Decision Making for Cancer Clinical Trial Participation: A Systematic Review

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Purpose/Objectives: To describe what is known about the factors that influence cancer clinical trial decision making.

Data Sources: PubMed database and reference lists of identified articles.

Data Synthesis: Variations in research design and methods, including sample characteristics, instrumentation, time between decision made and measurement of decision making, and response rates, have effects on what is known about decision making for cancer clinical trial participation. Communication, whether in the form of education about a cancer clinical trial or as a personal invitation to join, is an important factor influencing decision making. Personal and system factors influence the outcomes of decision making for cancer clinical trials.

Conclusions: The process of decision making for cancer clinical trials is understudied. Nevertheless, the currently available cancer clinical trial decision-making literature suggests a multitude of factors that influence the outcomes of the decision to accept or decline clinical trial participation, as well as the psychosocial consequences of decisional regret, pressures, and satisfaction.

Implications for Nursing: The decision-making process of cancer clinical trials is a fertile area for research and, subsequently, evidence-based interventions. Oncology nurses are in a position to facilitate the process and to relieve the pressures patients perceive regarding decision making for cancer clinical trials that will benefit individuals and, ultimately, society.

Increased participation in cancer clinical trials would benefit individuals with cancer and society by contributing to the understanding of the effects of new cancer treatments on patient outcomes (American Cancer Society, 2009; National Cancer Institute, 2009). Limited literature indicates that the process by which patients decide to join or decline participation in a cancer clinical trial is poorly understood. This systematic review attempts to identify the factors that influence clinical trial decision making among patients with cancer by critically evaluating relevant studies. Better understanding the decision-making process may help clinicians identify ways to improve patient-provider communication, possibly leading to increased clinical trial participation. Furthermore, such information may provide opportunities to create interventions to facilitate decision making and benefit the person with cancer as well as society.

Background

Considering just the interest of society, enhanced rates of participation in cancer clinical trials should not only hasten the testing and development of effective treatments, but also save cost and energy by discounting ineffective treatments more efficiently. For people with cancer, participating in clinical trials provides access to research with the hope of extending survival time, greater access to healthcare professionals, and altruistic satisfaction.

Tejeda et al. (1996) first reported a frequently cited historical estimate of cancer clinical trial participation of less than 3%. More recent studies have reported enrollment fraction, a value comparable to cancer clinical trial participation rate, as low as 1.7% (Murthy, Krumholz, & Gross, 2004) and 0.68% (Stewart, Bertoni, Staten, Levine, & Gross, 2007). Cancer clinical trial participation varies by cancer diagnosis: for example, 3.2% in breast cancer and 0.8% in prostate and lung cancers (Murthy et al., 2004).

Several patient and system barriers to clinical trial participation have been identified, including access, perceived harm, quality of life, and diversity. Limited access to clinical trials may be related to a lack of awareness, as well as physical and financial obstacles.

A common misconception exists that cancer clinical trial participation is harmful (Epstein & Street, 2007). In fact, studies have suggested a favorable risk-benefit ratio when patients with cancer consider a phase I cancer clinical trial compared with nonvalidated therapies in which the risks may be known but the benefits unknown (Joffe & Miller, 2006; Horstmann et al., 2005; Kurzrock & Benjamin, 2005).

Most (93%) phase I cancer clinical trial research participants indicated that their quality of life was at least as important as their length of life (Meropol et al., 2003).

Yet many research studies do not address quality of life (Wagner, Wenzel, Shaw, & Cella, 2007).

Diversity is an important challenge in clinical trial participation. Advani et al. (2003) noted that African American men with cancer were less likely to participate in cancer clinical trials. Education, income, and belief in God's role in determining their fate, not race alone, affected willingness to participate in cancer clinical trials.

Patient and system factors known to influence cancer clinical trial participation are diverse. However, little is known about decision making for cancer clinical trial participation. Therefore, the purpose of this systematic review is to describe the current state of the science regarding patient decision making for cancer clinical trial participation.

Methods

Search Strategy

With the assistance of an information specialist, the researcher designed a search strategy to maximize a yield of relevant studies. PubMed was examined for the following terms: *clinical trials*, *patient participation*, and *decision making*. Search-term criteria included articles published since 2004, human research, English language, and the topic of cancer. The search was supplemented with related articles identified by PubMed and the researcher's review of the reference lists in identified articles.

Articles had to (a) be written in English, (b) include an abstract, (c) be based on studies conducted in the United States, (d) address adults with cancer, (e) focus on cancer clinical trial participation, and (f) feature original quantitative or qualitative research. The researcher reviewed all abstracts for eligibility.

Exploring research conducted only in the United States limited the review to one health system, even though that one system has a plethora of options. The review focused on the years complementing recent biomedical research advances and the evolution of decision making. The National Institutes of Health (NIH) *Roadmap for Medical Research*, released in 2004, strengthened biomedical research through discoveries and emphasized the importance of human research participants to translational research (NIH, 2009). The concept of healthcare decision making has evolved from being physician focused to having additional facets, including evidence, patient preferences, or a combination of all three. Including literature beyond the past five years may not have provided an accurate representation of the current views on decision making for cancer clinical trial participation.

