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Running Head

Patients' understanding of cancer clinical trial

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Abstract

Patients' misunderstanding of cancer clinical trial participation is identified as a critical issue and researchers have developed and tested a variety of interventions to improve patient understanding. This systematic review identified nine papers published between 2000 and 2013, to evaluate the effects of interventions to improve patients' understanding of cancer clinical trial participation. Types of interventions included audio-visual information, revised written information, and a communication training workshop. Interventions were conducted alone or in combination with other forms of information provision. The nine papers, all with methodological limitations, reported mixed effects on a small range of outcomes regarding improved patients' understanding of cancer clinical trial participation. The methodological limitations included: 1) the intervention development process was poorly described; 2) only a small element of the communication process was addressed; 3) studies lacked evidence regarding what information is essential and critical to enable informed consent; 4) studies lacked reliable and valid outcome measures to show that patients are sufficiently informed to provide consent; and 5) the intervention development process lacked a theoretical framework. Future research needs to consider these factors when developing interventions to improve communication and patient understanding during the informed consent process.

Keywords: Cancer; clinical trial; understanding; informed consent; communication

INTRODUCTION

Informed consent in the context of clinical trials is a process aimed at: 1) providing participants with adequate information to enable them to make an informed decision as to whether to participate in a clinical trial; and 2) ensuring that people participate voluntarily and without coercion in research and only when the research is consistent with their values, interests, preferences (Emanuel et al. 2000). It is the physicians' obligation to disclose enough information for the patient to make an "informed" decision. Normally, detailed information about a trial is presented to potential participants through discussion and a Participant Information and Consent Form (PICF) during the informed consent process (Daugherty 1999; Emanuel et al. 2000). However, evidence indicates that overwhelming amounts of trial information and technical language used during oral discussion or included in the PICF may result in patients agreeing to participate in a trial without adequate understanding of the intervention to which they are consenting (Brown et al. 2011a). In addition, when a trial is the only treatment option, hope for extending survival may result in a patient ignoring important information such as the experimental nature of the clinical trial or the potential burdensome nature of a study (Brown et al. 2011a; Shannon-Dorcy & Drevdahl 2011; Wright et al. 2002). Valid consent may therefore be difficult to obtain in clinical practice.

Given that improving patients' understanding of clinical trial participation is a critical issue, researchers have set out to develop and test a variety of interventions to respond to this issue. Several systematic reviews have assessed whether evidence exists to support the type of interventions most likely to improve patient understanding (Falagas et al. 2009; Flory & Emanuel 2004; Ryan et al. 2009; Schenker et al. 2011). However, most of these reviews reported methodological limitations of studies reported as part of the reviews, which may impact reliable interpretation of the conclusions. Limitations include: 1) no reporting of the intervention development process; 2) no reporting of the content of intervention/information presented; 3) no reporting of the intervention/information delivery process; and 4) no consideration of the validity and reliability of outcome measures. One review that was rigorous and

credible was limited to interventions regarding audio-visual information (Ryan et al. 2009). In addition, no review had been undertaken that focused specifically on people with cancer participating in cancer clinical trials. This population of patients may face more challenges than other patient groups when considering trial participation, because of their disease status and potential for disease progression and the need for presentation of complex trial information (Brown et al. 2011a; Shannon-Dorcy & Drevdahl 2011; Wright et al. 2002). Therefore, this systematic review set out to address the research question: what interventions can improve patients' understanding of cancer clinical trial participation, during the informed consent process.

METHODS

Search strategy

The following databases were searched for articles published in peer-reviewed journals in English: Cochrane Library, CINAHL, MEDLINE, PsycINFO, and PubMed. The specific search strategies used for each database are detailed in Appendix 1. Reference lists of relevant publications of articles retrieved as part of the study were hand searched to identify additional articles.

Eligibility criteria

Inclusion criteria

This review included pre-post test, quasi-experimental, case-controlled or randomised controlled studies. Participants were limited to adults with cancer, participating in drug-related clinical trials (phase I, II or III). The types of interventions for the review included, audio-visual resources (such as DVDs), written information (such as booklets or information sheets), and oral information (such as face-to-face discussion). The interventions could be conducted alone or in combination with other forms of information provision. Studies that measured patients' knowledge, comprehension, or understanding of a clinical trial were eligible for inclusion. These were the primary outcomes of this systematic review. Studies that measured the above primary outcomes and patient satisfaction with information provided, satisfaction with the decision making process, or anxiety about the informed consent

process were also eligible for inclusion. Eligible papers were those published in a peer-reviewed journal in English with full text from 2000 to May 2013.

Exclusion criteria

Studies involving surrogates, health professionals, or family/friends were excluded, unless they were part of mixed populations that included people with cancer. Studies involving participants who were not potential clinical trial participants were excluded (e.g. simulated studies).

