Title

Development and testing of a guideline to provide essential information for patient decision making regarding cancer clinical trials

Running Head

Guideline development to inform a SPIF

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Conflict of interest

The authors declare that there is no conflict of interest.

Ethics approval

The study was approved by the Ethical Committee of the Peter MacCallum Cancer

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Abstract

Objective: To develop and test a guideline intended to provide information about the content of a summarized patient information form (SPIF) regarding cancer clinical trials.

Methods: Fifteen statements drawn from the Delphi study and participant commentary formed the basis of the content for the guideline document. Delphi participants contributed to a five-step process to complete the guideline document, including guideline formulation, application, revision, utility and clarity assessment, and finalization.

Results: After the draft guideline formulation, the Delphi participants were invited to complete the survey to test the draft guideline. Over 73% of the participants agreed that the summarized document could support patient decision-making. After the draft guideline revision, the researcher and four health professionals used the guideline to independently create a SPIF version. The Flesch-Kincaid reading ease scores of the sample SPIFs were between 61.3 and 66.5, with reading levels between 7.8 and 8.8, indicating that the SPIF guideline can assist health professionals with the generation of understandable information. The reference group members provided positive feedback,

and an expert on plain language in health care information proofread the guideline document.

Conclusion: The study approach used ensured equity of engagement on the part of all participant voices in the development of the SPIF and the production of a guideline to support provision of essential and understandable information intended to support patients' decision-making.

Key Words: Cancer, clinical trials, guideline, informed consent

1. Introduction

The Belmont Report indicated that information, comprehension, and voluntariness are three essential elements of the informed consent process (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978). For consent to be valid, the participant should receive sufficient information, understand the information provided, and make a decision without coercion. Provision of a consent form with detailed information is one part of the entire consent process to satisfy legal and ethical requirements intended to respect the autonomy of participants and protect them from harm by supporting them in making an informed decision (Beauchamp, 2017).

To help people understand health information and enhance comprehensive communication, plain language is recommended. In the USA, the Plain Writing Act was signed into law in 2010 to improve the effectiveness and accountability of Federal agencies to the public by promoting clear government communication that the public can understand and use (Koh et al., 2012). In Australia, the Office of Parliamentary Counsel actively encourages the use of plain language in legislation as well as the development and use of plain language techniques (Australian Office of Parliamentary Counsel, 2016). These findings and actions emphasize the importance of using plain language to deliver clear, understandable messages to improve effective communication.

In Canada and the US, it is recommended that reading materials meet a reading level target of sixth to eighth grade to reach people with low levels of literacy (Jindal & MacDermid, 2017; Stossel, Segar, Gliatto, Fallar, & Karani, 2012). Australians have similar reading level requirements (Jefford & Moore, 2008). There are several formulas available to help determine the approximate reading level of a document. The most commonly used method to determine readability is the Flesch-Kincaid formula (Jindal & MacDermid, 2017). The Flesch-Kincaid test provides a grade level score based on the USA high school grade level system (0-100 point scale). Higher scores indicate a more

readable text. Text with a score of 60 or greater is interpreted as plain language, easily understood by 13-15 year old students (Jindal & MacDermid, 2017).

Researchers have suggested that clinical trial consent forms do not adhere to best practice recommendations. Evidence shows medical jargon and the overwhelming nature of information provided limit the value of the consent form as a source of patient decision-making (Bleiberg et al., 2017). In a study analyzing 13 cancer trial consent forms covering phase I, II, and III trials, the average word count was 4,562 words or 18 pages (2,644-6,977 words, 11-28 pages). The average Flesch-Kincaid reading grade in the forms was 13, a reading level that requires college level comprehension skills (Armstrong, Dixon-Woods, Thomas, Rusk, & Tarrant, 2012). Twenty-six patients who had been invited to take part in a clinical trial were interviewed, and they indicated that the length and complex language of the consent form limited its function as a decision support document (Armstrong et al., 2012). Similarly, a US study analyzed informed consent documents from 33 phase I pediatric cancer trials. The median word count of 33 consent forms was 6,364 (4,185-8,873 words); the median Flesch Reading Ease score was 56.7 (49.2-69.4), and the median Flesch-Kincaid reading grade was 9.7 (5.8-11.7), indicating a difficult read with a reading level that requires 10^{th} to 12^{th} grade comprehension skills (Koyfman, Reddy, Hizlan, Leek, & Kodish, 2016). A Swedish study interviewed 14 patient representatives to determine their perceptions of consent forms used in cancer clinical trials. The results indicated that the medical terms and complexity of the words used failed to evoke patient interest in consent forms that were perceived to be important for comprehension. Patient representatives suggest summarizing informed consent forms with plain language and structured text in order to improve the informed consent process (Dellson, Nilbert, & Carlsson, 2016).

In response to this critical issue, many researchers have developed a range of interventions to improve the quality of information provided during the informed consent process. A summarized patient information form is one such intervention that aims to highlight important information in the consent form in order to supplement patients' understanding of cancer clinical trial participation (Bleiberg et al., 2017; Kim &

Kim, 2015). However, little evidence exists to inform the development of a summarized patient information form intended to enable informed consent. One response to this problem may be the development of a guideline document intended to help researchers and clinicians better understand the critical elements of informed consent (Kao, Aranda, Krishnasamy, & Hamilton, 2017). A guideline document could be used to develop a summarized patient information form (SPIF) that will enhance patient decision-making while ensuring that critical consent-related information is included.

