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Title

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Running Head

Essential information when considering trial participation

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Identifying essential information to support patient decision-making regarding participation in cancer clinical trials: a Delphi study

Abstract

Purposes: This research set out to contribute to ongoing efforts to improve the quality of informed consent information provided to patients by specifically focusing on establishing consensus with regard to essential information to enhance the informed consent process.

Design and Methods: A Delphi consensus method was used to conduct three rounds of online surveys. Five groups of experts directly or indirectly involved in the informed consent process were invited to participate: patients, family members/friends, physicians, other health professionals, and other key informants, including ethicists, contract research staff, and pharmaceutical company staff.

Findings: Of 156 eligible participants, 101 participants (64.7%) completed all three rounds. In round 1, 994 information items were reported and generated into 74 statements. These were grouped under eight headings essential to the informed consent process. In rounds 2 and 3, the list was reduced to 15 statements representing consensus on essential information to be included in a summarized patient information document to support decision-making regarding trial

participation. Risks and discomforts, participation requirements, and trial governance were identified as important considerations.

Conclusions: The 15 essential statements identified in this study could be used as components of a summarized information sheet given to potential cancer clinical trial participants, as an adjunct to the informed consent process. A robust evaluation of the impact of these statements on the quality of the informed consent process is needed.

Keywords: Cancer, Clinical trial, Consensus process, Delphi, Informed consent

1. INTRODUCTION

Cancer clinical trials are aimed toward finding new ways to improve treatment and quality of life for people with cancer (US National Institutes of Health, 2017). New drugs undergo three phases of knowledge development, each having particular goals and tasks. Phase I trials test a new drug or treatment for the first time in humans to evaluate safety, determine a safe dosage range, and identify side effects in a small group of usually 20-80 patients. Phase II trials continue to address drug safety, while also assessing the efficacy of the drug in a larger group (100-300) of participants. Depending on the results from Phase I and II trials, randomized controlled trials (RCTs) are the gold standard for Phase III trials (US National Cancer Institute, 2016). Phase III trials have a larger number of participants ranging from several hundred to several thousand. In Phase III, the efficacy and adverse effects of a new drug are compared to a standard, an experimental treatment, or a placebo (US National Cancer Institute, 2016). The results of Phase III trials become source data to determine final approval of drugs at the country level (Mulaje, Birajdar, Patil, & Bhusnure, 2013).

Informed consent issues arise during all trial phases. In Phase I and II trials, most participants have advanced cancer that is normally unresponsive to standard treatment, and the trial drug may offer the only form of treatment available. For consent to be informed patients need to understand that there may be no direct

benefit from the drug; yet the lack of a direct benefit does not prevent patients from entering trials in the hope of benefit. Phase I and II informed consent discussions are often difficult because participant's prognoses may be poor, and there are likely limited treatment options (Wall et al., 2015). In addition there is a requirement that clinicians can communicate subtle but important differences about the intent of trials according to their phase. Participants need to understand the genuine uncertainty about the benefits of one treatment over another with opportunities for alternatives to trial participation fully disclosed (Wells et al., 2012).

Studies report that misunderstanding of trial intent among trial participants is a critical issue impacted by the quality of the informed consent process. For example, patients seeking a cure may rely on an overly positive interpretation of the trial outcome (Barrett, 2005; Flynn et al., 2008; Jefford et al., 2011; Jenkins, Anderson, & Fallowfield, 2010). When patients view an invitation to participate as the last chance to be treated, they may not fully focus on trial requirements such as additional hospital visits interrupting their daily routine, and this can contribute to decisional regret (Cohn & Larson, 2007; Cox, 2002; Wootten, Abbott, Siddons, Rosenthal, & Costello, 2011). Given that Participant Information and Consent Forms (PICFs) are often lengthy and difficult to read, a range of interventions have been developed and tested to improve the quality of information provision during the informed consent process (Antoniou et al., 2011; Kao, Aranda, Krishnasamy, & Hamilton, 2017; Kirby, Calvert, McManus, & Draper, 2013; Nishimura et al., 2013). In a systematic review of 54 interventions tested in randomized controlled trials to improve understanding of informed consent, Nishimura et al. (2013) concluded that enhanced consent forms and extended discussion between participants and medical staff were most effective in improving participant understanding of research informed consent processes. More recently Kao et al. (2017) highlghted the lack of evidence regarding what constitutes essential information required by patients to make an informed decision regarding cancer clinical trial participation. They asserted that provision of or access to essential information would assist the patient in navigating complex informed consent information and would ensure that attention is paid to those elements likely to impact the patient's decision or those required for ethical research conduct (Kao

et al., 2017; Nishimura et al., 2013).