Study selection

Papers were screened by their title and abstract to identify whether they were potentially relevant. Three reviewers (CYK, MK and SA), then independently assessed the papers to determine if they met eligibility criteria for inclusion in the systematic review. Discrepancies were resolved by discussion. This process resulted in nine eligible papers for inclusion in the systematic review. Figure 1 outlines the stages of selection of papers for inclusion in the systematic review.

Data extraction and quality review

The study team developed a standardized data extraction template for review of each paper, based on the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0) (Higgins et al. 2011). All papers were reviewed by at least two reviewers. After completing the data extraction and quality review, the three reviewers met to ensure adequate inter-rater reliability of the data extraction process, with discrepancies resolved through discussion. The initial inter-rater reliability of data extraction was 85% and subsequently 100% after the discussion meeting. Data from the template were then entered into a table to enable comparison of the nine studies. Descriptive statistics were applied to present a summary of the information. These statistics included frequency and percentages.

RESULTS

Description of studies

Of 303 abstracts retrieved, nine studies (3.0%) met the inclusion criteria (Table 1). Of the nine papers, seven were RCTs (Agre & Rapkin 2003; Coyne et al. 2003; Hoffner et

al. 2012; Hutchison et al. 2007; Kass et al. 2009; Strevel et al. 2007; Wray et al. 2007) and the remaining two papers, were a pre-post test design (Brown et al. 2007), and a case-controlled study (Hietanen et al. 2007). Studies ranged in sample size from 49 to 441 participants; in total, 1615 people participated across the nine studies. Of the total sample, 1368 were people with cancer, who were invited to take part in a clinical trial. The other participants included 10 oncologists, 109 family members/friends, and 128 surrogates.

In terms of interventions to improve patients' understanding of trial participation, five of the nine studies used an audio-visual intervention: 1) alongside usual care or compared to usual care (Agre & Rapkin 2003; Hoffner et al. 2012; Hutchison et al. 2007; Kass et al. 2009); and 2) compared to a placebo DVD (Strevel et al. 2007). Two of the nine studies used revised written information interventions, compared to trial PICFs (Coyne et al. 2003) or a National Cancer Institute (NCI) booklet (Wray et al. 2007). Two studies held a communication skills training workshop regarding informed consent for doctors and nurses with patient outcomes assessed (Brown et al. 2007; Hietanen et al. 2007).

Assessment of study rigor

According to the Cochrane Handbook, eight specific domains were assessed for the study rigor, including random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, intervention development process, standardized intervention approach, and other bias. Results are presented in Table 2.

Random sequence generation, allocation concealment, blinding

Of the seven RCT studies, only two (Hoffner et al. 2012; Hutchison et al. 2007) described methods used to generate the random allocation sequence by contacting a central coordinating centre; these two studies also demonstrated adequate allocation concealment. The remaining five papers did not describe the randomization process or allocation concealment (Agre & Rapkin 2003; Coyne et al. 2003; Kass et al. 2009; Strevel et al. 2007; Wray et al. 2007). Of the nine reviewed studies, six used self-report questionnaires to assess intervention outcomes (Agre &

Rapkin 2003; Brown et al. 2007; Hietanen et al. 2007; Hutchison et al. 2007; Strevel et al. 2007; Wray et al. 2007), which potentially limited the influence of data collectors on participant responses, compared with being interviewed by an interviewer in three studies (Coyne et al. 2003; Hoffner et al. 2012; Kass et al. 2009). Self-report supports blinding and in that regard minimizes bias, as there is no direct contact between participants and the study researcher/data collector, which implies assessors are blind to participant responses. Self-report questionnaires can also help reduce potential for social desirability in answers, compared with interviews undertaken by a trained interviewer.

Rigor of the intervention development process

Only five studies described the process of intervention development with sufficient detail to assess the rigor of the development process (Brown et al. 2007; Coyne et al. 2003; Hoffner et al. 2012; Hutchison et al. 2007; Kass et al. 2009). Of these five studies, one followed the best practice principles of adult learning to conduct their communication skills training, including watching video scenarios about ideal informed consent behaviour, role-play practice, group discussion and reading materials (Brown et al. 2007). The other four of the five studies used a multidisciplinary panel, including health professionals and trial consumers to assist in the process of intervention development, revision of the intervention content, and provision of comments (Coyne et al. 2003; Hoffner et al. 2012; Hutchison et al. 2007; Kass et al. 2009).