In a previous study applying Delphi methodology, 15 statements were identified that could be used as components of a SPIF given to potential cancer clinical trial participants as an adjunct to the informed consent process (Kao, Aranda, Krishnasamy, & Hamilton, 2018). On the basis of the Delphi results, the goal of this study was to develop and test a guideline to inform the content of a SPIF regarding cancer clinical trials in order to contribute to ongoing efforts to improve the quality of informed consent information provided to patients.

2. Methods

A guideline document was based on the results of a previous Delphi study (Kao et al., 2018). The 15 statements retained from the Delphi study and participant commentary on each of the 15 statements formed the basis of the content for the guideline document. Five steps were conducted to complete the guideline document, including draft guideline formulation, application of the draft guideline, draft guideline revision, utility and clarity assessment, and guideline finalization (Figure 1). A reference group comprising a person with cancer, an oncologist, a clinical cancer nurse consultant, an academic specializing in cancer care and a senior researcher specializing in biomedical ethics and anticancer drugs oversaw the guideline development process. The reference group members were in addition to the research team.

2.1 Formulation of the draft SPIF guideline

To formulate the SPIF guideline document, a table listing the 15 statements was generated alongside the Delphi participant commentary responding to each statement. Participant comments formed the basis for decisions regarding combining or re-phrasing statements that had similar meaning. Statements were re-arranged into four main groups, and a heading given to each group. The Delphi participants' commentary was reviewed to inform the content of the guideline instructions and to ensure the content reflected the intent behind each statement. Guideline instructions were drafted under each heading, following the principles of how to write patient-appropriate, or consumer-friendly information. Key points were added about using plain language, and formatting of a SPIF to reflect best practice on how to create a SPIF. A background section was written about key processes to produce a set of guideline instructions. Four study researchers were involved in this process.

After the draft of the guideline document was complete, it was sent to the reference group to obtain further feedback on: 1) whether the language of the instructions was understandable; 2) whether they agreed with the ordering of the content, and 3) whether they had comments on the wording and the formatting of the instructions.

2.2 Application of the draft guideline

2.2.1 Preparation for online survey to test the draft guideline

The Clinical Trials Unit manager at the participating cancer center was consulted to identify a published Participant Information and Consent Form (PICF) from a recently completed cancer clinical trial. A double-blind randomized trial with a published PICF was chosen to test the utility of the SPIF guideline document. The researcher used the draft guideline document alongside the trial PICF to develop a sample SPIF. The sample SPIF was presented to the research team to ensure that the content followed the draft guideline document and that the wording and content were clear and understandable.

The next step was to prepare an online survey to elicit the original Delphi participants' feedback on the sample SPIF. The survey was designed in two sections. The first section was compulsory, and the second section was optional. In the first section, the participants were asked to focus on the information presented in the SPIF and to judge whether the information was sufficient to support patient decision-making regarding trial participation. Only the sample SPIF was provided. In the second section, participants were asked to compare the information presented in the sample SPIF with the original PICF to determine if any important information regarding trial participation had been omitted from the SPIF.

2.2.2 Data collection

An email invitation, including a URL to the online survey, along with a summary of the findings of the Delphi study was sent to the 153 participants in the original Delphi study. These participants were divided into four groups, including patients, physicians, allied health professionals, and other significant people involved in trials. In the first section of the online survey, the participants answered two questions with dichotomous options (yes or no): 1) Do you think this summarized document is able to support a patient's decision-making related to trial participation?; 2) is there any other important information a patient would still need in order to make a decision about trial participation?

The participants were asked to provide comments if they felt that important information was missing from the SPIF. After the participants completed the first section, they were invited to complete the second section. The second section asked them to read the full version of the PICF, and respond to the following question: "Is there any information in this consent form essential to support patient decisions that was not covered by the summarized version of the document?" Finally, they could provide any further general comments on the study.

2.2.3 Data analysis of participant feedback on the guideline application

Two types of questions were analyzed to assess the acceptability and completeness of the SPIF. The question about whether the SPIF was able to support patient decision-making regarding clinical trial participation was analyzed using frequencies and percentages related to whether respondents replied “yes” or “no.” The question regarding any missing essential information in the sample SPIF and general comments regarding the study were reviewed and analyzed to revise and enrich the draft guideline document.

2.3 Draft guideline revision

Comments from participants were discussed and analyzed. These comments helped the research team determine whether language issues and information included in the sample SPIF met patient needs. The draft guideline document was revised based on the participants’ comments.

2.4 Utility and clarity assessment

After the SPIF guideline document was revised, the researcher and four health professionals used the revised version of the guideline to independently create a SPIF version for the identified clinical trial. The testing of the application of the draft SPIF guideline allowed assessment of the reproducibility of the guideline.

Each SPIF was assigned a code as the SPIF number (SPIF#1 to SPIF#5). A checklist with 21 items was developed to assess whether the five versions of the SPIFs were consistent and contained key information from the PICF. A table was created to record whether each of the five versions of the SPIFs covered the 21 item requirements. If a SPIF included the key information from an item in the checklist, the key information was marked, and a “✓” was marked on the table corresponding to the SPIF number and item number. A descriptive analysis was conducted to show the inter-rater reliability.

2.5 Guideline finalization

The revised guideline document was presented to the reference group for final input regarding wording, structure, and general comments. In addition, an expert on plain language in health care information was invited to proofread the SPIF guideline document.

3. Results

3.1 Formulation of the draft SPIF guideline

A draft of the guideline instruction document included three sections: the background, instructions for the design of a SPIF, and suggestions for SPIF formatting. There were four headings in the section titled "Instructions for the design of a SPIF", including: 1) the purpose of the trial; 2) the design of the trial; 3) what happens as part of trial treatment, and 4) other information you may need to know.