In this research, the goal was to contribute to ongoing efforts to improve the quality of informed consent information provided to patients by specifically focusing on establishing consensus with regard to essential information intended to enhance the informed consent process. The research question posed to the study participants was: "If you were asked to take part as a patient in a cancer clinical drug trial today, please list what information would be essential to help you decide whether to take part or not." No specific trial phase was specified, as the intent was to generate consensus statements that could be of relevance to any potential cancer clinical trial patient.

2. METHODS

A three-round Delphi consensus process was used. The Delphi technique is a consensus method focusing on topics where evidence is uncertain due to a lack of scientific evidence or where there is controversy regarding the evidence. The technique is commonly used in the health sector for various purposes, such as developing nursing and clinical practice guidelines or clinical indicators (Campbell, Braspenning, Hutchinson, & Marshall, 2002). The Delphi method provides a structure for expert group decision-making using rating procedures to represent the extent of agreement (consensus measurement) and for resolving disagreements (consensus development) about pre-defined issues (Fretheim, Schünemann, & Oxman, 2006). Once the research question is determined, the main task is to select qualified expert participants with knowledge of the topic being investigated to participate in the Delphi surveys (Fiore, Bialocerkowski, Browning, Faragher, & Denehy, 2012). Delphi surveys are structured with three or more rounds, where each round builds on the results of the previous one, and a series of rounds are used both to gather and to provide information regarding the research question (de Villiers, de Villiers, & Kent, 2005).

The Delphi process for this study involved the use of online surveys to enable wide geographic participation and to overcome the potential power imbalance between patients and others. Ethical approval was obtained from the Cancer Center's Ethics

Committee.

2.1 Participants

A range of experts directly or indirectly involved in the informed consent process for cancer clinical trials were recruited to gather rich, comprehensive data about information required in the consent process. Five groups of participants were invited to take part in the study: patients, family members/friends, physicians, other health professionals, and other individuals involved in clinical trials, such as patient advocates, ethics committee members, contract research staff, pharmaceutical company staff, and academic researchers.

Patients were eligible if they were 18 years or older, diagnosed with cancer, had participated in a cancer clinical trial prior to recruitment for at least three months, could concentrate on study requirements up to 30 minutes, and could read English. Family/friends were eligible if they had supported a family member or friend receiving a trial treatment at least three months prior to being approached for recruitment and were able to read English. Physicians, other health professionals, and other individuals involved in clinical trials were eligible if they had more than three years of work experience in cancer clinical trials. Ethics committee members had to have had experience reviewing cancer clinical trials at least twice a year over the past three years. Details of how screening for eligibility took place are reported below.

The Delphi approach requires a sample of 15 to 30 carefully selected experts for a heterogeneous population (de Villiers et al., 2005; Loo, 2002; Murphy et al., 1998). Since the response rate for online surveys is low, reported to be between 20-30% (Nulty, 2008), to ensure a minimum sample of 30 participants after three rounds with a 10% attrition per round, a total of 150 participants across the five participant groups was required at round 1. A minimum sample of 30 participants at round 2 and round 3 was desired [formula = 150*0.2 (response rate)*0.9 (10% attrition) = 33).

2.2 Recruitment process

Purposive and snowball sampling approaches were used to recruit potential participants. Patients were recruited from Australia, Europe, the United States, and Taiwan via two metropolitan cancer centers and a range of patient organizations. Eligible patients were asked to identify family/friends interested in participating and to facilitate communication for recruitment purposes. Professionals were identified from cancer centers internationally, journal author lists, research team members' networks, and Human Research Ethics Committees (HRECs) at institutions in Australia. The Clinical Oncology Society of Australia (COSA) and pharmaceutical companies known to be active in cancer clinical trials in Australia, Europe, and Taiwan were also approached to provide information about the study to their members and staff. An individual invitation email containing a consent form was sent to potential participants. For those potential participants contacted via a support group or an organization, an invitation email containing a consent form was sent out via the organization/group on behalf of the study team.

