

Shared Decision-Making in Allergen Immunotherapy (AIT) Options Using a Questionnaire for Respiratory Allergic Patients: A Delphi Consensus Study

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Purpose: The objective of this study was to develop and validate a questionnaire, through a Delphi consensus, to be used by allergists in their routine clinical practice to assess the preferences of patients starting allergen immunotherapy (AIT) treatment using an objective approach.

Patients and Methods: A Delphi consensus-driven process was used. The scientific committee, composed of 15 allergists, led the study and participated in the preparation of the questionnaire. Two-hundred panelists from different Spanish regions were invited to complete a 16-item questionnaire on a nine-point Likert scale covering six topic blocks. Consensus was achieved if $\geq 66.6\%$ of panelists reached agreement or disagreement.

Results: Of the 200 experts invited to participate in the Delphi process, a total of 195 (97.5%) answered the questionnaire. The panel experts reached a consensus on “agreement” on a total of 12 of the 16 (75.0%) items, covering a total of six categories: (a) patient knowledge (2 questions), (b) barriers to patient adherence (3 questions), (c) patient behavior (4 questions), (d) future actions (3 questions), (e) treatment costs (2 questions), and (f) final patient preferences (2 questions).

Conclusion: This Delphi consensus study validated a set of twelve recommended questions for patients objectively assessing their preferences and suitability for the most common AIT options available. The questionnaire intends to assist allergists in making an objective, unconditioned decision regarding the best AIT option for each patient, after informing them about the different routes.

Keywords: allergen immunotherapy, Delphi consensus, shared decision-making, questionnaire

Introduction

Respiratory allergic illness is a global health concern affecting both industrialized and developing countries,¹ with an estimated prevalence of more than 20% of the worldwide population.² Allergic rhinitis and asthma are the most common respiratory allergic diseases, affecting hundreds of millions and 235 million individuals, respectively,^{2–5} with asthma causing 455,000 deaths in 2019.^{3,4}

Antihistamines and corticosteroids are the first-line therapy for allergic respiratory disorders. However, they are often insufficient to control symptoms. Allergen immunotherapy (AIT) treats respiratory allergic disease by modulating basic immunological pathways to induce immune tolerance, relieve symptoms, and improve disease control. This treatment has

shown long-term efficacy, resulting in improved prognosis and quality of life.⁶ Furthermore, AIT is the only treatment that modifies the natural history of allergic sensitization and may prevent asthma development.^{7,8} AIT therapies are commonly administered subcutaneously or sublingually for a 3–5 year period.^{9,10} Subcutaneous injections (SCIT) should always be administered at the doctor's and/or nurse's office, allowing 30 minutes to monitor adverse reactions. Therefore, patients receiving SCIT should attend the clinic during the 3–5 years of treatment.^{9,10} In contrast, the sublingual drops or tablets (SLIT-drops or SLIT-tablets) can be self-administered at home, only requiring daily patient involvement. Direct head-to-head studies comparing SLIT and SCIT are uncommon and small;¹¹ however, SLIT and SCIT differ in local reactivity. Current data indicate that the risk of systemic reactions with SCIT is quite low, but near-fatal and fatal anaphylaxis can occur.^{9,10} In contrast, SLIT has a higher incidence of local reactions, but severe anaphylactic events are very rare.^{9,10} Regarding the utilization of the most common routes, SLIT and SCIT prescription patterns vary by country.¹² In Spain, 85.5% of adults and 77.8% of children were administered SCITs,^{13,14} although a recent study indicates that patients prefer SLIT.¹⁵ Furthermore, few studies have been performed on patients' preferences, with mixed results.^{15,16} Hence, prescription patterns in Spain are not supported by clinical evidence or patient preferences. Altogether, these observations suggest a need for objective tools for the decision-making process on the route of AIT administration.