Four papers reported consumer involvement in the development of interventions (Coyne et al. 2003; Hoffner et al. 2012; Hutchison et al. 2007; Kass et al. 2009). However, none of these studies reported how they dealt with any consumer feedback if and when discordant views were presented between consumers, or between consumers and other informants, such as health professionals. Furthermore, no studies explored what information was considered essential for inclusion as part of study information and critical by consumers to enable informed consent.

Mixed interventions

The interventions from eight studies were delivered in conjunction with face-to-face oral discussions with health professionals as part of the informed consent process or usual care (Agre & Rapkin 2003; Brown et al. 2007; Coyne et al. 2003; Hietanen et al. 2007; Hoffner et al. 2012; Hutchison et al. 2007; Kass et al. 2009; Wray et al. 2007). However, none of these studies described details of the oral discussions, such as whether the health professionals received training in obtaining informed consent, details of the delivery of the intervention or usual care information, or whether they used an equivalent standard for the process of gaining informed consent. The potential lack of a standardized approach potentially affects the strength and rigor of the intervention. Furthermore, no studies examined the actual content of discussions, through processes such as audio recordings. The potential differences in the delivery of information by health professionals may dilute intervention effects as part of an intervention study, particularly where multiple health professionals are involved in information delivery.

Measurement rigor

A critical methodological issue from the reviewed papers was the use of outcome measures without reporting reliability and validity information related to the specific study population (Table 1). Most outcomes in the reviewed studies were situation specific, such as measuring patient understanding of a specific trial. Therefore, most studies used self-developed tools, without reporting on content validity or construct validity during the process of measurement development, and reliability for the use of the study sample (Brown et al. 2007; Coyne et al. 2003; Hoffner et al. 2012; Hutchison et al. 2007; Kass et al. 2009; Strevel et al. 2007).

Hietanen et al. (2007) and Wray et al. (2007) used a reliable tool, the Quality of Informed Consent (QuIC) (Joffe et al. 2001), to measure patients' knowledge of clinical trials without any relevant validity data. Three studies measured patient anxiety using the State-Trait Anxiety Inventory (STAI) state version (Brown et al. 2007; Coyne et al. 2003; Hutchison et al. 2007). The STAI is a valid tool to assess patient

anxiety (Spielberger 1983). However, none of the studies re-evaluated the reliability and validity of the STAI for use with the specific study population. Two studies used a previously published scale, the Satisfaction with Decision-Making Scale (SWD) (Holmes-Rovner et al. 1996) to assess patient satisfaction with the treatment decision (Brown et al. 2007; Wray et al. 2007), but only one paper reported its internal consistency within the study population(Wray et al. 2007).

Developing a measurement scale with good psychometric properties is time-consuming. This may be the reason why most studies used self-developed tools, without reporting on reliability and validity information. Careful consideration is therefore required as to whether these study results can be considered with confidence.

Conceptual frame

Another important study design issue is that none of the studies used a conceptual or theoretical framework to support the development of interventions. The complex components across a process of information exchange and subsequent informed consent are diversely conceptualized (Bhutta 2004). The lack of an explicit framework is a considerable limitation for the intervention literature reviewed, because if a study does not have a supporting conceptual or theoretical framework, researchers may be unable to describe, explain, or predict the study outcomes with accuracy.

Effects of interventions

The nine studies reported inconsistent effects of interventions on participants' knowledge, comprehension or understanding of clinical trials. However, satisfaction with the interventions, or with decision-making regarding whether or not to participate in a trial, was high overall. The details are described below:

Knowledge, comprehension or understanding of the trial

Four studies reported that participants had significant improvements in general or specific areas of understanding, or knowledge regarding a clinical trial after physicians had taken part in a communication skills training program (Hietanen et al.

2007), or after participants watched audio-visual information (Hutchison et al. 2007; Kass et al. 2009; Strevel et al. 2007). However, some misconceptions were still reported after participants had received the intervention.

In a study of 288 participants, people receiving an intervention delivered by physicians who had receiving communication skills training demonstrated better understanding of the main purpose of a trial (as measured by the QuIC), compared to participants in a control group (physicians without communication skills training) (89% vs. 78%, p=0.032) (Hietanen et al. 2007). However, questions about the details of the trial showed that participants in both groups had misconceptions. For example, 36% of the intervention group and 42% of the control group agreed, "All the treatment and procedures in my clinical trial are standard for my type of cancer" (Hietanen et al. 2007).