2.3 Preparation of the e-surveys

Each round of the study was administered through SurveyMonkey, an e-survey tool. To confirm participant eligibility, an electronic screening questionnaire was designed using skip logic. Skip logic directs respondents through different paths in a survey based on question logic (SurveyMonkey, 2017). This function allows the system to identify eligible participants using inclusion and exclusion criteria allowing participation to end when an individual is deemed ineligible.

Several strategies were used to increase the response rate. The introductory email was designed to engage the interest of potential participants through including details of the survey purpose and a clear explanation of participant contributions and requirements should they decide to take part in the study. The questions were kept concise, with a logical flow throughout, and a progress bar on each page enabled participants to monitor their progress through the e-survey (SurveyMonkey, 2017). A reminder email was sent to non-responders two weeks after the initial invitation.

One month later, a second reminder was emailed (SurveyMonkey, 2017).

A pilot test (n=10) assessed the wording and clarity of the questions, the flow of the questionnaire design, the links between each page of the questionnaire, and developed estimates of the time requirements. Pilot study participants included three research team members, four nurses, and three social workers from different hospitals. These data were not included in the final data set.

2.4 Delphi process

2.4.1 Screening process

After sending the invitation emails, participants were asked to click or enter the uniform resource locator (URL) attached in the email to record their consent and to complete the eligibility screening process. Participants were required to identify their primary role related to cancer clinical trials and to answer a series of questions to determine their eligibility as a member of that category of participants. If participants were eligible, they were automatically linked to the round 1 survey.

2.4.2 Round 1

The aim of round 1 was to generate an exhaustive list of statements about essential information that a patient would need to make an informed decision regarding participation in a clinical trial.

The round 1 survey consisted of a single question: “If you were asked to take part as a patient in a cancer clinical drug trial today, please list what information would be essential to help you decide whether to take part or not.” Participants were asked to record at least three essential items of information and to provide any comments they believed relevant to the topic. Responses from each of the five groups were managed separately and pooled within the respective group. Each response (words, phrases, or sentences) from a participant group containing more than one thought were expanded into different phrases or sentences to keep each single thought separate. Phrases/sentences from a participant group with the same or a very similar meaning were grouped together. An idea was generated to cover phrases/sentences

with the same or a very similar meaning.

Ideas were clustered and ordered into eight groups of related responses for logical flow when conducting informed consent, and a heading was given to each group. The ideas were clustered and ordered according to findings from a comprehensive literature review of 29 papers that focused on patient decision-making regarding participation in a cancer clinical trial and informed consent processes in cancer clinical trial contexts. Additionally, nine PICFs were reviewed from four Phase I, three Phase II, and two Phase III cancer clinical trials that had been completed over 5 years prior and without further follow up at a study cancer center. The authors analyzed the headings, subheadings, and content of the PICFs and compared these to findings from round 1, ensuring that the statements generated from round 1 covered relevant information related to the consent process. Four research team members were involved in this process.

A series of ideas under each heading was then re-phrased as question statements potentially asked by patients during the informed consent process. All statements from each participant group were pooled together, with duplicate statements eliminated. Before any duplicate statement was eliminated, the research team reviewed the statement against the original survey response to ensure any nuances of meanings were retained. Findings from the literature review and an analysis of the PICFs were reviewed and compared to the pooled statements to verify relevancy or missing concepts. Finally, a single list of statements related to essential informed consent information was generated.

An independent reference group, 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 anti-cancer drugs reviewed the analytical decisions at each round and provided comments for rounds 2 and 3.

2.4.3 Round 2

An email invitation with a URL to the round 2 survey, along with a summary of findings from round 1 was sent to eligible participants. In round 2, the list of

statements generated in round 1 was reduced by asking participants to rate the importance of each statement from the point of view of a patient considering participation in a clinical trial. Each statement was rated for importance on a five-point Likert scale ranging from 0 (not at all important) to 4 (extremely important) to a patient considering participation in a cancer clinical trial. The statements were presented under the eight headings.

After round 2 data collection, an inter-quartile range (IQR) and a box-plot were used to amplify distinctive features of group priorities. To reduce the number of items, a statement was considered highly important if its IQR was between 3 and 4 on the five-point Likert scale, which was equivalent to 75% of the group participants rating the statement as “very important” or “extremely important.” Data distributions of areas rated as “highly important” were similar between the family/friends and the other individuals. Family/friends were combined into the ‘other individuals’ group. Data in round 2 were presented as four groups, including patients, physicians, other health professionals, and other individuals.