Nature of the Scientific Literature

According to the described search strategy, 62 articles met the initial criteria. Twenty-four articles did not relate to cancer, and one was not in English. Twenty-four articles were rejected for the following reasons: no abstract (n = 5), location outside the United States (n = 11), not original research (n = 2), no cancer clinical trial participation option (n = 3), pediatric sample (n = 1), and sample that did not target people with cancer (n = 2). Only 13 articles from the initial search met all inclusion criteria. Three additional articles were identified via a review of references and from related articles. The final sample consisted of 16 eligible articles.

The strengths and limitations of the eligible literature are summarized in Tables 1, 2, and 3. Table 1 contrasts the factors affecting the rigor of the studies reviewed, including (a) design and method; (b) sample characteristics; (c) cancer diagnosis, clinical stage, and research phase; (d) response rate; and (e) time from decision to data collection. Table 2 summarizes the decision-making measures examined, including the (a) research question; (b) aspect of decision making; (c) instrument; (d) type of instrument, number of items, and points on scale; and (e) psychometric properties. Table 3 displays the studies' strengths and limitations and summarizes their key findings.

Sample Characteristics

Samples sizes ranged from 16 to more than 115,000 (median = 162). Thirteen of the 16 studies (81%) reported the race of the research participants. When race was reported, most participants were Caucasian (range = 69%–98%; median = 86%). One study recruited only Asian women. Thirteen studies (81%) reported gender; in eight studies (50%), most participants were men; three studies (19%) of gynecologic and breast cancers recruited only women.

Ten (63%) studies reported a mean age (range = 50–64 years, median = 57.6 years). One study (6%) reported a median age of 50 years. Three studies (19%) reported only age ranges (33–71; $\bar{X}$ = 46–55; and 72% younger than 56 years), and two (13%) did not report age.

Cancer diagnoses were reported in 10 studies (63%) and omitted in six (38%) studies. Most did not describe stage of cancer, although four (25%) reported advanced cancer. Six studies (38%) focused on cancer clinical trial participation for a phase I study, one for a phase III study, and one for a supportive care clinical trial. Eight studies (50%) did not report the phase of clinical trial.

Research Question and Variables

Thirteen studies sought to describe, assess, investigate, examine, characterize, and understand multiple aspects of cancer clinical trial participation. The aspects included the decision-making process, communication, educational interventions, perceptions, benefits and burdens, quality of life, reasons for declining participation, knowledge, relative health stock, timing of consent, satisfaction, and decisional regret. Although many studies focused indirectly on decision making, some

Table 1. Factors Reflecting the Rigor of the Studies Reviewed

Study	Design and Method	Sample Characteristics[a]	Cancer Diagnosis, Clinical Stage, and Research Phase	Response Rate	Time From Decision to Data Collection
Agrawal et al., 2006	Cross-sectional, descriptive; in-person interview with survey	N = 163 56% male 88% Caucasian $\bar{X}$ age = 58 years	NR NR Phase I	NR	Immediately after consenting to phase I research prior to treatment
Albrecht et al., 2008	Longitudinal, descriptive, mixed-method, observational; taped patient visits and follow-up phone interviews	N = 35 54% male 69% Caucasian $\bar{X}$ age = 58.9 years	NR NR NR	NR	First visit and two weeks later
Avis et al., 2006	Longitudinal, experimental; phone interview with surveys	N = 191 100% female 77% Caucasian $\bar{X}$ age = 51.5 years 42% decided not to join a cancer clinical trial	Breast Stage 2 (76%) Phase III (78%)	86%	0–50 days after decision, median = 13 days
Buss et al., 2008	Cross-sectional, qualitative, phenomenologic approach	N = 96 NR	Prostate, breast, lung Advanced (stage NR) Supportive care study	21%	At time of refusal to join supportive cancer study
Cohen et al., 2007	Cross-sectional, descriptive, mixed-method, phenomenologic approach	N = 16 62% male 88% Caucasian $\bar{X}$ age = 57 years	Solid tumors NR Phase I	NR	After the interventional trial was started
Daugherty et al., 2005	Cross-sectional, descriptive, mixed-method; semi-structured interviews	N = 162 55% male 84% Caucasian $\bar{X}$ age = 57.8 years	Solid tumors 49% gastrointestinal Advanced (stage NR) Phase I	95%	While receiving experimental agent
Gaskin et al., 2004	Cross-sectional, descriptive	N = 207 57% male 86.3% Caucasian $\bar{X}$ age = 56.4 years	Mixed, 21% colon Advanced (stage NR) Phase I	64%	NR
Hlubocky et al., 2007	Cross-sectional, descriptive, mixed-method; semi-structured interviews	N = 212 56% male 81% Caucasian $\bar{X}$ age = 59 years	Mixed, 47% gastrointestinal Advanced (stage NR) Phase I	95%	Within 7–10 days after signing consent within the first week of receiving experimental agent
Lara et al., 2005	Cross-sectional, descriptive; in-person, mailed, electronic, or telephone survey	601 were patients with cancer representing 51% of the sample NR	NR NR NR	NR	Not applicable
Markman et al., 2006	Cross-sectional, descriptive; interview for one structured question	More than 115,000 patients with cancer or family members representing patients with cancer NR	Mixed, 47% breast NR NR	NR	NR
Mathews et al., 2009	Cross-sectional, descriptive, comparative	N = 79 100% female 86% Caucasian Median age = 50 years	Gynecologic disorders, 55% had cancer diagnosis NR NR	NR	Immediately prior to the visit to discuss a cancer clinical trial

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[a] Sample characteristics included sample size, gender, race, and age as reported by the study. If not listed, the data were not reported. Other relevant sample characteristics may be included.