Hutchison et al. (2007) reported that participants who watched the audio-visual information and read the PICF had higher knowledge scores compared with those who reviewed the PICF only (p=0.0072) . Kass et al. (2009) reported that participants given an opportunity to take part in a video group, to watch a 20-minute presentation on early phase clinical trials, were 32 times more likely to believe that the purpose of an early phase trial was to examine safety, as opposed to the efficacy of study drugs (OR=32.31, p=0.005), compared with participants in a group given the NCI booklet. However, the video group tended to report that the reason they enrolled in an early phase trial was because their physician thought it would be a good idea (70.2% vs. 48.6%, p=0.045) and that patients might benefit from the drug (46.8% vs. 25.9%, p=0.02), compared to participants in the NCI booklet group (Kass et al. 2009). Strevel et al. (2007) reported that participants in an educational DVD group were less likely to believe that the goal of phase I trials was to determine drug efficacy (p=0.019), more likely to know phase I drugs had not been thoroughly studied in humans (p=0.003), and less likely to believe that these new drugs had proven activity against cancers (p=0.008) than those in a control group. However, there was no significant difference between physician groups reporting on their perceptions of patient understanding of phase I trials (Strevel et al. 2007).

Table 3 summarizes the effect of interventions on patients' knowledge, comprehension, and understanding of trial participation.

Satisfaction with intervention strategies or treatment decision

Five studies evaluated patients' satisfaction with informational interventions (Coyne et al. 2003; Hietanen et al. 2007; Hoffner et al. 2012; Strevel et al. 2007; Wray et al. 2007), and four studies demonstrated that the intervention group patients had higher overall satisfaction with information presented compared to those in the control group (Coyne et al. 2003; Hietanen et al. 2007; Hoffner et al. 2012; Strevel et al. 2007). Of three studies evaluating patients' satisfaction with the consent process or satisfaction with decisions (Brown et al. 2007; Hietanen et al. 2007; Wray et al. 2007), only Hietanen et al. (2007) reported that patients in the intervention group (physicians who had received communication skills training) thought the time given to them for decision-making was sufficient compared with the control group (98% vs. 90%, p=0.004). These results concluded that patients' satisfaction with intervention strategies was high overall. Table 4 presents the results of patients' satisfaction with the consent process, participation decisions, or interventions.

Anxiety

Three studies assessed patient anxiety and reported mixed effects (Brown et al. 2007; Coyne et al. 2003; Hutchison et al. 2007). Coyne et al. (2003) used a self-developed consent anxiety scale to measure distress regarding giving consent to treatment, one week after the consent process and reported that patients in the easy-to-read consent statement group had significantly lower consent anxiety (p=0.016), compared with the standard PICF group. Three studies used STAI state version to measure patient anxiety after delivery of an intervention (Brown et al. 2007; Coyne et al. 2003; Hutchison et al. 2007). Hutchison et al. (2007) reported that patients who received an audio-visual intervention plus had read a PICF had lower anxiety scores (p=0.011) than those who read a PICF only at one week.

DISCUSSION

The effect of intervention strategies to improve patients' comprehension,

understanding, or knowledge with regard to clinical trial information remains unclear. The paucity and inconclusive nature of the effects reported made it difficult to draw conclusive results with regard to effect and as such the design of the interventions became a focus in order to try to understand why effects were inconsistent. The intent is to draw researchers' attention to design flaws that may hamper further progress in this area.

Nine studies, all with methodological limitations, reported mixed effects on a small range of outcomes (understanding, satisfaction and anxiety). The methodological limitations of the papers reviewed included: 1) the intervention development process was poorly described; 2) only a small element of the communication process was addressed; 3) studies lacked evidence regarding what information is essential and critical to enable informed consent; 4) studies lacked reliable and valid outcome measures to show that patients are sufficiently informed to provide consent; and 5) the intervention development process lacked a theoretical framework.

Studies without sufficient detail to describe the development of interventions do not allow assessment of the rigor of the development process (Craig et al. 2013). Informed consent is a communication process. None of the reviewed studies examined the content of the intervention discussion, or the modes of delivery of that information. Potential differences in the delivery of information by health professionals are likely to confound outcomes measured as part of the intervention studies reported. Studies reviewed lacked convincing evidence regarding what information is essential to enable informed consent and as such, may explain the results of the reviewed studies with regard to the failure of the information presented to meet patients' information needs. In addition, a lack of reliable and valid outcome measures may have compromised the ability to measure intervention effects. Finally, it is important to have a conceptual or theoretical framework to provide an organizing structure for the development of the intervention, to guide the development and testing of hypotheses, explain how the intervention works and which factors facilitate or inhibit the effectiveness of the intervention. The Medical Research Council (MRC) guidance also points out the importance of using an appropriate theory. This is more likely to resulting in an effective intervention than is

a purely empirical or pragmatic approach (Craig et al. 2013).