Two criteria were used to inform consensus decision-making for statement retention for round 3: any statement with an IQR of 3-4 across the four participant groups or an IQR of 3-4 across the patient group and any other two groups. Statements meeting the first criterion showed that 75% of participants from each group agreed that retained statements were “very important” or “extremely important.” The second criterion was intended to support retention of patient prioritized statements with sufficient across group consensus. The inclusion of the IQR rule for “any statement with an IQR of 3-4 across the patient group and any other two groups” for carrying forward statements ensured that there was focus on the primacy of patient responses across the study rounds.

2.4.4 Round 3

An email invitation, with a URL to round 3, along with a summary of anonymous findings from round 2 was sent to eligible participants. Round 3 was intended to refine and further reduce the statements retained after round 2. Round 3 consisted

of dichotomous choice questions comprising “essential” or “optional” attached to each statement retained from round 2. The goal was to reduce the statement list to only those items considered essential to patient decision making. If a statement was selected as “optional,” participants were encouraged to comment on the circumstances where this statement may be essential. Participants could argue for the inclusion of any statements excluded after round 2 that they felt were essential to summarized patient information.

Data from the dichotomous choice questions were analyzed based on the frequency of options rated as essential or optional. To avoid downplaying the family/friends’ views, data distribution between the family/friends, and the original other individuals was examined in round 3 to see whether they remained similar. Given that they continued to hold the same views, their data were combined into the ‘other individuals’ group again. A statement was considered for retention if it was rated as “essential” by 80% of participants across all groups or by 80% of the patient group and any other two groups. Additionally, statements identified as essential by the physician group and the other health professional group were discussed with the research team and the reference group to inform judgements about inclusion. Participant comments on re-inclusion of statements excluded from round 2 were also analyzed.

3. RESULTS

3.1 Participants

A total of 222 people agreed to participate in the study with 156 meeting eligibility to participate (70.3%). Figure 1 shows the completion rates from screening to round 3. Of the 156 eligible participants, 28 were patients (17.9%), 15 were family/friends (9.6%), 32 were physicians (20.5%), 56 were other health professionals (35.9%), and 25 were other individuals involved in trials (16.0%). Most participants (55.4%, n=31) from the other health professional group were nurses, including nurses working in a cancer unit (n=17) and nurses involved in cancer clinical trials (n=14). The rest of the participants from the other health professional group were 20 clinical trial

coordinators and 5 pharmacists. Finally, 101 (64.7%) participants completed all three rounds of the Delphi surveys. Of these 101 participants, 21 were patients (20.8%), nine were family/friends (8.9%), 25 were physicians (24.8%), 31 were other health professionals (30.7%), and 15 were other individuals involved in trials (14.9). All responses at each round were included in the analysis.

3.2 Round 1

In response to the question, "If you were asked to take part as a patient in a cancer clinical drug trial today, please list what information would be essential to help you decide whether to take part or not.", round 1 produced 831 individual words, phrases, or sentences across the five groups with 994 different information items capturing all individual responses. Phrases or sentences containing more than one information item were expanded into multiple statements to keep each information item separate, explaining that 994 different information items formed 831 responses. The 994 items were then grouped into 131 individual ideas, with 26 from the patient group, 12 from the family/friend group, 30 from the physician group, 39 from the other health professional group, and 24 from the other individuals. These ideas were re-phrased into question statements under eight headings. The statements from each group were pooled together, and duplicate statements were eliminated. The retained statements reflected findings from the literature review and information presented in the PICFs reviewed for the study. A list of 74 statements, framed as questions potentially asked by patients during the informed consent process was generated and grouped under the eight headings (Table 1). The 74 statements formed the basis of the survey content for round 2.