All reference group members agreed that the language in the instructions was comprehensible and that the order of the content was logical. The group also provided comments on minor changes to wording and suggestions for formatting the instructions. After the draft guideline was complete, a published PICF was chosen to test the application of the draft SPIF guideline.

3.2 Application of the draft guideline

3.2.1 Online survey ample characteristics

A total of 104 participant responses were collected from the 153 eligible participants. Of these 104 responses, only 100 completed the first section of the survey with a completion rate 64.5% (100/153). Of the 100 complete responses; 18% were patients; 24% were physicians; 35% were allied health professionals, and 23% were other significant people, including family members and other individuals involved in trials (Table 1). One physician and two allied health professionals did not complete the second section. The completion rate for Section 2 was 63.4% (97/153).

3.2.2 Acceptability

The SPIF achieved a high level of acceptability from participants (Figure 2). Over 73% of all participants agreed that the summarized document could support patient decision-making regarding clinical trial participation.

3.2.3 Completeness

Fifty-five participants provided comments on essential information they believed to be missing from the sample SPIF. These comments were grouped into two themes: 1) issues excluded from the Delphi consensus process and 2) issues with the draft SPIF guideline content.

1) Issues excluded from the Delphi consensus process

Three areas of missing content were identified, including costs, participant confidentiality, and conflict of interest. After discussing all of the participant comments, the research team decided to add information about costs associated with trial participation to the guideline document. Cost issues were related to the statement "will I have any costs to pay?" and was excluded at round 3 of the Delphi study because only the patient group and the physician group identified this statement as essential (>80%) to a SPIF. Clinical trial participation often increases the frequency of clinic visits for extra tests or assessments as compared with standard treatments. This can result in extra expenses, such as transportation costs. These costs may influence a patient's decision as to whether to participate in a clinical trial.

Information about participant confidentiality, and conflicts of interest were not added to the guideline document. These statements were not rated as "highly important" (IQR 3-4) by the patient group in round 2 of the Delphi study. The scores of importance varied across the four participant groups, and therefore, the rationale to retain these issues in the guideline list was not strong.

2) Issues with the SPIF guideline content

The participants listed five main issues included in the guideline document that were missing from the sample SPIF. This information included trial requirements, patient benefits, patient rights, contact person information, and the randomized procedure process. Participant comments on these issues indicated that the guideline instructions needed more precision and refinement to ensure that specific information requirements were addressed. These comments were used by the study team to further refine the guideline document.

3.2.4 Improvements to the structure/wording/language

Twenty-eight participants provided optional comments on the structure/wording/language of the sample SPIF. The two largest groups of comments related to wording suggestions and the structure of the section on risks and side effects. Suggestions focused on improving the plain language of the document, such as using "orally" instead of "by mouth," and "eaten" instead of "ingested." Regarding risks and side effects, the decision initially was only to list common or severe risks/side effects in the sample SPIF. Most participants suggested providing the percentage occurrence of common or severe risks/side effects in order to add to patients' understanding of risks and side effects.

The participants' comments indicated that the guideline instructions needed more precision and refinement to ensure that specific information requirements were addressed.

3.3 Draft guideline revision

The original guideline document included three sections: the background, instructions for the design of the summarized patient information for cancer clinical trials, and suggestions for SPIF formatting. Considering that the function of this guideline is to assist health professionals with creating a SPIF, instructions about using the guideline were added to the document to help health professionals gain a better understanding of

how to use the guideline document and extract the most important information from a PICF.

During the pilot testing process, the feedback indicated the need for more details about and strategies related to the presentation of complex information. The original section, "Suggestions for SPIF formatting" was changed to "Recommendations for use of plain language in a SPIF." Examples were attached to each recommendation in this section to explain the differences between technical language and plain language and to assist health professionals with the development of plain language statements. Further, an introduction to undertaking a readability check was added.

With regard to the complexity of the trial information, a recommendation to use bullet points to simplify complex information was added (Plain English Campaign, 2009). A recommendation on the use of locally applicable language was also added to assist with the international applicability of the guideline.

3.4 Utility and clarity

The results indicated that the five SPIFs had a high level of consistency, with extraction of key information from the PICF. The researcher and four health professionals correctly followed the guideline instructions to present key information against 15 of the 21 items in the checklist. An additional four items were correctly presented by the researcher and three health professionals. Of the remaining two items related to cost and common risks and side effects of the standard treatment, only the researcher and two health professionals correctly followed the instructions to present relevant information. In response to these results, the study team modified parts of the guideline content to improve the clarity of the instructions for these two items.

Table 2 lists the results of the readability tests for the sample PICF and the sample SPIF created by the researcher (SPIF #1), as well as the versions of the SPIFs created by the four health professional volunteers (SPIF #2-5). In this study, the Flesch-Kincaid reading ease score for the sample PICF was 58.7, and reading level was 9.3, which equates to

being fairly difficult to read (Ridpath, Greene S. M., & Wiese C. J., 2007). After following the SPIF guideline, the ease of reading scores of the SPIFs created by the researcher and four health professional volunteers were between 61.3 and 66.5, with reading levels between 7.8 and 8.8. These data indicate that the SPIF guideline can assist health professionals with the generation of understandable information using plain language.