The informed consent discussion is a complex engagement process and the final goal is to assist potential participants to understand information about clinical trial participation and then make a decision regarding trial participation (Bhutta 2004). Often patients are asked to consider taking part in a clinical trial at a key time point, such as very soon after diagnosis, or at a time when the disease has progressed. At these times, people may be unprepared or unable to deal with new and often complex information about trial treatments, processes and procedures (Stevens & Ahmedzai 2004). They may need more opportunity and time for discussion to clarify any questions or concerns regarding trial participation across several clinical visits (Beadle et al. 2011; Hietanen et al. 2000; Jaspers et al. 2006; Wright et al. 2002). Patient understanding of trial participation is an early outcome to assess whether the informed consent process is successful. However, most studies reviewed used invalid tools to measure patient understanding. It is necessary to develop a reliable and valid measure to assess patient understanding of trial participation.

Satisfaction with the intervention strategies was significantly higher for participants in intervention groups than for participants receiving usual care. This demonstrates that satisfaction with intervention strategies may be a poor indicator of intervention impact on targets of comprehension and understanding (Jefford et al. 2011). Evidence supports that patients with cancer participate in a trial based on hope for personal benefit or trust in their physicians' recommendation (Brown et al. 2011b; Madsen et al. 2007). However, they may also feel regret about their decision to participate, particularly in an early phase trial (Cox 2002; Wootten et al. 2011). If the interventions reviewed offer limited capacity to improve patients' understanding or knowledge of clinical trial participation, even though patients may report improved satisfaction with the intervention strategies offered, patients may still feel frustrated or unhappy with their decision to take part in a trial. Therefore, in line with measuring patients' understanding or knowledge of clinical trial participation, level of comfort with the decision made or decisional regret should be considered as a key indicator of success when assessing the effects of intervention strategies. Overall, there is a lack of studies focusing on decisional comfort or regret and other factors,

such as participants' physical or psychological distress as key variables of interest in the development and measurement of effective interventions.

CONCLUSIONS AND RECOMMENDATIONS

To date there are no guidelines to advise health professionals about what critical information regarding clinical trial participation should be included in information or new interventions developed to enhance potential trial participants' understanding and knowledge. The results of this systematic review indicate the necessity for development of new testable interventions based on an explicit conceptual frameworks, that recognize the relationship of specific elements of a new intervention to other important variables in obtaining consent, and that use robust outcome measures to assess the relationship between variables and the impact of any new intervention on predefined study outcomes. In addition there is a need to understand and refine the focus of complex information, with attention to consumer perspectives. Future research needs to consider these factors when developing interventions to improve communication and patient understanding during the informed consent process.

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Table 1. Summary of the included studies

Study	Design	Participants	Types of interventions (oral discussion)	Content of interventions	Outcomes of interest	Outcome measures (reliability/validity)	Timing and number of evaluations
Agre et al. (2003)	RCT	204 patients 109 family/friends 128 surrogates	● Booklet ● Video ● CAI program ● PICF (control group)	● Unclear	● Knowledge	● Multiple-choice quizzes developed by the study team to assess knowledge(+/-)	● Once, immediately after the consent process.
Brown et al. (2007)	Pre-post test	10 oncologists 90 patients	● Communication skills training workshop for physicians	● Watching video scenarios about ideal informed consent behavior ● Role-play practice ● Group discussion ● Reading materials.	● Knowledge ● Anxiety ● Satisfaction with decision	● Ellis Clinical Trial Knowledge Scale (-/-) ● STAI (state version) (-/-) ● SWD (-/-)	● Four times, at baseline, two days after physician consultation, two weeks and three months after the consultation.

Coyne et al. (2003)	RCT	226 patients	● Easy-to-read consent statement ● PICF (control group)	● Unclear	● Comprehension ● Anxiety ● Satisfaction with decision ● Satisfaction with interventions	● True/false and multiple-choice questions developed by the study team to assess comprehension (-/-) ● STAI (state version) (-/-) ● Satisfaction scale developed by the study team (+/-) ● Consent anxiety scale developed by the study team (+/-)	● Once, 1-2 weeks after the intervention.

Hietanen et al. (2007)	Case-controlled trial	288 patients	● Communication skills training workshop for health professionals	● Lectures covering the psychological reaction to somatic disease, interviewing techniques and patients' needs when receiving trial information. ● Illustrating poor quality of informed consent. ● Role play ● Group discussion ● Reading material	● Understanding ● Satisfaction with informed consent	● QuIC (-/-) ● Satisfaction questionnaire developed by the study team (-/-)	● Once, 3.5 months after patients were randomized.
Hoffner et al. (2012)	RCT	90 patients	● Video + PICF ● PICF (control group)	● Unclear	● Understanding ● Satisfaction with interventions	● QuIC (modified version) (-/-) ● Satisfaction questionnaire developed by the study team (-/-)	● Once, within a week after the intervention to evaluate understanding and next clinic visit to evaluate satisfaction.