NR—not reported

Table 1. Factors Reflecting the Rigor of the Studies Reviewed *(Continued)*

Study	Design and Method	Sample Characteristics[a]	Cancer Diagnosis, Clinical Stage, Research Phase	Response Rate	Time From Decision to Data Collection
Nguyen et al., 2005	Cross-sectional, descriptive, mixed-method	N = 19 100% female 100% Asian Age range = 33–71 years	NR NR NR	NR	NR
Quinn et al., 2007	Cross-sectional, quasiexperimental, mixed-method; educational intervention	N = 43 59% male 87% Caucasian $\bar{X}$ age = 64 years	Lung NR NR	86%	NR
Stryker et al., 2006	Longitudinal, descriptive	N = 57 78% female 98% Caucasian 72% less than 56	Breast and prostate cancer and sarcoma NR NR	First survey, 73.7%; second survey, 65.5%; overall, 42.3	Shortly after participants were identified (exact time unknown) in person or by mail, and then six weeks later by mail
Weinfurt et al., 2005	Cross-sectional, descriptive	N = 328 56.1% male 85.1% Caucasian $\bar{X}$ age = 57.4 years	NR NR Phase I	55%	NR
Wray et al., 2007	Longitudinal, experimental	N = 118 75% female 90% Caucasian Age range = 46–55 years	NR NR NR	78%	Two and eight weeks after initial appointment when patients were identified as cancer clinical trial candidates

[a] Sample characteristics included sample size, gender, race, and age as reported by the study. If not listed, the data were not reported. Other relevant sample characteristics may be included.

NR—not reported

specifically examined the psychosocial consequences of cancer clinical trial decision making, including pressures when making decisions (Agrawal et al., 2006), decisional regret (Stryker, Wray, Emmons, Winer, & Demetri, 2006), and satisfaction with the decision (Stryker et al., 2006; Wray, Stryker, Winer, Demetri, & Emmons, 2007).

Instrumentation

The studies provided limited information on instrumentation. The most common decision-making instruments were the Llewellyn-Thomas one-item, unnamed instrument (Daugherty et al., 2005; Hlubocky, Ratain, Wen, & Daugherty, 2007) and the Homes-Rovner et al. Satisfaction with Decision Scale (Stryker et al., 2006; Wray et al., 2007). Other instruments included Joffe et al.'s Understanding of Clinical Trial Scale (Wray et al., 2007), the Decisional Regret Scale (Stryker et al., 2006), and the Karmanos Accrual Analysis System (Albrecht et al., 2008). Most studies used a single question to assess willingness, interest, or knowledge about cancer clinical trials or did not include information about the research instrument. Most studies reviewed did not report psychometric measures. Only two studies (13%) provided information on instrument reliability (Stryker et al., 2006; Wray et al., 2007).

Procedures

Design and methods: Most studies were descriptive. Five employed a mixed-methods design, using a quantitative survey or interview with observed, taped interviews. Three studies tested an educational intervention. Two studies used an experimental design (Avis, Smith, Link, Hortobagyi, & Rivera, 2006; Wray et al., 2007), and one used a quasiexperimental design (Quinn et al., 2007).

Time between decision made and measurement of decision making: Eight studies (50%) did not report any information on the timing of their research in relation to the decision regarding cancer clinical trial participation. For the studies that reported a time interval, timing ranged from prior to discussing a cancer clinical trial (Mathews, Restivo, Raker, Weitzen, & DiSilvestro, 2009) to immediately after making a cancer clinical trial decision (Agrawal et al., 2006; Buss et al., 2008) to as long as 50 days after a decision was made (Avis et al., 2006). The median time from decision to data collection regarding the decision was 11 days. Three studies used a single, repeated measure at either two, six, or eight weeks after a decision (Albrecht et al., 2008; Stryker et al., 2006; Wray et al., 2007).

