immunologists from the study team. The objective of the mock treatment-choice discussions was to evaluate the patient perspective on using the aid and the resulting personalized output in a scenario that was similar to a real treatment-choice discussion.

Both immunologists reviewed the patient outputs from the prototype SDM aid and engaged with the patients in treatment-choice discussions that were intended to be as natural as possible. Before the mock treatment-choice discussions began, the study team obtained feedback from the participating patient and immunologist regarding the prototype SDM aid and the personalized outputs. After the mock treatment-choice discussions were completed, patients and immunologists were debriefed separately on their experience of using the personalized rankings of treatment-choice features and feedback was sought on the helpfulness of the prototype SDM aid in the discussions.

Revisions were considered and implemented based on insights gathered from the mock treatment-choice discussions.

Results

First round of interviews & mock treatment-choice discussions

The first round of interviews was conducted between 30 May 2019 and 26 June 2019. Supplementary Table 1 shows characteristics of the 19 patients who participated in the interviews (first interview round, n = 14; second round, n = 5). Patients in this first round had a median age of 41 years (range: 19–84 years), were mostly (79%) female and had received IGRT (including both IV and SC routes of administration) for a median of 10

years (range: 0.7–17.0 years). Each interview was ~60 min in duration. Several patients recommended including more educational content regarding IGRT options. A few patients appeared to have difficulty considering treatment features separately, such as treatment frequency and duration, because they perceived the features to be linked. Patients reported that the BWS component helped them to organize their thoughts, understand their priorities and empowered them to ask questions, but included too many tasks without a clear indication of the purpose of the exercise; these questions were, therefore, perceived to be redundant.

Web-based, mock treatment-choice discussions between five patients from the first round of interviews and two immunologists were conducted between 1 June 2019 and 21 June 2019. During these discussions, patients also suggested providing additional educational materials regarding IGRT options but reported that the tool and associated output were useful, particularly for those who were newly diagnosed or had less experience making treatment choices.

The two immunologists involved in the mock treatment-choice discussions, who also played an advisory role in the study, provided feedback on the prototype SDM aid and mock treatment-choice discussions. One immunologist found the personalized outputs useful to launch SDM discussions and target them to the factors most important to the patient, while the other believed that patient preferences reflected their current treatment choices rather than their treatment-choice priorities. This immunologist believed that administration features should be better explained to prepare patients for decision-making. Both immunologists recommended providing additional educational materials regarding IGRT options and common side effects.

Revisions to the prototype SDM aid

Based on the feedback and findings from the first round of interviews and mock treatment-choice discussions, three key changes were made to the prototype SDM aid. First, treatment frequency and duration features used in BWS questions were decoupled to ensure patients considered them independently (thus increasing the number of administration features included in the BWS exercise from 9 to 12) (Table 1). Second, a table was added to summarize IGRT options. Third, the introduction to the BWS activity was revised with a clearer purpose statement.

Several other changes shortened the time required to use the prototype SDM aid in response to patient feedback regarding the length of engagement with the aid. Introductory information in the aid was revised to remove instructions that were found to be unnecessary. During the first round of interviews, the number of BWS questions was reduced from 18 to 9. In the second round of interviews, the number of BWS questions in the design was increased to 12 to accommodate an increase in the number of items from 9 to 12. Consequently, a revised prototype SDM aid with 12 BWS questions using 12 administration features was created for the second round of interviews. Reducing the length and complexity of the SDM aid also lessens the cognitive burden on patients (i.e., the time and attention required by patients to complete the prototype SDM aid).

Second round of interviews

The revised prototype SDM aid was then assessed in a second round of interviews conducted between 23 September 2019 and 30 September 2019. Patients participating in the second round of interviews (n = 5) were broadly similar to those participating in the first round (Supplementary Table 1).

When queried about the revised BWS exercise, patients reported no difficulty in completing the 12 BWS questions. They reported no challenges with considering the decoupled treatment frequency and treatment duration features separately when answering the BWS questions. Patients also reported that the summary table of IGRT options was useful and in accordance with their own experience. Patients in both rounds found the personalized output to be intuitive and generally thought the aid would be more useful for patients with newly diagnosed disease or patients with relatively little experience with IGRT than for those with more IGRT experience.

Discussion

Patient and HCP SDM is increasingly employed to improve treatment-choice decision-making and clinical outcomes, especially in populations with chronic diseases. We identified the need for decision support in PID based on clinician/patient feedback, a targeted literature search that found no existing SDM decision support aid for PID [16], one study on the topic of SDM in PID [17] and one study with survey data indicating misalignment of patient and HCP perceptions of SDM [18]. The development of the prototype SDM aid for PID described in this study is intended not only to meet the need for a decision support aid for PID treatments but also to present a novel way to quantify patient values, concerns and goals with the preference assessment component using BWS

methodology. Our use of formative research helped make the aid more user-centered, with interviews and mock treatment-choice discussions providing greater understanding of how the prototype SDM aid may be used in clinical practice. Additional input from patients with newly diagnosed PID who are beginning to consider IGRT may also generate useful insights.