Hutchison et al. (2007)	RCT	173 patients	● AVPI + PICF ● PICF (control group)	● AVPI covering generic and cancer site-specific trial information.	● Knowledge ● Anxiety	● Knowledge questionnaire developed by the study team (-/-) ● STAI (state version) (-/-)	● Twice, at baseline and one week after baseline.
Kass et al. (2009)	RCT	130 patients	● Computer-based presentation ● NCI booklet (control group)	● Computer-based presentation describing trial purposes, risks/benefits, and emphasizing voluntary of trial participation. ● NCI booklet describing trial purposes, randomization, participant protection, and benefits/ risks in trial participation.	● Understanding	● Multiple-choice questions developed by the study team to assess understanding (-/-)	● Once, immediately to 1 week after the intervention and discussion with an oncologist about trial participation.

Strevel et al. (2007)	RCT	49 patients	● Educational DVD* ● Placebo DVD (control group)*	● Educational DVD including trial types/purposes, early phase drug development, trial requirement, toxicity, side effects, and possible outcomes. ● Placebo DVD describing research accomplishments of scientists and investigators at the study team's institute.	● Knowledge ● Satisfaction with interventions	● True/false and multiple-choice questions developed by the study team to assess knowledge (-/-) ● Satisfaction questionnaire developed by the study team (-/-)	● Once immediately after viewing the DVD

Wray et al. (2007)	RCT	118 patients	● Trial tailored brochure ● NCI booklet (control group)	● Brochure addressing elements of the PICF for each trial. ● NCI booklet addressing information that cancer patient need to know in trial participation.	● Understanding ● Satisfaction with decision	● QuIC (+/-) ● SWD (+/-)	● Twice, 2 and 8 weeks after informed consent and the interventions and discussion with an oncologist about trial participation.

CAI program: computer-assisted instructional program; PICF: participant information and consent form; AVPI: audio-visual patient information

NCI booklet: US National Cancer Institute booklet; *interventions delivered without face-to-face oral discussions as part of the informed consent process

STAI: Spielberger State and Trait Anxiety Inventory; SWD: Satisfaction with Decision Scale; QuIC: Quality of Informed Consent

"+" with outcome measure reliability or validity data for the study sample; "-" without outcome measure reliability or validity data for the study sample

Table 2. Methodological quality summary

Study	Random sequence generation	Allocation concealment	Blinding (outcome assessors)	Incomplete outcome data	Selective reporting	Intervention development process	Standardized intervention approach	Other bias
Agre et al. (2003)	●	●	●	●	●	●	●	●