Table 2. Measures of Decision Making Used in the Studies Reviewed

Study	Research Question	Aspects of Decision Making	Instrument	Psychometric Properties
Agrawal et al., 2006	To assess the decision-making process of patients who participate in phase I research	Options and alternatives, pressures when making decision, understanding of purpose and risks, and assessment of benefits	Instrument not named; 61-item survey; details not reported	Standard and behavioral pretesting; details not reported
Albrecht et al., 2008	To investigate how communication influences decision making about clinical trials	Three decision-related outcomes: enroll or not, affect and cognition, reasons for decision	Instrument not named; 10-item survey with fixed responses	Details not reported
Avis et al., 2006	To assess whether an educational intervention influences cancer clinical trial participation	Trial participation (agree, decline, no longer available); factors on personal decisions and feelings about cancer clinical trials	Instruments not named 22-item survey of knowledge of clinical trials, 4-point Likert-type scale 22-item survey (7 items on benefits and 15 items on drawbacks) of attitudes toward clinical trials, 5-point Likert-type scale 9-item survey on factors in personal decisions, 5 point Likert-type Survey on feelings about knowing about clinical trials	Details not reported
Buss et al., 2008	To explore reasons why patients would decline a supportive cancer study	Reasons for declining supportive care study may provide insight into refusals for cancer clinical trial participation	Instrument not named 1-item, closed-ended interview ("Do you want to disclose reason for not participating?")	Not applicable
Cohen et al., 2007	To describe benefits and burdens and perceived quality of life	Identification of benefits and burdens	Instruments not named 5-item semistructured interview Survey, details not reported	Not applicable Details not reported
Daugherty et al., 2005	To examine the role of spirituality in terminally ill patients who volunteer for cancer clinical trials	Preference for medical decision making	Instrument not named 1-item survey with fixed responses Llewellyn-Thomas, first author	Details not reported; article said that it had "undergone significant prior study and validation" (p. 138).
Gaskin et al., 2004	To test the hypothesis that relative health stock affects patients' decisions regarding participation in phase I clinical trials	Relative health stock (expectation of longevity and quality of life) may impact decision making	Instrument not named 7-item survey with numerically rated responses	Details not reported
Hlubocky et al., 2007	To describe differences in treatment decision-making preferences associated with complementary and alternative medicine use	Medical care decision control preferences	Instrument not named Llewellyn-Thomas, first author	Details not reported; article reported "validated instrument."
Lara et al., 2005	To describe knowledge of clinical trial options	Awareness and willingness	Instrument not named 7-item survey with fixed responses	Details not reported
Markman et al.,2006	To provide insight into variables in the decision-making process	Influence of tumor type, disease status, and age	Instrument not named 1-item, closed-ended interview	Not applicable
Mathews et al., 2009	To describe willingness to participate	Influence of demographics	Instrument not named 12-item survey with fixed responses	Details not reported
Nguyen et al., 2005	To describe barriers to Asian women's participation in cancer clinical trials	Influence of barriers	Instrument not named 3-item, closed-ended interview	Not applicable

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Table 2. Measures of Decision Making Used in the Studies Reviewed *(Continued)*

Study	Research Question	Aspects of Decision Making	Instrument	Psychometric Properties
Quinn et al., 2007	To examine perceptions, barriers, and benefits in cancer clinical trial participation	Impact of educational intervention	Instrument not named 11-item, open-ended interview Accrual rate	–
Stryker et al., 2006	To describe the relationships among timing of consent, subjective knowledge, satisfaction with decision making, and decisional regret	Subjective informed consent, satisfaction with decision making, decisional regret, and timing of consent	Satisfaction with Decision Scale: 6-item survey, Likert-type scale Subjective Informed Consent, a subscale of the Quality of Informed Consent Scale: 14-item survey with fixed responses Decisional Regret: 10-item survey with numeric responses	Cronbach alpha: previous, 0.85; current, 0.86 Intraclass correlation: 0.77 Cronbach alpha: current, 0.89
Weinfurt et al., 2005	To characterize the frequency-type of numeracy of patients who are considering a phase I cancer clinical trial	Interpretation of hypothetical statement of treatment benefits	Instrument not named; details not reported	Details not reported
Wray et al., 2007	To compare effects of print materials on satisfaction and understanding related to cancer clinical trial decision making	Satisfaction and understanding	Satisfaction with Decision-Making Scale: 6-item, Likert-type scale Joffe et al.'s Understanding of Clinical Trial Scale: 14-item survey, details not reported	Cronbach alpha: 0.94 Cronbach alpha 0.91

Response rates: Response rates varied by the type of measure and study design. Only eight studies (50%) reported response rates (range = 21%–95%, median = 71%). Verbally asking for decision-making preferences yielded the 95% response rate (Daugherty et al., 2005). Participants declined research participation because they had no interest (29%) or they gave no reason (24%). However, upon further exploration, patient and system factors, including time commitment and discomfort using or learning to use a computer, were the major reasons people declined participation (Buss et al., 2008). No study explored the difference in response rates between an anonymous, mailed survey and a face-to-face interview.

One study captured satisfaction shortly after a decision was made and followed up in two weeks to measure decisional regret (Stryker et al., 2006). Multiple timed measurements have the potential to reduce response rates. For example, in Stryker et al.'s (2006) research, the response rate was reduced from 74% with the first survey to 48% with the second.

Clinical Trial Decision Making

Clinical trial decision making is the process leading to accepting or declining clinical trial participation. This review revealed three main factors influencing clinical trial decision making: patient, provider, and treatment (see Figure 1). Patient factors were clinical trial information, decision-making style preferences, decisional regret, disease characteristics, optimism, quality of life, relative health stock (a measure of estimated longevity and quality of life), satisfaction with decision making, sociodemographic profile, spirituality, trust in God or medicine, and understanding of purpose. Provider factors were clinical trial information, coercive pressure, communication, and recommendation for participation. Treatment factors were alternative treatment options, benefits and risks, clinical trial information, phase of cancer clinical trial, and time and travel considerations.

Patient Factors

Two studies specifically explored decision making for clinical trial participation. Stryker et al. (2006) reported that understanding the risks and benefits of cancer clinical trials had an impact on decision-making satisfaction and decisional regret. Wray et al. (2007) established the value of trial-specific materials in facilitating clinical trial decision making. Educational interventions have increased clinical trial enrollment 8%–33% (Quinn et al., 2007). Clinical trial information can be considered a patient, provider, and treatment factor because information about a clinical trial must be available on the treatment, disseminated by the provider, and converted to knowledge by the patient.