Consideration of patients' viewpoints and preferences and joint decision-making increase treatment adherence.^{17–20} The cultural, social, and democratic growth of the last several decades has led to a transformation in the physician-patient interaction, where various decisions can be taken collaboratively, as reflected in the latest clinical guidelines.²¹ Previous research has shown diverse patients preferences and benefits of the different AIT treatments.^{15,22–26} Mode of administration, efficacy, risk of adverse events, and direct and indirect expenditures may determine which AIT patients prefer.¹⁵ In this regard, SCIT treatment is burdensome due to time spent on each appointment and travel expenses, affecting patients' adherence.²²

Despite the potential benefits of shared AIT decision-making, a physicians' guide on patient-related criteria and preferences is missing. Furthermore, AIT prescription patterns and patient preferences seem disconnected. The objective of this study was to develop and validate a questionnaire, through a Delphi consensus, that can be used by allergists in their routine clinical practice to objectively assess the preferences of patients starting AIT treatment. In order to express the need for reaching an agreement, the project was called ALLIANCE (ALIANZA in its Spanish version).

Materials and Methods

Study Design

A Delphi consensus is a structured technique used in different fields to collect relevant information on a specific issue, which consists of a series of questions targeted at experts.²⁷ The key features of this method are anonymized responses and controlled feedback.

The ALIANZA project was carried out in four phases. In Phase 1, a literature review was performed.^{26,28–32} During Phase 2, the Delphi questionnaire was developed based on the review of the literature and the scientific committee's experience. In phases 3 and 4, the Delphi questionnaire was answered by a panel of experts, results were analyzed, and the manuscript was prepared.

Study Phases

A diagram of the study phases is presented in [Figure 1](#). In the initial phase, conducted between March and June 2021, the literature regarding adherence and patients' preferences and shared decisions on allergy and AIT treatment was reviewed, with a special focus on factors related to the socioeconomic and health system factors and on aspects related to the characteristics of the patient and the treatment. In the second phase, the scientific committee developed the Delphi questionnaire based on the literature review (June 2021). The questions were generated based on the relevant factors identified in the literature review, and considering patients' preferences and situation. The final version of the Delphi questionnaire included 16 items written as questions to be asked by allergists to patients when informing them about the different AIT routes. The questions included in the Delphi were answered on a nine-point Likert scale, where 1 was

	Actions	Performed by
Phase 1	<ul style="list-style-type: none"> Review of the literature 	Scientific committee
Phase 2	<ul style="list-style-type: none"> Preparation of the the Delphi questionnaire 	Scientific committee
Phase 3	<ul style="list-style-type: none"> Delphi questionnaire 	Panel experts
Phase 4	<ul style="list-style-type: none"> Analysis and discussion of the results of the Delphi questionnaire Conclusions 	Scientific committee

Figure 1 Diagram of study phases.

Abbreviations: AIT, allergen immunotherapy; Cns, consensus measure; GPPR, General Data Protection Regulation; SCIT, subcutaneous injections; SLIT, sublingual.

“Strongly disagree” and 9 “Strongly agree”. The third phase was the Delphi phase, conducted between September and October 2021, in which the panelists selected by the expert panel answered the questionnaire. During Phase 4 (October to November 2021), the scientific committee analyzed the results of the Delphi phase, resulting in the final ALIANZA questionnaire, and the manuscript was prepared.

Scientific Committee

The project was led by a scientific committee that was comprised of a team of fifteen allergists from sites located across the Spanish territory, experts in the physician-patient relationship. All the members of the scientific committee have proven experience using SLIT and SCIT with a median experience in the allergy field of 25 years (IQR, 19–30) and a median prescription of allergen immunotherapy of 180 (IQR, 120–200) per year.

Expert Panel

A group of 200 allergy experts were invited among the 1200 allergists of Spain, ensuring representation of all regions of Spain. The criteria for their selection included professional knowledge and experience in the field of allergy and AIT treatment. The geographic distribution of the panelists is displayed in [Supplementary Table 1](#).

Consensus Definition

A statement was considered consensual if the panelists' votes outside one of the three-point regions ([1–3], [4–6], [7–9]) containing the median were less than one-third of the responses (<33.3%). The median value defined group consensus: majority “disagreement” if the median was within 1–3 and majority “agreement” if it was within 7–9. Cases with a 4–6 median were considered “doubtful”. When one-third or more of panelists scored [1–3] and another third scored [7–9], “discordance” was considered. The remaining assertions without concordance or discordance were considered as “undetermined” consensus.

Items were recommended when the voting result reached consensus in the “agreement” region (votes outside region [7–9] were <33.3%). Strong consensus was defined as 80% of panelists rating the statement 7 or above. When 67–79% of panelists evaluated a statement 7 or above, a moderate consensus was reached. Statements that did not reach this level of agreement were interpreted as “undetermined”.