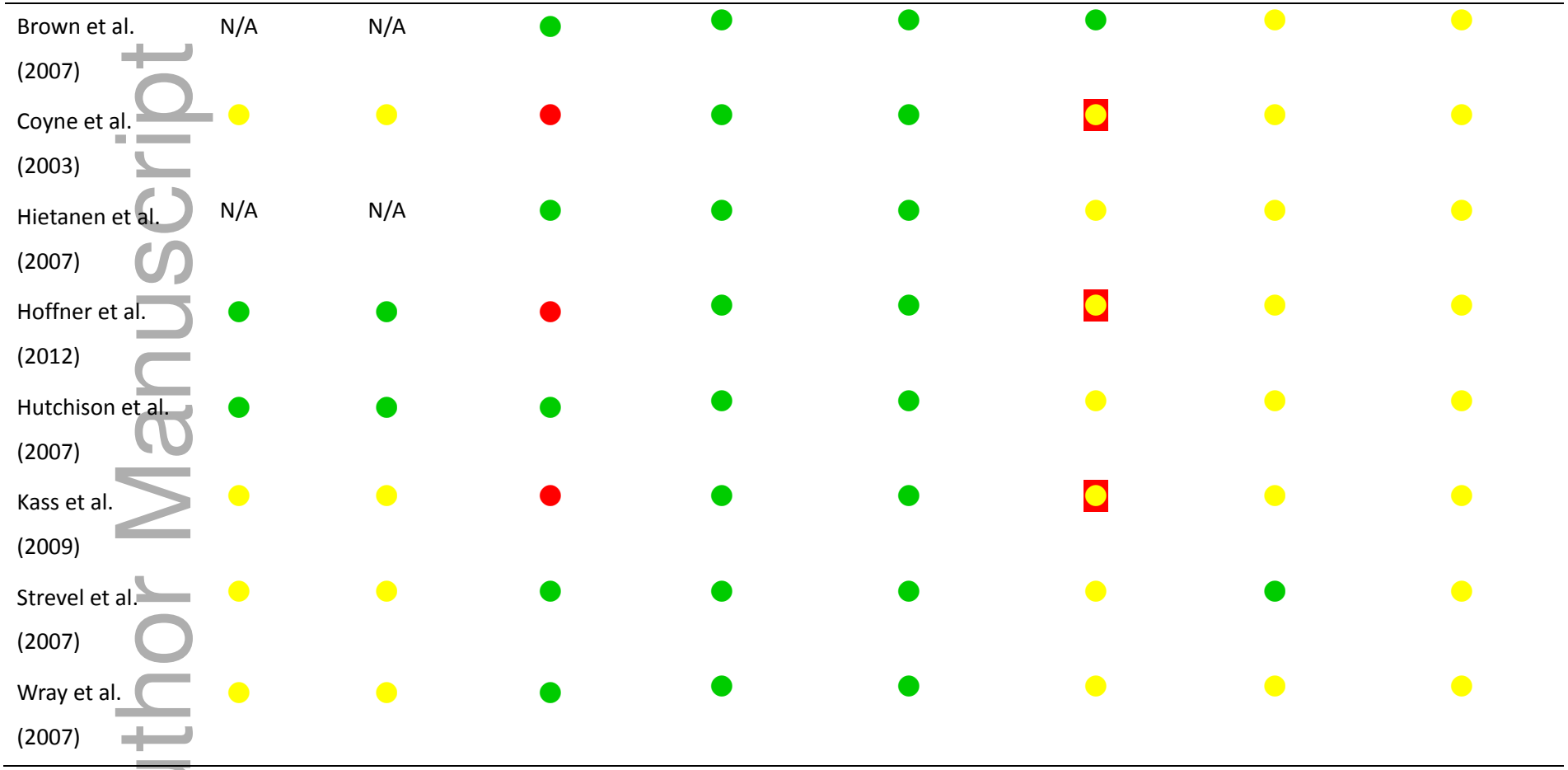

Table 3. Intervention effects on knowledge, comprehension or understanding of clinical trial participation

Author (Year)	**Endpoint**	**Results**
Agre et al. (2003)	Knowledge	No significant difference in proportion of correct responses to knowledge quizzes among four types of interventions, PICF, booklet, video and CAI program, across patients from 18 clinical trials.
Brown et al. (2007)	Knowledge	No significant difference on patients' knowledge scores before and after physicians' participation in a communication skills training workshop.
Coyne et al. (2003)	Comprehension	No significant difference in number of correct responses to 23 true/false and multiple-choice questions between groups who read the easy-to-read consent statements and those given the PICFs.
Hietanen et al. (2007)	Understanding	Patients treated by the physicians who received communication skills training (the intervention group), demonstrated better understanding of the main purpose of the trial as measured by the QuIC than control group participants (89% vs. 78%, p=0.032). However, questions about the details of the trial showed that participants in both groups had misconceptions. For example, 36% of the intervention group and 42% of the control group agreed, "All the treatment and procedures in my clinical trial are standard for my type of cancer".
Hoffner et al. (2012)	Understanding	No significant differences in scores on the modified QuIC between a group of participants who watched a video plus reading a PICF and a group who only read a PICF.
Hutchison et al. (2007)	Knowledge	Results from a 12-item knowledge questionnaire showed that participants who watched audio-visual information and read the PICF, had higher knowledge scores compared to those who reviewed the PICF only (p=0.0072).
Kass et al. (2009)	Understanding	Results from a self-developed questionnaire showed that participants in the video group were 32 times more likely to believe that the purpose of an early phase trial was to examine safety, as opposed to efficacy of study drugs (OR=32.31, p=0.005), compared with participants in an NCI booklet only group. However, the video group tended to report that the reason they enrolled in an early phase trial was because their physician thought it

Author (Year)	Endpoint	Results
		would be a good idea (70.2% vs. 48.6%, p=0.045) and patients might benefit from the drug (46.8% vs. 25.9%, p=0.02) compared to those in the NCI booklet group. Many other aspects of understanding remained unchanged in both groups.
Strevel et al. (2007)	Knowledge	Results from a self-developed questionnaire showed that participants in an educational DVD group were less likely to believe that the goal of phase I trials was to determine drug efficacy (p=0.019), more likely to know phase I drugs have not been thoroughly studies in humans (p=0.003) and less likely to believe that these new drugs have proven activity against human cancers (p=0.008). However, there was no significant difference between the two groups on physician perception of patient understanding of phase I trials.
Wray et al. (2007)	Understanding	No significant differences in subjective QuIC scores were reported between participants who received only the NCI booklet and those who received the tailored brochure.