Provider Factors

Provider factors may have a positive or negative influence on decision making. Whether a provider's

Table 3. Strengths, Limitations, and Key Points of the Studies Reviewed

Study	Strengths and Limitations	Key Findings
Agrawal et al., 2006	Strengths: Included information on pressures to join a cancer clinical trial; sample had a long history of treatments (average of 4.8 years) and consulted with an average of three doctors before deciding on this study. Limitations: In-person interview may have affected participants' responses; participants may not have been reflective of most clinical trial participants.	Information that the "drug kills cancer cells" is most important. Pressure occurs from tumor burden. Research participants, not others, benefit. Participants were labeled as therapeutic optimists. Particpants had pressure from others to participate.
Albrecht et al., 2008	Strengths: Observation and coding of actual consenting visits provided insight into the impact of communication on decision making; included those who chose to participate in a cancer clinical trial as well as those who denied participation Limitations: Information was not provided on the development of the un-named survey used to illicit decision-related outcomes; small sample, many were lost in follow-up.	Communication and errors in understanding were important. 77% of those offered cancer clinical trial participation enrolled. 14% offered participation denied being offered cancer clinical trial participation. 74% were accompanied by at least one person. Alliance building decreased the influence of families and the concerns about costs and adverse events.
Avis et al., 2006	Strengths: Practical recommendations for improving cancer clinical trial participation based on findings Limitations: Established and psychometrically sound tools were not used.	Research participants had higher benefit scores and lower drawback scores. Time and travel considerations were significant drawbacks. Drawbacks were more important than benefits. Benefits to others and themselves, trust, and recommendations from others were associated with decision to participate. Knowledge was not a factor that influenced clinical trial participation.
Buss et al., 2008	Strengths: Reasons for low accrual to supportive care study; strategies developed to boost accrual	Most patients indicated that they were not interested (30%) or had no reason (24%) for declining participation in a supportive care study. Time commitment was the overall major factor why people declined participation. Discomfort using and learning to use a computer was a major reason for people with lung cancer to decline participation in the supportive cancer study.
Cohen et al., 2008	Strengths: Through in-depth interviews, researchers identified that the process of clinical trials is burdensome.	The process of trial participation, including travel and time away from home, job, leisure activities, family, and friends, produced a burden that adversely impacted quality of life.
Daugherty et al., 2005	Strengths: Included concept of spirituality within the context of cancer clinical trial participation Limitations: Did not assess spirituality in those who chose not to participate; findings may be similar or divergent from those who decline participation.	Research participants who had a collaborative religious problem-solving style strongly considered the doctor's opinion when making medical healthcare decisions.
Gaskin et al., 2004	Strengths: Included those who declined participation and those who participated in the cancer clinical trial; first testing of new survey to measure relative health stock; researchers included sample of instrument to facilitate further development and use.	Study suggested that relative health stock, a measure of anticipated longevity, and quality of life form an independent construct that is not dependent upon probabilities of benefits or risks associated with cancer clinical trial participation.
Hlubocky et al., 2007	Strengths: Used validated decision-making scale, although it was not identified in the article.	Decision-making preferences were not statistically associated with use of complementary and alternative medicine. Most cancer clinical trial participants preferred shared medical decision making.
Lara et al., 2005	Limitations: Data from patients with cancer reported in aggregate with data from family, friends, general public, and others; unable to ascertain data specific to people with cancer	African Americans, Asians, and young people's willingness to participate in cancer clinical trials was not related to their knowledge of clinical trials.

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Table 3. Strengths, Limitations, and Key Points of the Studies Reviewed *(Continued)*

Study	Strengths and Limitations	Key Findings
Markman et al., 2006	Strengths: Study used a large data set to determine new information and to confirm that older adults are less interested in cancer clinical trials; participants included patients with cancer and a family member. Limitations: Information is not available on the characteristics of the sample; family member reported on behalf of the patient; unable to ascertain whether the family members' perceptions were similar to the patients'; data were not separated into results from patients and those of family members reported on patients' behalf.	Patients with cancer older than 80 years were less interested in cancer clinical trials. Patients and family members representing patients with some tumor types (e.g., non-small cell lung cancer) were more interested in cancer clinical trials. Patients and family members representing patients with the same cancer diagnosis but a more serious condition were more interested in cancer clinical trials.
Mathews et al., 2009	Strengths: Surveys were distributed by receptionist to new patients at a gynecologic oncology office. Limitations: Only half of the surveys were completed by patients with cancer.	20% indicated prior to consulting with oncologist that they would participate in a cancer clinical trial. 42% were unsure whether they could change their minds.
Nguyen et al., 2005	Strengths: Researchers studied minority sample to find barriers common with other minority cultures. Limitations: Small sample size	Asian women reported fear of side effects, language problems, competing needs, fear of experimentation, family wishes, and distrust as barriers to cancer clinical trial participation.
Quinn et al., 2007	Strengths: Provided educational intervention that significantly increased the clinical trial enrollment rate. Limitations: Lacked scientific rigor of a quantitative study	Reasons for coming to the hospital included looking for hope and options. Trust and words used by the doctor influenced decision to join the cancer clinical trial. Educational letter mailed just before first consultation increased clinical trial enrollment from 8% to 33%.
Stryker et al., 2006	Limitations: Small sample size; limited power; no control for demographic variable in bivariate analysis; response to cancer clinical trial may affect decisional regret measured at six weeks and was not reflective of decision-making process.	Early signers were less informed. Subjective informed consent and satisfaction with decision making were strongly associated with later decisional regret. Older participants signed consent earlier than younger participants.
Weinfurt et al., 2005	Limitations: A nonresponse bias inflates the average numeracy for patients considering cancer clinical trials.	75% responded correctly to interpret the aggregate probability of benefit in a hypothetical treatment statement. Adequate numeracy skills are needed to comprehend data presented to make informed decisions regarding cancer clinical trial participation.
Wray et al., 2007	Limitations: Participants were only surveyed after the intervention; preintervention testing would have allowed for greater understanding of baseline knowledge and preferences.	High overall levels of satisfaction with decision making, satisfaction with materials, and understanding in control and intervention group