Alternatively, we used the consensus measure (Cns) developed by Tasle et al for the analysis of ordinal scales.³³ For its calculation, we adapted the original formula, developed for 5-point scales, to apply it to a 9-point scale ([Supplementary Figure 1](#)). Using the Cns, results of ≥ 0.80 indicated consensus agreement.

Data Analysis

SPSS Statistics version 20 (IBM; Armonk, NY, USA) was used to create and analyze the database. The median and the percentage of responses in the 7–9 range were calculated, and their values were used to define consensus. For the Cns, the formula was calculated using SAS Version 9.4 software (SAS Institute, Inc, Cary, NC, USA).

Ethical Aspects

The study was carried out according to the Helsinki Declaration. Data from the Delphi questionnaire were anonymized during processing and analysis; therefore, personal data were dissociated from the results in compliance with the EU General Data Protection Regulation (GDPR).

Results

A total of 16 questions were developed by the scientific committee as part of a questionnaire to be administered by the physician when informing the allergy patient about the AIT (Table 1). The questions covered a total of six categories: (a) patient knowledge (2 questions), (b) barriers to patient adherence (3 questions), (c) patient behavior (4 questions), (d)

Table 1 Level of Consensus Reached with Proposed Questions

Question	CM	Median	Consensus (%)	Result	Consensus Level
Patient knowledge (Block a) Questions should be accompanied by information provided to the patient by the physician on both routes of administration (efficacy, safety, adverse effects, dosage, costs, etc.).					
1. Are you familiar with the different routes of IT administration?*	0.94	9	93.8	A	S
2. Are you familiar with the pros/cons of each of the different routes of IT administration?*	0.93	9	92.8	A	S
Barriers to patient adherence (Block b)					
3. Do you have any work/school/family constraints or commitments that make it difficult for you to attend scheduled IT treatment appointments?	0.86	8	82.6	A	S
4. If you live far from the health center, the cost of travelling to the health center and/or hospital is affordable for you in terms of time and/or money? In your answer, consider the time it takes you to travel, the cost of travel, including any associated costs (parking, bus, cab, etc.).	0.82	8	73.8	A	M
5. Do you believe that in your work and/or school and/or personal situation you have the availability/flexibility to attend your medical appointments in the health centers and/or hospital for the periodical administration of IT? Keep in mind that there are alternatives that require travel for administration, and the commitment you must make to scheduling and treatment appointment.	0.85	8	80.5	A	S
Patient behavior (Block c)					
6. Do you consider yourself an organized person and do you stick to your routines?	0.76	7	60.5	UD	UD
7. Do you use any method to remember medical appointments and/or treatment guidelines? Consider as a method of appointment reminders the use of a cell phone, agenda, etc.	0.72	7	50.3	UD	UD
8. If you are under treatment for other conditions (eg, HTA, cholesterol, contraceptives.), do you feel that you are adequately compliant with the prescribed medication?	0.77	7	62.6	UD	UD

(Continued)

Table 1 (Continued).

Question	CM	Median	Consensus (%)	Result	Consensus Level
9. Are you following the prescribed medication guideline for the treatment of your allergy?	0.86	8	81.5	A	S
Patient future attitudes (Block d)					
10. If you were prescribed a subcutaneous vaccine, would you be willing to become actively involved in the treatment by timely attending appointments at the health center and/or hospital?	0.91	8	91.3	A	S
11. If you were prescribed a sublingual vaccine, will you be able to commit to taking it at home on a daily basis as prescribed?	0.95	9	97.4	A	S
12. Would you be concerned about having to keep the treatment in the refrigerator if required and having to maintain the cold chain while travelling?	0.77	7	64.1	UD	UD
Treatment costs (Block e)					
13. Do you consider that the cost of acquiring the treatment at the pharmacy is a potential limitation to continue with the treatment for a period of 3 years?	0.88	8	85.6	A	S
14. Do you consider that the indirect cost derived from the administration of the IT (including travel, loss of work or school hours) may have an impact on your choice of the administration route?	0.80	7	68.7	A	M
Final patient preferences (Block f)					
15. Taking into account the side effects discussed for each route of administration, which option would you prefer?	0.90	8	87.7	A	S
16. Having all the information about efficacy, security and characteristics of the two IT routes of administration, which IT management solution do you think best suits your lifestyle and best meets your needs?	0.95	9	94.9	A	S

Note: *The question should be accompanied by information provided to the patient by the physician on both routes of administration (efficacy, safety, adverse effects, dosage, costs, etc).