3.3 Round 2

A total of 117 participants completed the round 2 survey for a 75% completion rate, with 30 statements retained. Twelve statements achieved an IQR over three across

all participant groups. Most of these statements related to the trial design (chance of receiving the trial drug/placebo), trial participation (requirements to participate and costs), and risk/discomforts/benefits. Eighteen statements achieved an IQR over three across the patient group and two other groups. Of these statements, the largest group related to trial participation (7/18, 38.9%). Only two statements showed concordance between the patient group and the physician group, possible benefit of participation (Q45) and the contact person for further information (Q63). However, nearly all statements (16/18, 88.9%) indicated concordance between the patient group and the other professional group and the other significant people group. Statements excluded in round 2 related to the communication of trial results, detailed information about sponsors, trial investigators and institutions, and other specific questions with regard to specific medical conditions.

The 30 statements retained from round 2 reflected informed consent content often highlighted in published literature. Thirty statements formed the survey content for round 3 (Table 2).

3.4 Round 3

In round 3, 114 usable responses were collected, representing a completion rate of 73.1%. Eight statements were rated as “essential” by 80% of participants across all groups while three statements were rated as “essential” by 80% of the patient group and two other groups. Three additional statements were identified as essential by the physician group and the other health professional group and were retained at this stage after discussion between the research team and the reference group (Table 2). Most of these statements related to possible risks and discomforts (4/14, 28.6%), details of trial participation (3/14, 21.4%), and the ethics and governance of the trial, including future treatment options, differences between trial care and standard care, and contact persons (3/14, 21.4%). The remaining four statements related to the purpose of the trial, trial design (chances of receiving the trial drug or the placebo drug), and personal benefit.

Eleven participants suggested re-inclusion of four statements excluded from round 2.

Of these, statement Q55, “What are my rights to enroll or withdraw from the trial?” was retained because it was rated “as highly important” (IQR 3-4) by three participant groups, but not the patient group, in round 2. The statement is fundamental to the protection of participants’ rights in research and is critical to ethical approval. The remaining statements were determined by the research team as not having a strong case for retention.

A final fifteen statements were retained from the Delphi process, comprising the essential content of a summarized patient information document to support patient decision-making related to cancer clinical trial participation.

4. DISCUSSION

The provision of a consent form with detailed information is one part of the entire consent process required to satisfy legal and ethical obligations and to respect participants’ autonomy and protect them from harm by supporting them in making an informed decision (Beauchamp & Childress, 2013). However, researchers have noted that information and consent forms are often lengthy and complicated (Antoniou et al., 2011). Summarized patient information sheets or plain language sheets are extensively used in clinical practice to assist patients with understanding and making decisions about clinical trial participation (Gillies, Skea, MacLennan, Ramsay, & Campbell, 2013; Jefford & Moore, 2008). However, no robust evidence has previously existed to help health professionals integrate essential information into clinical interventions, which may account for the reported lack of efficacy in improving patient understanding of clinical trial participation and ability to give informed consent (Kao et al., 2017). This study provided an opportunity for a broad range of participants experienced in clinical trials to voice their views and demonstrated both differences and similarities across and between participant groups when discussing essential information pertinent to recruitment to a cancer clinical trial. In addition, nearly 65% of participants completed all three rounds of Delphi surveys. This high level of participant engagement across the entire study demonstrates the trustworthiness of the results and speaks to the importance of the research, which kept participants interested in contributing their knowledge to this

important research question over time (Fiore et al., 2012).

The study generated a list of information regarding clinical trial participation from five different perspectives, which was condensed through a consensus process into a series of essential information statements. Patients are the main consumers in the informed consent process. To ensure patient needs remained at the center of the process, patient voices were privileged during rounds 2 and 3 of the decision-making process through a priori decision-making for the selection criteria for each round. However, despite the primacy given to the patient voice, there were some examples where items were carried forward from round to round based on important ethical, policy, or legal requirements. For example, issues such as randomization and patients' rights in trial participation were carried forward even though they were not rated as "highly important" by patients. Through two survey rounds, a list of 994 information items was narrowed to 15 statements that represented consensus on the information regarded as essential to support a patient's decision-making related to cancer trial participation. These essential statements could be applied and presented to potential trial participants in a concise document to be used as an adjunct to the informed consent process.