clinical trial information is interpreted by a patient as coercive (Agrawal et al., 2006) or as an invitation to join the cancer clinical trial (Albrecht et al., 2008; Avis et al., 2006; Nguyen, Somkin, Ma, Fung, & Nguyen, 2005) may be dependent upon the provider's communication style (Albrecht et al., 2008; Nguyen et al., 2005) and the patient's decision-making style preferences (Daugherty et al., 2005; Hlubocky et al., 2007).

Treatment Factors

Treatment factors also may be considered system factors or research participation burdens. Time and travel considerations can adversely affect quality of life and deter cancer clinical trial participation (Avis et al., 2006; Buss et al., 2008; Cohen et al., 2007). Research participation burdens can be more important than clinical trial benefits (Avis et al., 2006).

Positive Decision-Making Outcomes

Studies reported several factors that were associated with a positive decision-making outcome (enrollment in the cancer clinical trial) or with the decision-making process (see Figure 2). Positive patient factors included being more spiritual (Daugherty et al., 2005); being younger and having more advanced cancer (Markman, Petersen, & Montgomery, 2006); having a lower relative

health stock (Gaskin et al., 2004); having adequate information (Lara et al., 2005; Mathews et al., 2009); and seeking a positive benefit, being well-informed, and not being deterred by risks (Agrawal et al., 2006). Positive decision-making outcomes occurred when providers invited patients to join cancer clinical trials (Albrecht et al., 2008). User-friendly clinical trials and a reduction in personal and system burdens promoted research participation (Avis et al., 2006; Buss et al., 2008; Cohen et al., 2007).

Discussion

Multiple Outcome Factors

As noted earlier, clinical trial decision making is the process leading to accepting or declining clinical trial participation. The decision-making process was a secondary focus of most of the studies reviewed, and its influence on clinical trial participation is a silent variable. Additional prospective studies with a primary focus on decision making are needed to better elucidate the factors influencing clinical trial participation.

This review demonstrates that healthcare professionals who communicate information and recommend cancer clinical trials influence cancer clinical trial participation. Reducing personal and system barriers can further influence the decision. This review suggests that patients with cancer—even those with advanced disease—can make their own decisions about whether to participate in cancer clinical trials. When given the option, patients with cancer may choose to participate more often rather than when someone else predetermines their candidacy for clinical trial participation (Albrecht et al., 2008).

Although other systematic reviews have added to the knowledge regarding the risks and benefits of, barriers to, and attitudes toward cancer clinical trials, as well as decision making in advanced cancer, none has focused primarily on patient decision making regarding participation in cancer clinical trials. Some systematic reviews have included factors associated with cancer clinical trials but did not include data on decision making for cancer clinical trial participation (Gaston & Mitchell, 2005; Horstmann et al., 2005; Humber et al., 2007; Koyfman et al., 2007; Kumar, Soares, Balducci, Djulbegovic, & National Cancer Institute, 2007; Mills et al., 2006; Todd et al., 2009). The variety of research questions explored in the studies included in this systematic review demonstrate the multifactorial nature of decision making for cancer clinical trials. However, the varied focus on multiple aspects of the decision-making process and the different instruments used have hampered the advancement of the understanding of the cancer clinical trial decision-making process. A comprehensive approach to explore the decision-making phenomenon with validated instruments will instruct interventional studies that facilitate the decision-making experience.

Patient Factors

- Benefits and risks preferences (Albrecht et al., 2008; Avis et al., 2006; Gaskin et al., 2004; Nguyen et al., 2005; Quinn et al., 2007; Weinfurt et al., 2005)
- Clinical trial information (Lara et al., 2005; Quinn et al., 2007)
- Decision making style preferences (Daugherty et al., 2005; Hlubocky et al., 2007)
- Decisional regret (Stryker et al., 2006)
- Disease characteristics (Agrawal et al., 2006; Buss et al., 2008; Markman et al., 2006)
- Optimism (Gaskin et al., 2004)
- Quality of life (Cohen et al., 2007; Daugherty et al., 2005; Gaskin et al., 2004; Hlubocky et al., 2007)
- Relative health stock (Gaskin et al., 2004)
- Satisfaction with decision making (Stryker et al., 2006; Wray et al., 2007)
- Sociodemographic profiles (Agrawal et al., 2006; Albrecht et al., 2008; Avis et al., 2006; Daugherty et al., 2005; Gaskin et al., 2004; Hlubocky et al., 2007; Lara et al., 2005; Markman et al., 2006; Mathews et al., 2009; Nguyen et al., 2005; Stryker et al., 2006; Weinfurt et al., 2005)
- Spirituality (Daugherty et al., 2005)
- Trust in God or medicine (Avis et al., 2006; Daugherty et al., 2005; Nguyen et al., 2005)
- Understanding of purpose (Agrawal et al., 2006; Avis et al., 2006; Quinn et al., 2007; Wray et al., 2007)