Abbreviations: A, agreement; UD, undetermined; CM, consensus measurement; M, moderate; S, strong.

future actions (3 questions), (e) treatment costs (2 questions), and (f) final patient preferences (2 questions). Of the 200 experts invited to participate in the Delphi process, a total of 195 (97.5%) answered the questionnaire. The panel experts reached a consensus on “agreement” on a total of 12 of the 16 questions (75.0%), with a strong consensus on 10 questions (85.71%) and a moderate consensus on 2 questions (14.29%). Key results for each block are detailed below.

Patients' Knowledge

A 100% consensus was obtained across block a, with agreement on the 2 questions, and both were categorized into the strong consensus range (Table 1, Block a). The panelists agreed that the physician should ask the patients whether they are familiar with the different routes of AIT administration, as well as whether the knowledge of the pros/cons of each of the different routes of AIT administration. For both questions, experts agreed that the physician must provide information to the patient on both routes of administration, including efficacy, safety, adverse effects, dosage, and costs.

Barriers to Patients' Adherence

The panelists reached a consensus agreement on all 3 questions (100%) of block b, of which 1 (33.33%) had a moderate consensus and 2, a strong consensus (66.67%) (Table 1, Block b). The question regarding the barrier of treatment adherence related to the costs of travel to the health center and/or hospital, in terms of time and/or money, was the one

that reached a moderate consensus (question 4). The panelists agreed and showed a strong consensus on the questions of barriers to adherence related to the work/school/family constraints or commitments (questions 3 and 5).

Patients' Behavior

Agreement was reached on 1 (25.0%) of the 4 block c questions, with strong consensus (Table 1, Block c). The panelists strongly recommended that the physicians should ask the patients if they followed the prescribed medication guideline for the treatment of their allergy (question 9). Instead, the experts did not agree on the relevance of asking the patients about aspects of their behavior, related to their organizational skills and ability/method to remember medical appointments and/or treatment schedules, and if they feel that they are adequately compliant with medication prescribed for other pathologies (if applicable).

Patients' Future Attitudes

A total of 2 of the 3 questions (66.67%) reached consensus agreement by the panelists, as shown in Table 1 (Block d), both with strong consensus. The question related to the concern of the patient about having to keep the treatment in the refrigerator if required and having to maintain the cold chain while travelling reached an indeterminate agreement by the experts consulted at the Delphi (question 12). On the contrary, it was strongly recommended that patients be asked about future compliance with aspects related to subcutaneous (question 10) and sublingual (question 11) treatment.

Treatment Costs

Consensus was reached on 2 questions in block e (100%), with 1 considered a strong consensus and the other a moderate consensus (Table 1, Block e). The panelists strongly recommended that the physicians ask the patients if they consider that the cost of acquiring the treatment at the pharmacy is a potential limitation to continue with the treatment for a period of 3 years. The experts moderately agreed on asking the patients if they consider that the indirect cost derived from the administration of the AIT (such as travel and loss of work or school hours) may have an impact on their choice of administration route.

Patient Preferences

The results of the block regarding final patient preferences are shown in Table 1 (Block f). The total of the 2 questions reached an agreement, both with strong consensus. The experts consulted in the Delphi strongly recommended that physicians ask the patients about AIT treatment delivery route preferences, taking into account side effects and efficacy, security and characteristics of the two AIT routes of administration.

Final ALIANZA Questionnaire

Finally, based on the results obtained, a patient questionnaire to assess patients' preferences regarding AIT route was validated (Table 2). The questionnaire, which includes a total of 12 questions, considered socioeconomic and health system factors, as well as aspects related to patient and treatment characteristics.

Discussion

To our knowledge, this is the first study to validate a questionnaire aiming to guide physicians in making shared decisions regarding the optimal AIT for patients with respiratory allergy. A total of 195 physicians, allergy specialists based in Spain, validated the questions of the questionnaire through a Delphi methodology. The experts reached a consensus on questions to be asked to capture patients' preferences regarding AIT routes to guide decisions on AIT therapy alternatives in the allergist's office (Table 2).