3.5 Guideline finalization

The revised guideline document was presented to the reference group, seeking final input regarding wording, structure, and other general comments. Overall, the reference group members provided positive feedback. A few minor changes to the wording were made, and more examples were added to the guideline instructions to prompt health professionals on how to convey clear, understandable information. In addition, an expert on plain language in health care information proofread the SPIF guideline document. Appendix 1 presents the final version of the SPIF guideline document.

4. Discussion

The study involved guideline formation, application, revision, and utility, and clarity assessment. After the draft guideline was formulated, it was applied to a sample PICF to create a sample SPIF for further feedback and revision from the participants. The researcher and four health professionals used the revised guideline to create five versions of the SPIF based on a sample PICF. This was done to assess the utility and clarity of the guideline. The final guideline presents information that can be regarded as understandable as a result of the consensus process, as well as information considered to be the most relevant to supporting patient decision-making when considering clinical trial participation.

In the guideline development process, the target audience, and the desired outcomes need to be clear (World Health Organization, 2014). The SPIF guideline is aimed toward assisting health professionals create a short and concise SPIF as an adjunct to the full PICF to support patient decision-making related to trial participation. Therefore, health

professionals are the main audience for the guideline, and the outcome is that the SPIF can be reliably used as a communication tool between health professionals and patients during the informed consent process.

According to the National Health and Medical Research Council (NHMRC) standard, clinical practice guidelines must make clear and actionable recommendations in plain English for health professionals practicing in an Australian health care setting and must be easy to navigate for end users (National Health and Medical Research Council, 2016). If health professionals merely copy key information from a PICF and paste it into a summarized document, the technical language or medical jargon will still limit patient understanding. Therefore, the summarized document should include plain language, short sentences, diagrams, and bullet points (Kim & Kim, 2015). To address this, the guideline includes recommendations for plain language and examples to assist health professionals with preparing the information in plain language. The results of the study indicate that the SPIF guideline can assist health professionals with generation of understandable summarized information since the use of plain language lowered the original reading level (the sample PICF) from a Flesch-Kincaid score of 9.3 to between 7.8 and 8.8. The results from the study indicate that the SPIF guideline document meets these criteria and can be used as a tool to communicate with patients considering participation in a clinical trial.

If English is not a patients' first language, physicians may feel that communication with this patient group about clinical trial participation is too challenging and may in turn not offer trial participation. Nguyen, Somkin, Ma, Fung, & Nguyen (2005) conducted a pilot study to assess barriers to participation in cancer research for Asian-American women. Oncologists and patients agreed that language discordance is an important barrier to physician-patient communication. Their results also indicated that more Asian oncologists than non-Asian oncologists had referred (75.0% vs. 9.5%, $p \leqq 0.001$) and enrolled (40.0% vs. 9.5%, $p<0.05$) Asian-American women in industry trials (Nguyen et al., 2005). An US study explored the clinical trial enrollment rates according to the participants' primary language. English speakers comprised 92% (n=1421) of the trial

participants. For the remaining 8% of the participants, their first language was not English (Staples et al., 2018). However, if there is a plain language document summarizing key information about clinical trial participation, physicians may be more willing to provide the plain language document about trial participation to non-English speaking patients and to consider them as potentially eligible for inclusion. These documents may also be easier and less costly to have translated for use in clinical trials and can be created in a digital form.

Summarized patient information documents or plain language sheets are extensively used in clinical practice to assist patients with understanding and making decisions about clinical trial participation (Jefford & Moore, 2008; Kim & Kim, 2015). However, no robust guideline has previously existed to help health professionals create a summarized document. This may in turn have implications for the outcomes of research previously undertaken to test the impact of summarized patient information on patient outcomes, such as retention of key study messages. The current study participants were the previous Delphi study members, and the response rate was 64.5%. The high response rate indicates that participants were willing to be involved in this research over time. Over 62% of participants consistently participated in the Delphi study, whereas nearly 50% of participants were involved in both the Delphi study and the guideline testing. The high level of participant engagement across the whole study adds to the trustworthiness of the results.

A limitation of the study is that it only focused on application, utility, and clarity of the guideline. The guideline document has not been tested in a real trial environment to determine whether the document (SPIF) fulfills requirements as a patient decision support tool and enhances the understanding and communication of patients. Even though the study team provided a set of recommendations for developing a SPIF for health professionals, and there is early evidence of the reliability of the SPIF development process using the guideline, further work is needed to test application of the guideline in various cancer trial environments. Future researchers could consider utilizing or applying these critical elements in content design as an audio-visual resource

through DVDs or videos or as an enabler of discussion with patients during the consent process. Currently, the SPIF guideline document is only available in English. Future work might usefully involve translating the SPIF guideline into other languages, where the document could assist health professionals in non-English speaking countries to condense complex trial information and initiate enhanced informed consent for patients and families.

This manuscript presented the processes followed to develop the SPIF guideline document, including formulation, application, revision, utility and clarity assessment, and finalization. The development process ensured equity of voice engagement and produced essential, understandable information to support patients' decision-making process. When patients read a SPIF, the intent is that it will assist them gain an understanding of the essential requirements for clinical trial participation. This development process produced a reliable guideline document to guide health professionals to create their own SPIF from a PICF in their setting. This document was aimed toward supporting patient understanding of cancer trial participation during the informed consent process. Ongoing updates of the guideline document and further testing of the SPIF in clinical practice is recommended.