Strengths of this patient-centered, qualitative research and development of an SDM aid include immunologist involvement, direct feedback from real patients and the inclusion of a BWS exercise to facilitate user understanding of their own decision-making priorities. Development of this prototype SDM aid with iterative involvement from immunologists and patients with PID is consistent with IPDAS guidelines for conducting a systematic development process [11]. The BWS exercise offers unique advantages to the prototype SDM aid for PID treatment, as preference elicitation is not typically applied to the development of a patient decision support aid nor is it typically used to support SDM. BWS is less cognitively taxing than other preference elicitation techniques such as discrete choice experiments, and a simple analysis allows individual-specific preference data to be analyzed without advanced statistics [19]. The advantages that BWS methodology brings may help patients with PID and their HCPs identify treatment-choice preferences when using the prototype SDM aid.

The formative approach had limitations. Nevertheless, the authors (several of whom are experienced with SDM for considering IGRT modes of administration) believe that the SDM aid facilitates discussions of elements of typical patient and HCP SDM discussions. Furthermore, the BWS approach is potentially appropriate to provide useful information to patients as they engage with their clinician in the choices of modes of administration, frequency of administration and site of care to facilitate discussion, and is presented here as a proof of concept exercise and not a data-proven tool. Future research with this SDM aid could evaluate both the satisfaction of making a treatment choice, and assess whether patient treatment preference changed after using the aid.

Owing to the qualitative nature of interviews, the sample sizes for interviews and mock treatment-choice discussions were small, and may not represent all adults with PID considering IGRT treatment. As an example, our sample was primarily female and all patients had previous IGRT experience. However, interviews are not intended to be generalizable, but rather to test the user experience and content. Further research is needed to validate the contents of the prototype SDM aid in other countries. Another limitation is that the prototype SDM aid did not include all features of IGRT, as only the features that were thought by the content experts to have the biggest impact on preference were included. When considering limitations of the SDM aid, the prototype and any resulting final aid will require continuous updating as new treatments become approved with innovative features. Most interviewed patients, however, supported the study team's selection of features to include. Finally, this study focused on formative research for the development of the prototype SDM aid. Future well-powered studies should assess the impact of this prototype SDM aid on how patients assimilate information, identify treatment harms and benefits, and make choices consistent with their preferences, as well as investigate use of the aid in patients prior to starting treatment or at the time of diagnosis.

Conclusion

We developed a novel prototype SDM aid to facilitate discussions between patients with PID who are considering IGRT and their HCPs. We used expert engagement and formative research activities to develop the prototype SDM aid, which included a BWS activity. The decision aid was found to be useful in eliciting patient values during formative research and supported decision-making. Future research should investigate whether the use of this prototype SDM aid facilitates alignment between preferred and actual IGRT choices, and how it may enable patient choice in treatment decision-making or improve patient adherence to IGRT.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/imt-2022-0193

Author contributions

S Tzivelekis, J Orange, C Poulos, LM Meckley, H Peay, J Sutphin, VP Hernandez-Trujillo and RL Wasserman were responsible for study conception and design. C Poulos, H Peay, J Sutphin, VP Hernandez-Trujillo and RL Wasserman were responsible for data collection and analysis. S Tzivelekis, C Poulos, H Peay and J Sutphin were responsible for interpretation of data. All authors reviewed and contributed to revisions of the manuscript.

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Ethical conduct of research statement

RTI International's institutional review board (IRB) determined that the study met the criteria for exemption from IRB review.

Summary points

- Shared decision making (SDM) is a patient-centered approach to support healthcare decision-making between patients and healthcare providers (HCPs).
- Among patients with primary immunodeficiency diseases (PID), SDM may be used to help better align choice of immunoglobulin replacement therapy (IGRT) with a patient's individual concerns, preferences, goals and values.
- Expert engagement and qualitative formative research were used to develop and assess a novel prototype SDM aid.
- The prototype SDM aid included educational patient content on IGRT, an object-case best–worst scaling (BWS) exercise to prioritize IGRT features and a graphic output that yielded personalized importance rankings of IGRT administration features.
- Following interviews with patients with PID, the aid was generally reported to be useful and accessible.
- The interviews and discussions confirmed the feasibility and supported the utility of BWS methodology for eliciting and summarizing patients' personalized rankings of treatment features.
- Results suggested that the aid may be particularly helpful to patients with newly diagnosed disease or those who have less treatment experience, and can facilitate HCP–patient discussions in a way that promotes efficient use of time.
- Future research is warranted to evaluate the impact of the SDM aid on informed choice and decision satisfaction at the time of diagnosis or prior to starting treatment.

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