Provider Factors

- Clinical trial information (Lara et al., 2005; Quinn et al., 2007)
- Coercive pressure (Agrawal et al., 2006; Albrecht et al., 2008; Nguyen et al., 2005)
- Communication (Albrecht et al., 2008; Nguyen et al., 2005)
- Recommendations for participation (Albrecht et al., 2008; Avis et al., 2006; Nguyen et al., 2005)

Treatment Factors

- Alternative treatment options (Agrawal et al., 2006)
- Clinical trial information (Lara et al., 2005; Quinn et al., 2007)
- Phase of the cancer clinical trial (Avis et al., 2006)
- Time and travel considerations (Avis et al., 2006; Buss et al., 2008; Cohen et al., 2007)

Figure 1. Factors Associated With the Decision to Participate in a Cancer Clinical Trial

Patient and System Barriers

Identifying patient and system barriers and intervening may promote greater cancer clinical trial participation, better quality of life, and longer survival (Cheng et al., 2000; Horstmann et al., 2005; Wagner et al., 2007). Lack of information about and access to cancer clinical trials, as well as uncertainty about third-party insurance coverage and fear of side effects, are important reasons for reduced participation in cancer clinical trials (Meropol et al., 2007; Umutyan et al., 2008).

Access: Challenges in access to cancer clinical trials can be financial, physical, or informational. The

- Being more spiritual (Daugherty et al., 2005)
- Being younger and having more advanced cancer (Markman et al., 2006)
- Having a lower relative health stock, a measure of estimated longevity and quality of life (Gaskin et al., 2004)
- Having adequate information (Lara et al., 2005; Mathews et al., 2009)
- Being invited to a cancer clinical trial (Albrecht et al., 2008)
- Making clinical trials more user friendly and reducing the personal and system burdens (Avis et al., 2006; Buss et al., 2008; Cohen et al., 2007)
- Seeking a personal benefit, being well informed, and not being deterred by risks (Agrawal et al., 2006)

Figure 2. Factors Associated With a Positive Decision-Making Outcome

financial burden can be great for cancer care as well as participation in clinical trials. The obvious healthcare costs associated with cancer clinical trials include deductibles and copayments for patients who have healthcare insurance coverage for clinical trial participation. Physical barriers include reduced geographic access to cancer clinical trial locations and variations in practice settings.

Prior to the 2004 statement from the International Committee of Medical Editors, clinical trials usually were not registered. That practice limited not only public access to information about available clinical trials, but also outcome data that could be helpful in evidence-based healthcare decisions (DeAngelis et al., 2005).

Media and electronic technology provide new venues for information about treatment options, including cancer clinical trials (Gren et al., 2009; Lai et al., 2006; Umutyan et al., 2008). A positive decision-making outcome is associated with adequate information (Lara et al., 2005; Markman et al., 2006).

Perceived harm: Although none of the studies in this systematic review explored perceived harm in an analysis of 460 cancer clinical trials involving 11,935 participants, Horstmann et al. (2005) ascertained an 11% clinical response rate even though clinical benefit is never an objective of a phase I study. The chance of death resulting from toxicities from the phase I research products was less than half a percent. Therefore, phase I cancer clinical trial participation provides a favorable risk-benefit ratio.

Quality of life: As with other reports, quality of life was not a frequently reported variable (Wagner et al., 2007). Only four studies (25%) that were reviewed explored quality of life (Cohen et al., 2007; Daugherty et al., 2005; Gaskin et al., 2004; Hlubocky et al., 2007). A lower relative health stock, a measure of longevity and quality of life, was associated with a positive decision-making outcome (Gaskin et al., 2004).

Diversity: The published studies are notable for their lack of age, race, and ethnic diversity. The focus on Caucasian, middle-aged individuals precluded inclusion of the older population, in which cancer is most prevalent. Cancer is the number one cause of death among those aged 60–79 years and the second leading cause of death in those older than 80 years, surpassed only by heart disease (Jemal et al., 2009). Although the death rate from heart disease has declined steadily in the past 30 years among those aged 85 years and older, cancer deaths have increased (Jemal et al., 2009).

Cancer death rates also have racial disparities. African American men are diagnosed with and die from cancer more often than Caucasian men. Yet, although African American women have a 6% lower cancer incidence rate than Caucasian women, they actually have a 17% higher death rate (Jemal et al., 2009). Decreased cancer clinical trial participation among minorities inhibits the ability to understand reasons for disparities in cancer death rates.

This systematic review found insufficient detail regarding racial characteristics. Although information regarding race may have been omitted because of space limitations, including the participants' racial profiles would have provided greater insight into the studies. Even when race of the participants was known, small to moderate sample sizes did not allow for analysis of race, ethnic, or age differences. However, the known sociodemographic variables within this systematic review are not consistent with those of a vulnerable population (Seidenfeld, Horstmann, Emanuel, & Grady, 2008).

Underrepresented groups include racial and ethnic minorities, as well as older adults and those with low socioeconomic status. A systematic review of almost four decades of literature on cancer clinical trials participation among underrepresented groups indicated that awareness, opportunity, and acceptance of research improved enrollment into both preventive and clinical intervention trials (Ford et al., 2008).