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Guideline document for informing the content of a Summarized Patient Information Form (SPIF) regarding cancer clinical trials

Authors:

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Table of Contents

1. Background

Ethical review processes support the need to present comprehensive information to enable cancer patients to make informed decisions about whether or not to participate in a clinical trial. Evidence indicates that many people affected by cancer find Participant Information and Consent Forms (PICFs) hard to read and understand. As a result, researchers have tried a variety of interventions to enhance patient understanding of the information provided in these forms. Studies indicate that these interventions have not improved patient comprehension. One possible reason for the limited success to date is a lack of evidence regarding what information is essential to enable informed consent. Such evidence could be used to guide the development of more user-friendly Summarized Patient Information Forms (SPIFs).

To address this knowledge deficit, we undertook a study using a Delphi process to establish consensus on essential elements of a SPIF, as defined by key groups (Kao, Aranda, Krishnasamy, & Hamilton, 2018). These groups included patients with cancer and their families, multidisciplinary health care professionals, ethics committee members, and representatives from pharmaceutical companies. The Delphi process generated 30 highly important statements. These were reduced (through the Delphi methodology) to a final list of 15 essential statements (Kao et al., 2018). We developed a guideline (presented below) that explains how researchers and clinicians may use the statements to generate a SPIF. Note that a SPIF should be used in conjunction with a full PICF.

2. Instructions on using the SPIF guideline

On the following pages, we provide advice to guide the development of your SPIF, including:

- "preferred language" (in italics and bold)

- format (in standard black text)
- examples of key words and phrases (in the box).

The guideline addresses four main sections of the SPIF. It is recommend that you follow the guideline instructions and highlight essential information from the PICF before you start drafting your own SPIF. Ensure that you use plain language in your SPIF to convey and explain information contained in the detailed PICF, in order to enhance patient understanding. Please ensure that all sections relevant to your study are included and numbered appropriately in the final SPIF.

In the final section of this document, we provide recommendations for how to use plain language in the SPIF. We strongly advise that you read and follow these recommendations before you develop your own SPIF in order to maximize the usefulness of the document for patients.

3. Instructions for the design of a SPIF for cancer clinical trials

Summarized Patient Information Form

Study title:

Study number:

Contact person: ***Telephone:***

List the study title, study number, and contact details for the key contact person. Consider directing patients to the relevant page on the PICF for further information.

1) What is the trial for?

Write the purpose of the trial here, explaining what this trial aims to do and how trial care differs from standard care.

For a phase I trial, explain that the purpose is to determine the maximum dose at which a study drug or new treatment can be given safely. For a phase II trial, explain that the purpose is to test the efficacy of a drug or treatment with a larger sample of patients than previously tested in a phase I study and to further evaluate its safety. For a phase III trial, explain that the purpose is to find out which of two or more treatment options offers the best change of cure or disease control through comparing the efficacy of the study drug or new treatment with the current standard treatment/care.

Examples: essential plain language statements for phase I, II, and III trials

[Phase I]
The purpose of this study is to find out:
- the best dose (or dose range) of the study drug
- the safety and side effects of the study drug in your type of disease
- how the body absorbs and handles the study drug.

[Phase II]
The purpose of this study is to find out if the drug we are testing is safe and is effective at treating your type of cancer.

[Phase III]
The purpose of this study is to find out which treatment is best for treating a specific condition. To find out which one is best, we need to compare different treatments. To do this, we put people into groups and give each

group a different treatment. Then, we compare the results from each group to see if one treatment is better.

2) What is the trial design?

If the trial is an early phase trial without randomization or a placebo, state that all patients in the study will receive the study drug with or without standard treatment.

If the trial is a randomized controlled trial (RCT) or includes a placebo, explain random allocation, including the patient's chance of receiving the trial drug and their chance of receiving a placebo drug. Explain whether a patient receiving a placebo drug will still receive standard treatment or not. Also explain what the placebo is.

Example: randomized controlled trial design

You have an equal chance of receiving the study drug with the usual chemotherapy we give to people or a placebo (a liquid or tablet that has no effect) with the usual chemotherapy we give to people. Neither you nor your doctor can choose what group you will be in. Neither you nor your doctor will know what group you will be in.

3) What will the trial mean for me?

State the requirements of the trial treatment early in the SPIF. Then, list any likely discomforts resulting from the study procedures and possible risks of participation. State any possible benefits of participation. Below are examples of questions to include as subheadings in this section:

a) What will I have to do?

Include here the frequency of trial treatment, the time requirements of each hospital visit, and the cost of trial participation. These items provide an indication of the demands of participation. Details include:

- how the trial drug is administered (e.g. intravenous [‘in a vein’] or oral [‘by mouth’])
- the number of cycles in the trial
- how often the patient has the trial treatment (e.g. daily or weekly)
- whether an overnight stay at hospital is needed
- how often the trial schedule assessments are required (e.g. blood tests, scans, questionnaires, etc.)
- how long the hospital visit will be for each treatment and during follow-up (e.g. blood samples, waiting time, time required to rest before they can be discharged, etc.)
- the length of the trial treatment overall (e.g. in weeks, months, years?)
- the costs for participants if the sponsor does not fully support costs (e.g. transportation costs).

Examples: trial requirements

[Screening]

You will have these tests at the hospital or clinic to make sure that the study is suitable for you:

- blood tests
- urine tests
- physical examination
- pregnancy test (for women who may become pregnant)
- computed tomography (CT) scans
- electrocardiogram
- multi-gated acquisition scan (MUGA) (a heart scan), if you have a history of heart disease.

You may have more than one of some tests during the study. You may also have some tests more frequently than if you were receiving the standard

treatment.