In rounds 2 and 3 of the Delphi survey, the participant groups all identified issues related to the trial purpose, risks and discomforts related to trial participation, and requirements for trial participation, as high priority issues for patients. Patient misunderstandings or misinterpretations of the unproven nature of trial interventions has been repeatedly noted as an issue (Burke, 2014; Jefford et al., 2011). Patients' desire to survive may reduce the importance they place on the experimental nature of clinical trials, potentially leading them to overestimate trial benefits and underestimate trial burdens (Howie & Peppercorn, 2014). For example, patients have expressed that being offered an early phase trial with limited treatment benefits was like, "the light at the end of the tunnel," but evidence shows that many patients are unable to describe the purpose of an early phase trial offered to them (Cox, 2000). The findings from this study demonstrate that knowing the purpose of a trial is a key component of the informed consent process.

Clinical trial participation can be time consuming and can also result in physical and emotional burdens for patients and their support networks, such as extra visits for side effect management, additional scans, and repeated blood draws. Evidence suggests that some patients start questioning their decision or experience decisional regret after commencing a trial as a consequence of unanticipated issues (Cox, 2002; Wootten et al., 2011). Essential resources required for participation including transportation, child care, and the ability to manage extra expenses in terms of time, energy, and money may be overlooked or unexpected (Cohen et al., 2007; Cox, 2000). During the consensus process, all participant groups reported that knowing all of the trial participation requirements was highly important for decision-making. However, information about the requirements of trial participation is underrepresented among existing informed consent documents (Dellson, Nilbert, Bendahl, Malmström, & Carlsson, 2011). The relevant information in a patient consent document is often spread across various sections of the document, making it difficult for patients to generate an accurate understanding of the requirements and potential impact of trial participation.

The results of round 2 indicate that the other health professionals and other individuals group had opinions much closer to the patient group than the physician group. Most participants (55.4%) from the other health professional group were nurses. Nurses support patients not only physically and medically, but also emotionally (Gordon, 2006). During the informed consent process, nurses are often the patients' key contact for clarification of questions or concerns (Murff et al., 2006). They understand the day-to-day challenges patients face as part of trial participation (Beadle, Mengersen, Moynihan, & Yates, 2011), including clinic visits, tests, and adverse events management, all of which are essential to adherence to all research protocol procedures (Kao, Huang, Dai, Pai, & Hu, 2015). Such experiences help nurses understand patients' concerns regarding trial commitments, perhaps explaining the concordance between the patient and other health professional views in this study.

Family members and ethics/human subjects committee members were important study participants. Family members were identified by patients in this study as their key support when taking part in a cancer clinical trial. Evidence indicates that family

members usually assist patients with activities of daily life and accompany them to trial treatments (Wootten et al., 2011). Ethics/human subjects committee members have a responsibility to ensure that cancer patients, as vulnerable individuals, are provided with sufficient information to protect their decision-making rights (Howie & Peppercorn, 2014).

The physician group had lower concordance with the patient group in terms of the requirements of trial participation, particularly in the round 2 results. Physicians are commonly trial investigators who seek and recruit patients for a clinical trial. They are invested in health research, which is a morally grounded and morally justified enterprise (Ghooi, 2015). Evidence indicates that physicians are concerned about whether the study design minimizes risks and maximizes benefits to patients (Emanuel, Wendler, & Grady, 2000; Howie & Peppercorn, 2014). However, ethicists have raised concerns that trial investigators may offer a trial treatment to patients for reasons other than the treatment of a patient's disease, including the impact of a successful trial on their research career or because of a direct interest in a pharmaceutical company (Emanuel et al., 2000; Korn, 2000). These interests differ from patients' concerns, such as whether clinical trial participation will cure their cancer or whether side effects of treatments will prevent enjoyment of their remaining life (Cohen et al., 2007).

According to the round 2 and 3 of results, patients placed little emphasis on randomization, use of placebos, and their rights, yet these areas were priorities for other participant groups. Qualitative studies report that patient decision-making is mostly driven by their hope to survive as well as patient trust in their oncologist's recommendations (Brown et al., 2011; Shannon-Dorcy & Drevdahl, 2011). The other explanatory factor may be that patients misunderstand the concept of random allocation or the use of placebos (Behrendt, Gölz, Roesler, VBertz, & Wünsch, 2011), further complicating their ability to make informed decisions about trial participation. To improve the quality of informed consent, researchers have used a diverse range of interventions, such as audio-video presentations and communication training to improve patients' understanding of clinical trial participation (Brown, Butow, Boyle, & Tattersall, 2007; Hoffner et al., 2012; Kass et al., 2009; Wray, Stryker, Winer, Demetri,

& Emmons, 2007). The limited effects of these interventions may be due to issues with the quality of information or the focus of information as it relates specifically to them.