Within the process of incorporating patients' preferences, it is essential to be aware of patients' knowledge.^{34,35} In this case, patients' knowledge about the different AIT options is very important for deciding the best treatment alternative. It is probably for this reason that a 100% agreement and a strong consensus were obtained for questions assessing patients' knowledge (Block a).

Table 2 Validated ALIANZA Questionnaire

Question
1. Are you familiar with the different routes of IT administration?*
2. Are you familiar with the pros/cons of each of the different routes of IT administration?*
3. Do you have any work/school/family constraints or commitments that make it difficult for you to attend scheduled IT treatment appointments?
4. If you live far from the health center, the cost of travelling to the health center and/or hospital is affordable for you in terms of time and/or money? In your answer, consider the time it takes for you to travel, the cost of travel, including any associated costs (parking, bus, cab, etc.).
5. Do you believe that in your work and/or school and/or personal situation you have the availability/flexibility to attend your medical appointments in the health centers and/or hospital for the periodical administration of IT? Keep in mind that there are alternatives that require travel for administration, and the commitment you must make to scheduling and treatment appointment.
6. Are you following the prescribed medication guideline for the treatment of your allergy?
7. If you were prescribed a subcutaneous vaccine, would you be willing to become actively involved in the treatment by timely attending appointments at the health center and/or hospital?
8. If you are prescribed a sublingual vaccine, will you be able to commit to taking it at home on a daily basis as prescribed?
9. Do you consider that the cost of acquiring the treatment at the pharmacy is a potential limitation to continue with the treatment for a period of 3 years?
10. Do you consider that the indirect cost derived from the administration of the IT (including travel, loss of work or school hours) may have an impact on your choice of administration route?
11. Taking into account the side effects discussed for each route of administration, which option would you prefer?
12. Having all the information about efficacy, security and characteristics of the two IT routes of administration, which IT management solution do you think best suits your lifestyle and best meets your needs?

Note: *The question should be accompanied by information provided to the patient by the physician on both routes of administration (efficacy, safety, adverse effects, dosage, costs, etc).

The reasons for the lack of treatment adherence by patients are varied and depend on individual factors, requiring a case-by-case assessment.^{36,37} Aside from improving individual patient outcomes, overall treatment adherence helps to determine the best treatment modalities and reduces the burden of disease on society.³⁸ Consequently, factors associated with patient adherence should be carefully considered to guide decisions regarding the best therapeutic option for each patient. Accordingly, panelists agreed on the three questions related to exploring potential barriers to AIT adherence. The aim of assessing patients' behavior regarding treatment adherence should be for physicians and patients to take these factors into consideration when deciding the AIT treatment. Like with any other treatment, adherence to AIT is crucial to ensure effectiveness. SCIT requires monthly visits to the health center, while SLIT does not require regular visits to the doctor. Several studies have concluded that non-adherence to an AIT schedule and early discontinuation are common problems.^{24,39–47} These could be reduced by engaging patients in the decision-making process for the selection of AIT route of administration, as some studies have concluded.^{26,40}

Patient behavior is directly related to the definition of adherence, according to the World Health Organization.⁴⁸ However, the experts consulted agreed on recommending only one of the four suggested questions on patients' behavior. The three questions that did not reach agreement address issues of a personal nature or about other therapies, which some of the experts consulted may not have considered necessary for the evaluation of the AIT decision. Conversely, the panelists strongly recommended that the physicians should ask the patient if they followed the prescribed medication guideline for their allergy treatment. Although a doubt as to whether the patient's answers regarding adherence to treatment are always truthful cannot be ruled out,^{49,50} if patients acknowledge a lack of treatment compliance, physicians and patients can develop together a therapeutic strategy that will help them comply with AIT in the future.

Patients' attitudes and beliefs impact medication adherence.⁵¹ For this reason, three questions on patients' future attitudes have been included, two of which have been recommended by the experts, related to SCIT and SLIT treatment. In particular, the

questions that were considered relevant were related to actions required specifically for adherence to the SCIT or SLIT. SCIT has the inconvenience of requiring visits to the physician's office, whereas compliance with SLIT is contingent on the patient decision to take the recommended doses.⁵¹ Patients responding affirmatively to only one of these two impediments will therefore have expressed their preferences, and the physician will be able to guide them appropriately.^{17,18}