[Treatment period]

If this study is suitable for you:

- You will need to come to the hospital to have your chemotherapy every 3 weeks. You will have your chemotherapy by a needle in your arm. It will take about 4 hours each time for the chemotherapy to go into your body.
- You will need to come to the hospital for your chemotherapy four to six times.
- Chemotherapy is very helpful in treating cancer but sometimes it can also make people sick. If you get side effects, your doctor may recommend that you go into hospital for treatment.
- You will need to take tablets as part of your treatment. It is IMPORTANT that you know when to take the tablets and which ones and how many to take. If you do not understand how to take the tablets or what they are for, please ask your doctor or nurse.
- Keep a diary of the time you take your tablets each day. Bring this with you each time you come for chemotherapy. We will give you a new diary each time we give you more tablets.
- Fill out questionnaires about your quality of life each time you come for your chemotherapy.
- You do not need to pay for any study tablets or study treatments when taking part in the study. You may need to pay for any standard treatment that is not part of the study.
- You will not receive any money for taking part in the study.
- Taking part in the study may result in extra costs to you, such as parking or food while you are at the hospital.

b) What are the likely discomforts from study procedures?

In this section, briefly outline any possible discomforts from the trial procedures.

Include discomforts relating to trial participation as *immediate* (during the procedure), *short term* (soon after the procedure) and *long term* (after completion the trial participation or throughout the length of the trial period).

Example: how to present likely discomforts from study procedures

During the blood test, you may feel some pain when the needle is placed in your arm. This pain will go away quickly. Some people get a bruise after having blood taken. You are unlikely to get an infection from having blood taken. Infection of the area is very rare.

c) Are there any possible risks to me from joining the trial?

Briefly outline the common risks and side effects related to the trial treatment, and describe the percentage of people who experience the side effects. If risks and side effects related to the treatment are not common, but may be severe if they occur, you still need to list them.

List the risks and side effects of the study drug and the standard treatment separately.

We recommend that you refer to the page number of the PICF for detailed information about risks and side effects related to the study treatment.

Example: explaining possible risks

Below, you will find a list of the most common side effects associated with the study/usual care drug/treatment. There is a more detailed list of possible side effects on pages XX-XX of the Participant Information and Consent Form. You should read these pages before deciding whether to take part in this study or not. ➢ *Risks and side effects related to the <u>study drug A</u>:* *Very likely – that is, 21% of people (or 1 in 5 people) taking this drug get these side effects:*

- tiredness
- nausea
- diarrhea that could cause dehydration and may be severe
- high blood pressure, which may be severe with effects on kidneys or lead to strokes
- vomiting
- decreased appetite (may lead to loss of weight)

Less likely – that is, less than 21% (or fewer than 1 in 5 people) taking this drug get these side effects:

- hand and foot syndrome (the palms of the hands or soles of the feet tingle, become numb, painful, swollen, or red. These side effects may be severe.)

➢ *Risks and side effects related to <u>CARBOPLATIN</u>:*

Very likely – that is, 21% of people (or 1 in 5 people) taking this drug get these side effects:

- a drop in the number of blood cells in your body, causing a risk of infection, bleeding, or anemia
- vomiting
- changes in kidney function as seen by blood tests (including loss of calcium or magnesium that may require treatment)
- tiredness

d) Are there any possible benefits to me from joining the trial?

List intended clinical benefits. You need to state that all trials are experimental. If the trial is a determining the maximum tolerated dose (e.g. a phase I study without the standard treatment), clearly state that the trial is experimental and that personal benefits from the trial are unlikely.

If there are no anticipated benefits, we recommend that you state that the trial will lead to new knowledge and may have a potential benefit for future patients.

Example: presenting possible benefits

The trial treatment is experimental. The benefit of the study drug to patients is unknown. We cannot promise you will receive any benefit from this study. We hope that the information we learn from this study will benefit future cancer patients.

4) Other information you may need to know

Use the questions below as sub-headings.

a) If I join the trial affect my future treatment options?

If the trial treatment will affect a patient's future treatment options, it is important to include details of the impact. List other treatment options available after the trial treatment.

If participation in the trial will not affect the patient's future treatment, it is also important to state this before the patient takes part in the trial. For example: "Before you decide whether to take part, ask your doctor if this trial could affect your future treatment options and if so, how."

b) Do I have to join the trial? Can I leave the trial after I have joined?

Briefly explain what the patient's rights are with regard to enrolling or withdrawing from the study and refer to detailed information provided in the PICF (give relevant page number).

Example: presenting participants' rights

Taking part in this study is voluntary. You may choose not to take part or to leave the study at any time. Deciding not to take part or deciding to leave the study before it has finished will not result in any penalty. You will still receive the correct medical care for your cancer. Read about your rights as a participant on page XX of the Participant Information and Consent Form. You should read this page before deciding whether to take part in this study.

4. Recommendations for use of plain language in a SPIF

Using plain language in health information resources is very important to deliver clear, understandable messages and to achieve effective communication between health providers and patients (Australian Office of Parliamentary Counsel, 2016).

Listed below are evidence-based recommendations for achieving plain language health resources. These recommendations have relevance for developing a SPIF (Australian Office of Parliamentary Counsel, 2016; Jefford & Moore, 2008; Plain English Campaign, 2009).

1) Use "you" and "we"

Call patients "you," and call your organization or your research team "we." This will add a "personal touch" and help you avoid using passive voice.