Table 4. Satisfaction after receiving the intervention strategies

Author (Year)	Endpoint	Results
Brown et al. (2007)	Satisfaction with treatment decisions and the informed consent process	No significant difference in participants' satisfaction whether physicians had received the communication skills training or not.
Coyne et al. (2003)	Satisfaction with the ease of reading consent statements	Patients who received the easy-to-read consent statements had higher satisfaction (p=0.004) compared participants who read the PICFs.
Hietanen et al. (2007)	Satisfaction with the informed consent process	Patients treated by the intervention group (physicians receiving communication skills training) had higher satisfaction with the information given to them (73%) than the control group (56%)

Author (Year)	Endpoint	Results
		(p=0.003). Patients in the intervention group thought the time given to them for decision-making was sufficient compared with the control group (98% vs. 90%, p=0.004).
Hoffner et al. (2012)	Satisfaction with the DVD	Generally participants reported a favorable experience in watching the Clinical Trial Video: 85% found the video was an important source of information about clinical trials; 81% felt better prepared to discuss the trial with their physician; 89% of those who watched the video with family indicated that it helped family better understand clinical trials; and 73% indicated it helped the family to accept their decision about trial participation.
Strevel et al. (2007)	Satisfaction with the DVD	Compared with patients randomized to a placebo DVD group, participants in the educational DVD group were more likely to agree/strongly agree the video provided useful information (p<0.001); agree/strongly agree with the DVD as a good source of knowledge about phase I clinical trials (p<0.031); agree/strongly agree they will have more questions to ask their physicians (p=0.017) and; agree/strongly agree that a DVD helped them decide whether to enter a phase I clinical trial or not (p=0.011).
Wray et al. (2007)	Satisfaction with decisions and reading materials	No significant difference was found between both groups in this study to assess a NCI booklet or a tailored brochure. High levels of satisfaction with decision-making and with materials were reported between the NIC booklet group and the tailored brochure group.

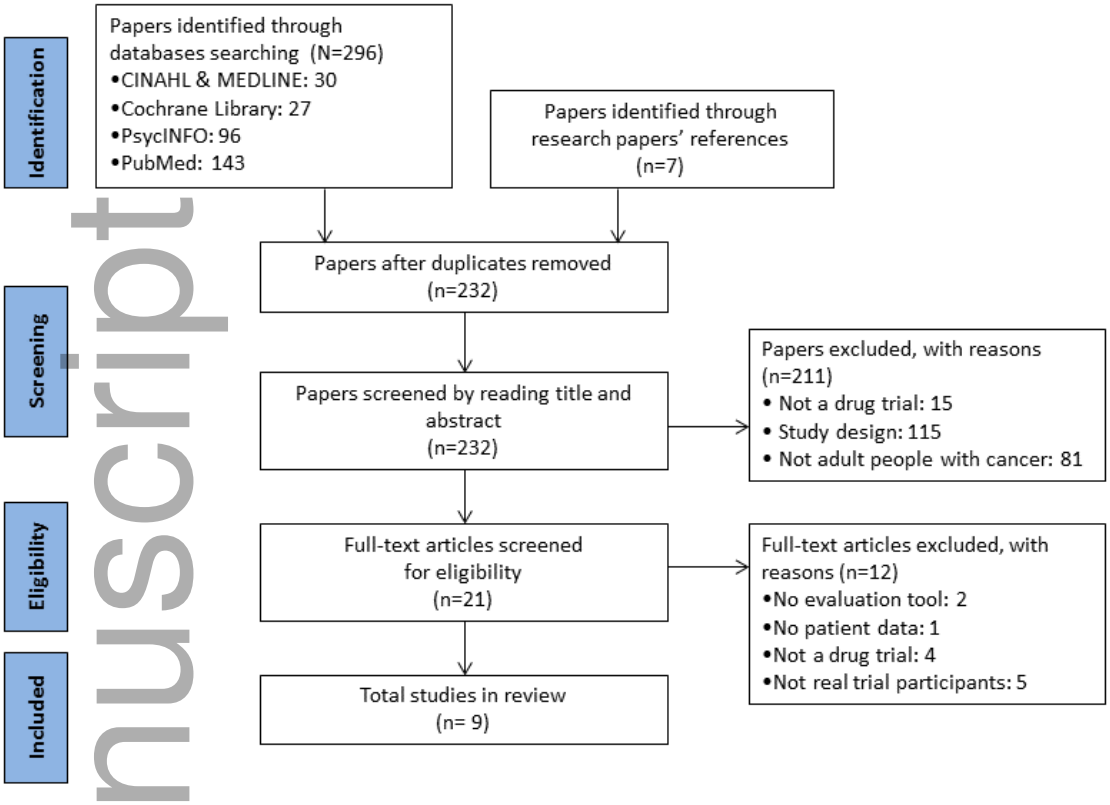

Figure 1. Flow chart drawing the main stages of the systematic review