4.1 Limitations

This study has limitations that must be considered. Unlike face-to-face meetings, the e-survey method used for the Delphi process could not benefit from full vocal and visual communication, including drawing on vocal and visual cues from the audience to better understand and interpret what was being said, having more opportunities to respond to complex statements, and gaining quick, immediate feedback to clarify statements about controversial or significant issues (Storper & Venables, 2004). Face-to-face communication facilitates a dynamic and meaningful exchange of views. However, research also reports disadvantages of face-to-face communication, including inhibiting minority expression, inhibiting trust in heterogeneous groups, and creating unequal participation and power relationships amongst group members (Krebs, Hobman, & Bordia, 2006). These disadvantages could be overcome through online Delphi surveys through removing coercion and equalizing potential power differences between participant groups. While the focus of the study was on the production of essential information as the foundation of informed consent, these essential statements require further testing to evaluate their impact on the quality of the informed consent process.

5. CONCLUSIONS

Risks and discomforts, participation requirements, and trial governance are important considerations for participants associated with cancer clinical trials. The 15 essential statements identified using a Delphi method in this study could be used as an adjunct to the informed consent process. Further testing to evaluate the impact of these statements on the quality of the informed consent process is required.

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Table Legends :

Table 1: Round 1 Headings and Statements

Table 2 Rounds 2 and 3 consensus results

Figure Legends:

Delphi participation rate over three rounds

Table 1: Round 1 Headings and Statements*

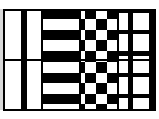
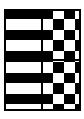
Headings and statements	
Background and purpose of the trial	
Q1	Why is the trial important?
Q2	What is this trial aiming to do?
Q3	Why am I being offered this trial?
Understanding the trial drug	
Q4	How does the trial drug work
Q5	What is the dose of the trial drug?
Q6	How is the trial drug administered?
Q7	How does the trial drug differ from the standard/other treatment?
Understanding the trial design	
Q8	What is the phase of the trial?
Q9	Does the trial design include randomization?
Q10	How are patients randomly allocated to one study group or another?
Q11	Does the trial design include the possibility of random allocation to a placebo group?
Q12	What is my chance of receiving the trial drug?
Q13	What is my chance of receiving a placebo drug if part of the trial?
Participation in the trial	
Q14	What is required of me if I choose to participate in this trial?
Q15	How long does it take to administer the trial drug?
Q16	How often is the trial drug administered?
Q17	Is an overnight stay at hospital needed?
Q18	How many appointments will I have?
Q19	How many blood tests will I have?
Q20	How many examinations will I have?
Q21	How many questionnaires will I need to complete?
Q22	How many follow-up appointments after completion of trial treatment will I have?
Q23	What is my time commitment as a result of trial participation?
Q24	What is the rationale for the trial requirements?
Q25	What is the length of trial treatment?
Q26	What is the length of follow-up period?
Q27	What do I do if I miss a dose of the trial drug?
Q28	Will I be able to receive other treatments during trial participation?

Headings and statements	
Q29	Will I be able to have a holiday/break from the trial treatment for a special occasion?
Q30	Can I be re-screened for participation in the trial if I fail initial eligibility screening?
Q31	Will I have any costs to pay?
Q32	What costs are covered by the trial sponsor?
Q33	What happens if I am injured as a result of participating in the trial?
Q34	What happens to me at the end of the trial if the drug has been beneficial?
Q35	What happens at the end of the trial if the drug has not been beneficial for me?
Q36	What happens to me if I have been withdrawn from the trial before end of the trial?
Q37	What happens to me if the study is stopped unexpectedly?
Possible risks and discomforts	
Q38	Will the trial drug have any interaction with other drugs I may be taking?
Q39	What are the situations for withholding the trial treatment/drug (contraindications)?
Q40	What are the possible risks to me of participation?
Q41	What are the possible side effects of the trial drug?
Q42	What is the likely impact of participation on my daily life?
Q43	What are the likely discomforts from study procedures?
Q44	What are the likely discomforts from study participation?
Possible benefits to me and future patients	
Q45	What are the possible benefits to me of participation?
Q46	What are the possible benefits of participation to my survival?
Q47	What are the possible benefits of participation to my quality of life?
Q48	What are the possible benefits to me of participation in the trial compared with standard treatment?
Q49	What is the anticipated efficacy of the trial drug?
Q50	What are the possible benefits of my participation in the trial to future patients?
Ethics and governance of the trial	
Q51	What are the alternative treatment options if I do not want to participate in the trial?
Q52	Will participation in the trial affect my future treatment options?
Q53	How does trial care differ from standard care/practice?
Q54	Is there any possibility that the trial is inferior to standard treatment?
Q55	What are my rights to enroll or withdraw from the trial?
Q56	How do I enroll or withdraw from the trial?
Q57	What happens if I choose to withdraw from the trial?