Examples: using "you" and "we"

[Instead of:]

Study participants will receive the study medication intravenously. (X)

[Use:]

You will have the drugs through a needle in your arm. (√)

[Instead of:]

The study team cannot promise study participants will benefit from this study. (X)

[Use:]

We cannot promise you will receive any benefits from this study. (√)

2) Use "active" voice wherever possible

Using the active voice is a direct way of expressing ideas and making them clearer. Using the passive voice can sometimes make sentences longer and their meaning less clear for the reader.

Examples: passive versus active voice

[Instead of:]

This medication is to be taken before every meal. (X)

[Use:]

Take this medicine before every meal. (√)

[Instead of:]

You have been invited to participate in the study. (X)

[Use:]

The trial might be suitable for you. (√)

3) Use short sentences

Most experts agree that an average sentence length between 15–20 words enhances understanding.

Example: shorter sentences

[Sentence of 53 words]

Whether you are randomized to Group A or Group B, your chemotherapy treatment will last for a maximum of 4.5 months (6 cycles of 3 weeks), and your treatment with the study drug or placebo will last until your cancer gets worse, or you are unable to tolerate this study drug.

[Same information in five sentences of no more than 19 words]

Your treatment will take place over about 18 weeks. You will have chemotherapy every 3 weeks. This 3-week period is called a treatment cycle. You will have 6 treatment cycles. You will also have the study drug or placebo until your cancer gets worse, or you cannot tolerate it.

4) Use words that are appropriate for the reader

Cancer patients will be the main audience for the SPIF. Use language that patients understand and keep the ideas you present clear. The recommended reading level for health information resources is grade 8 or below (Jindal & MacDermid, 2017; Stossel, Segar, Gliatto, Fallar, & Karani, 2012). The grade level is equivalent to the number of years of education a person has had. For example, grade 8 would indicate that the text is expected to be understandable by an average student in year 8 in the United Kingdom or an 8th grade student in the United States.

Use a readability formula to assess the reading level if possible. Flesch reading ease and Flesch-Kincaid grade level are two popular reading formulas. You can access these two formulas from Microsoft Word or some free online readability calculators.

Extracts from Microsoft Word and websites about free readability calculators

[Word]

1) Click the Microsoft Office Button  , and then click Word Options.
2) Click Proofing.
3) Make sure "Check grammar with spelling" is selected.
4) Under the section of "When correcting grammar in Word," select the Show readability statistics check box.

After completing a check of spelling and grammar, a box will report the results of Flesch reading ease score and Flesch-Kincaid grade level. The scores of Flesch reading ease test are 0–100. Higher scores indicate the texts are easier to read (60–70: understood by students aged 13–15 years, 90–100: understood by students aged 11 years).

[Free websites to check readability]

www.readability-score.com

www.read-able.com

5) Use bullet points instead of complex information

If you have a lot of information to present, use bullet points to divide the information into logical "stepping stones." This is easier for the reader to understand and can help keep the reader's attention.

6) Use local language

If the PICF is developed in another country, the SPIF provides an opportunity to ensure language is context-specific, e.g. "nurse baby" in Canada is equal to "breastfeeding" in Australia.

7) Keep a SPIF between 2–4 pages

The purpose of this document is to assist patients with understanding essential information about a trial in which they might participate. This is a supportive document, read in conjunction with a PICF. We recommend that

the document be no longer than 4 pages. Remember you can encourage the patient to refer back to the full PICF for detailed information at any time.

5. References

Australian Office of Parliamentary Counsel. (2016). *Plain English manual*. Canberra, Australia: Australian Office of Parliamentary Counsel. Retrieved from https://www.opc.gov.au/publications/plain-english-manual

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Stossel, L. M., Segar, N., Gliatto, P., Fallar, R., & Karani, R. (2012). Readability of patient education materials available at the point of care. *Journal of General Internal Medicine, 29*(9), 1165-1170. doi:10.1007/s11606-012-2046-0

TABLE 1 Online survey sample characteristics

	Patients	Physicians	Allied HPs	Others
Gender				
Male	6	17	2	12
Female	12	7	33	11
Age				
18-30	1	--	1	--
31-40	--	7	11	5
41-50	3	12	17	1
51-60	10	4	6	10
61-70	3	1	--	6
71+	1	--	--	1
Education				
High school	3	--	--	1
Technical school/ apprenticeship	1	--	--	2
Diploma	3	--	2	3
Undergraduate	3	1	16	5
Master	4	7	10	4
PhD/Doctorate	3	13	3	8
Other	1	3	4	--

Allied HPs: Allied health professional group, Others: other significant people

TABLE 2 Readability test results

Items	Sample PICF	SPIF#1	SPIF #2	SPIF #3	SPIF #4	SPIF #5
Words	4061	787	909	998	1110	773
Paragraphs	237	44	26	47	56	60

Sentences	177	49	56	45	57	42
Flesch-Kincaid reading ease scores	58.7	65.9	61.3	63.5	66.5	62.4
Flesch-Kincaid reading levels	9.3	8.1	8.7	8.4	8.8	7.8