The cost of medications is one of the factors that may impact treatment adherence. Cost-related medication non-adherence is a problem that has been described by several studies in the literature, and which affects a wide range of patients.^{52–55} In the field of AIT, there is also evidence regarding the possible impact of treatment costs on adherence to treatment regimens.^{45,56–59} The experts consulted in this Delphi are probably aware of the importance of this factor and have therefore agreed to recommend that patients be asked if they consider that the cost of acquiring the treatment at the pharmacy is a potential limitation to continue with the treatment for a period of 3 years (the typically recommended AIT treatment period). In addition to the direct costs of treatment, if the treatment requires visits to the health center, such as for SCIT administration, various indirect costs can be added, including the cost of travel itself and the time lost for other activities (work, social, school, etc.). In fact, the inconvenience related to patient time and travel is the most frequently cited reason for SCIT discontinuation in several studies.^{45,59–61} In this regard, experts have recommended asking the patient if they consider that the indirect cost derived from the administration of the AIT may have an impact on their choice of administration route.

The two final questions directly asked patients about their preferred AIT option and were both recommended by the experts. The shared decision-making process should end with a final assessment and decision after discussing all the information with the patient,^{62,63} and this is reflected in the position of the panelists.

Finally, it is worth mentioning that there was a total of four items on which no consensus was reached. Therefore, additional research and studies must be conducted on these topics in order to provide further evidence. Future expert discussions should be held with the purpose of reaching an agreement on these concerns.

The Delphi consensus technique is widely used in health studies as a method to obtain an agreement from experts on topics where the published body of evidence is incomplete.^{27,64} One of the limitations of the study is related to the definition of consensus, which is not standard for the Delphi technique.⁶⁵ To overcome this issue, we used two different approaches to determine consensus. In one of them, we defined two categories of consensus, moderate and strong, and in the other one, we considered the use of Cns, a method proposed by Tastle et al.³³ The Cns has been used in studies using the Delphi technique on questions/statements graded on a 5-point scale^{66,67} and, therefore, we adapted the formula for a 9-point scale. Both methods yielded similar results in terms of agreement, strengthening the agreed questions. To our knowledge, this is the first time that the results of both methodologies are shown on a 9-point scale Delphi study. Future studies may validate the equivalence of the results of both methods. Additionally, due to the methodology and the characteristics of the experts who answered the Delphi questionnaire, it is necessary to point out certain limitations of the recommendations obtained through this technique. In this study, the panelists were exclusively from Spain and, thus, their experience with the patient was focused on the Spanish healthcare system. Therefore, although we believe that this questionnaire could be used in other healthcare settings, the validation of the questionnaire presented here should be considered only for the Spanish healthcare system. Clinicians with experience in other healthcare systems should assess whether each question in this paper can be translated into their clinical allergy practice and adapt or discard those that they do not consider appropriate. They should also verify that the validated questionnaire presented here complies with the ethical and regulatory framework of the country where the physician-patient relationship is assessed.⁶⁸ However, regarding the representativeness of the panelists in the Spanish context, the high number of allergy specialists responding to the Delphi questionnaire should be noted. In Spain, it is estimated that there are around 1200 allergy specialists, which means that the 195 included in this study account for a percentage of more than 15%. In addition, the unique characteristics of the Spanish healthcare system, fragmented into autonomous communities, has also been taken into account, with representatives from all the territories. Therefore, although the extrapolation of the results to other healthcare systems should be done with caution, the high representation in the Delphi process means that it can be applied anywhere within the Spanish territory.

Conclusion

Patients' perspectives and preferences should be considered for a shared decision-making process between the patient and the allergologist to promote treatment compliance and AIT adherence. This Delphi consensus study validated a set of twelve recommended questions for patients with the intention of assessing their preferences and suitability for the most common AIT options available. The questionnaire enables an objective approach to the patient, thus resulting in a decision not conditioned by other external factors, but by the patient's preference after being informed of the characteristics of the different routes. This questionnaire, validated by 195 Spanish allergy experts, can be used in the daily clinical practice at the allergist's consultation and may help improve treatment adherence and, therefore, health-related outcomes. The intention of the questionnaire is not to decide the treatment based on a specific number of questions answered but to be aware of the patient's needs and expectations.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics

Review and approval for this research were not needed because the study does not include information on specific patients. It is a review of suggested questions which could be theoretically asked to patients in clinical settings.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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