Headings and statements
Q58 What alternative options are available to me if I choose withdraw from the trial?
Q59 Is the confidentiality of any personal information collected as part of the trial assured?
Q60 How will my personal information be collected?
Q61 What will happen to any information about me?
Q62 How can I access my information?
Q63 Who can I contact for further information or if I have any questions?
Q64 Who is the sponsor of the trial?
Q65 Who are the trial investigators?
Q66 What are the institutions at which the investigators work?
Q67 Who will conduct the trial?
Q68 Who will monitor my cancer progress?
Q69 What is the institution's responsibility in administering the trial?
Q70 Is there any conflict of interest between the sponsor, the researcher or the institution?
Q71 Has the trial been approved by an ethics committee?
Communicating the result of the trial
Q72 If new information arises during the trial participation or after completion of the trial, how will I be informed?
Q73 How long will I have to wait to be informed of the final result of the trial?
Q74 How will I be informed the final result of the trial?

* The statements reported in Table 1 were generated from responses across each of the five participant groups

Table 2 Rounds 2 and 3 consensus results

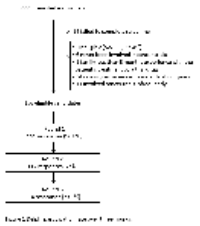
Headings and statements	IQR 3-4 in Round 2	>80% as essential in Round 3
Background and purpose of the trial		
Q2 What is this trial aiming to do?		
Understanding the trial drug		
Q7 How does the trial drug differ from the standard/other treatment?		
Understanding the trial design		
Q12 What is my chance of receiving the trial drug?		
Q13 What is my chance of receiving a placebo drug if part of the trial?		

Headings and statements	IQR 3-4 in Round 2	>80% as essential in Round 3
Participation in the trial		
Q14 What is required of me if I choose to participate in this trial?		
Q16 How often is the trial drug administered?		
Q17 Is an overnight stay at hospital needed?		
Q25 What is the length of trial treatment?		
Q28 Will I be able to receive other treatments during trial participation?		
Q31 Will I have any costs to pay?		
Q35 What happens at the end of the trial if the drug has not been beneficial for me?		
Q36 What happens to me if I have been withdrawn from the trial before end of the trial?		
Q37 What happens to me if the study is stopped unexpectedly?		
Possible risks and discomforts		
Q38 Will the trial drug have any interaction with other drugs I may be taking?		
Q40 What are the possible risks to me of participation?		
Q41 What are the possible side effects of the trial drug?		
Q42 What is the likely impact of participation on my daily life?		
Q43 What are the likely discomforts from study procedures?		
Q44 What are the likely discomforts from study participation?		
Possible benefits to me and future patients		
Q45 What are the possible benefits to me of participation?		
Q46 What are the possible benefits of participation to my survival?		
Q47 What are the possible benefits of participation to my quality of life?		
Q48 What are the possible benefits to me of participation in the trial compared with standard treatment?		
Q49 What is the anticipated efficacy of the trial drug?		
Ethics and governance of the trial		
Q51 What are the alternative treatment options if I do not want to participate in the trial?		
Q52 Will participation in the trial affect my future treatment options?		
Q53 How does trial care differ from standard care/practice?		
Q54 Is there any possibility that the trial is inferior to standard treatment?		
Q55 What are my rights to enroll or withdraw from the trial?		

Headings and statements	IQR 3-4 in Round 2	>80% as essential in Round 3
Q63 Who can I contact for further information or if I have any questions?		
Q68 Who will monitor my cancer progress?		

the patient group the physician group the other health professional group the other individuals group

Black writing on a gray background indicates the final statement retained from the Delphi consensus process.



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