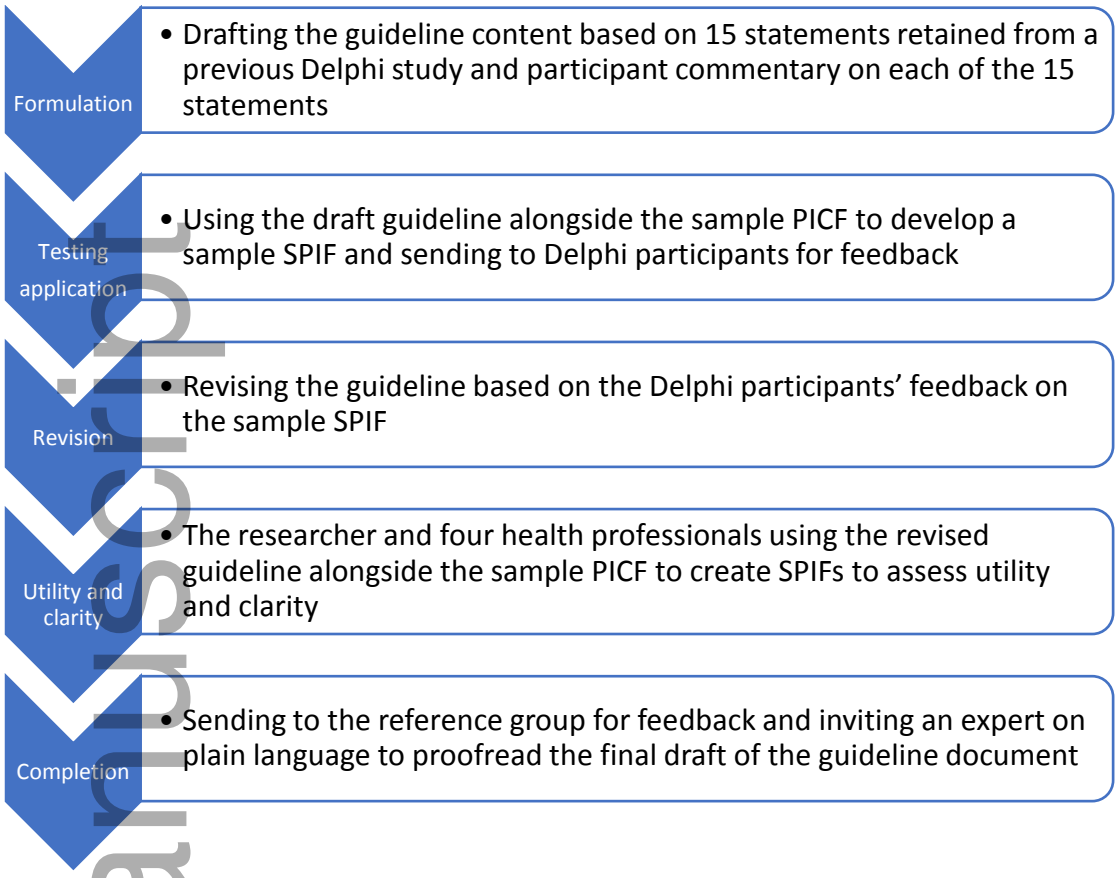

FIGURE 1 The five step process used to complete the guideline document

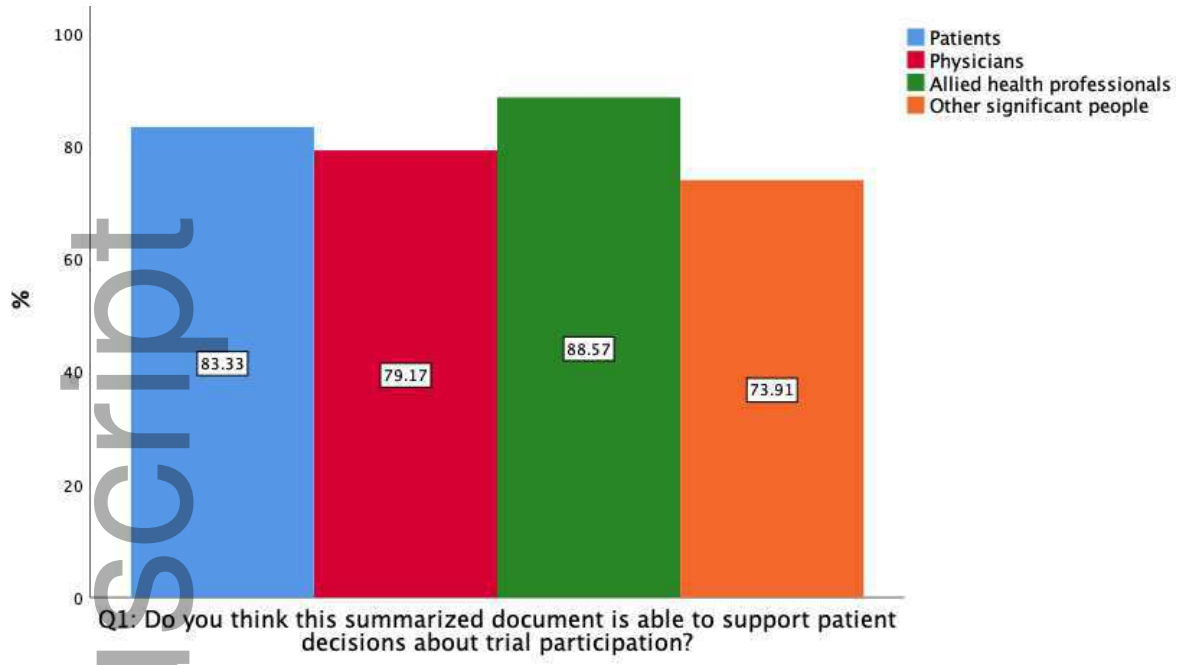

FIGURE 2 Acceptability of the SPIF

Author/s:
Kao, C-Y; Aranda, S; Krishnasamy, M; Hamilton, B

Title:
Development and testing of a guideline document to provide essential information for patient decision making regarding cancer clinical trials

Date:
2020-06-18

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http://hdl.handle.net/11343/275924