In summary, patient and system factors that influence cancer clinical trial participation are diverse. The influence of information dissemination through educational interventions, awareness of available trials, perceived unfavorable risk-benefit ratios, anticipated effects on quality of life, and the impact of diversity has been examined. Although some factors may be amenable to change, others (e.g., age, race, socioeconomic status, cancer diagnosis) are not modifiable.

Decision-Making Preferences

One factor that did not surface in this review was the process by which patients make the decision to join a cancer clinical trial. The ideal decision-making style for cancer clinical trial participation was not identified. Although many studies indicated that shared decision

making between a patient and a healthcare provider or a patient and a family member was ideal, little data were available about the extent to which the contributing party should control the ultimate decision. Patients understand their values best but may either lack (Stacey, Samant, & Bennett, 2008) or have (Agrawal et al., 2006) adequate knowledge, therapeutic optimism (Agrawal et al., 2006), or decisional conflict (Stacey, Samant, et al., 2008), which may bias their decision making.

Although informative and preferred by some, a shared decision-making style may be more challenging and potentially inhibit clinical trial participation rates. For example, the lowest response rate (21%) was seen when dyads of patients with advanced cancer and their caregivers were invited to evaluate an Internet-based decision support program (Buss et al., 2008). Studies in which only patients were recruited had higher rates.

The role and impact of decision-making preferences, a component of the decision-making process, are not clear. Although some patients have the necessary baseline knowledge and receive adequate study information to provide informed consent, whether they would prefer advice or collaboration from a family member or healthcare provider to make a shared decision is unclear. Consenting for research participation is an autonomous process (NIH National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979), one that clinical researchers have been cautioned to avoid affecting for fear of paternalism or conflict of interest. Also, healthcare providers are not optimal decision makers for patients because they often lack thorough understanding of the patients' values. The current healthcare system seldom provides opportunities to learn more about patients' values.

Research Bias

Because most of the studies conducted were in person and not confidential, a potential existed for social desirability bias. Research participants may have felt obligated to provide the positive responses they anticipated that the researchers were hoping for instead of their honest responses. The use of an anonymous survey may reduce bias. The potential for such bias or strategies to offset it were not addressed.

Recall bias also may adversely affect decision-making research. The optimal time to assess satisfaction with decision making for cancer clinical trial participation is unknown. If evaluation is too close to the actual decision, an inflated response may occur because of the fleeting satisfaction of accomplishment in making a decision and, perhaps, pleasing the researchers. If too long of an interval passes before an evaluation of the decision-making process, researchers risk recall bias and the influence of the research study's clinical risks and benefits. Half of the studies in this review did not provide data on the timing of their research in relation to the decision. Recall bias was not addressed at all.

Limitations

This systematic review had several limitations. Variability within the construct and with the instruments of decision-making research for cancer clinical trial participation hampers conclusive findings.

Other factors not identified through this systematic review also may influence decision making for cancer clinical trial participation. Geographic barriers and financial concerns such as traveling, insurance coverage, unreimbursed time away from family and work, and other out-of-pocket expenses that are known to impede access to health care were not identified within this review. Healthcare insurance coverage can contribute to or restrict clinical research participation (Bennett et al., 2001; Simon et al., 2004; Unger et al., 2006). Some patients may pursue research participation for the benefit of free health care; others may have their insurance coverage denied if they participate in a clinical trial; others may join a clinical trial only after their insurance supports their cancer clinical trial interest (Unger et al., 2006).

The decision to include only research conducted within the United States limits generalizability. However, established decision-making support systems, universal health coverage, and cultural and societal norms would have further complicated this review by including decision-making practices not common in the United States. For example, Canada supports nurses as decision coaches (Stacey, Murray, et al., 2008), and Canada and the United Kingdom are well noted for contributions to the psychosocial oncology research literature (Travis, 2009). In developing countries, clinical trial participation may be the only option to receive any health care (de Cenival, 2008). Some countries may have cultural or compulsory preferences, including social and hierarchical norms for healthcare decision making that contrast with those common in the United States (Moazam, 2006), such as Japan's long-standing paternalistic decision-making practices (Watanabe, Takahashi, & Kai, 2008).

Gaps in the Literature

A lack of consistency among studies stifles the building of scientific knowledge regarding decision making for cancer clinical trial participation. This systematic review highlights that decision making for cancer clinical trial participation research is incomplete because of (a) a lack of adequate data on sample characteristics,

including cancer diagnosis, stage of cancer, and phase of cancer clinical trial being offered; (b) unspecified and varied times between decision making and the measure of decision making; (c) homogeneous sampling; (d) use of research instruments that lack psychometric soundness; (e) use of unidentified measurement tools; (f) the potential for social desirability response bias from in-person interviews and surveys; and (g) an unclear focus on the decision-making process. Decision-making research that employs a quantitative design using psychometrically sound instruments focusing on self-report responses from a diverse sample in as close to real time as possible with a repeated measure is needed.

Conclusions

This systematic review provides a summary of the current body of knowledge on patient decision making for cancer clinical trial participation. Future research with a sound construct for decision making, psychometrically sound instruments, clarity in process and outcome factors, and sample diversity will define the state of the science for decision making in cancer clinical trial participation. Further research in this area will enhance knowledge, strengthen interventions, and improve cancer clinical trial participation.

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