

Attitudinal Clustering of Research Participants to Optimize Patient Recruitment and Retention Programs: A Review of the Literature

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Abstract

A literature review has been performed as the first step in a scientifically based study to explore the basis for decision-making processes undertaken by individual patients seriously considering clinical research study participation. Envisioned to build on the findings of past studies of patient participation phenomena, and involving the completion of a patient survey encompassing questions focused on the elucidation of various individual-specific attitudes and preferences, this study differs in that it includes an additional dimension which will attempt to actually identify and characterize a series of "attitudinal clusters" into which groups of individuals fit. These clusters will serve to describe how certain types of patients approach, and sometimes avoid, participation in clinical research opportunities. A literature review indicates that no such study has been undertaken before. Research sponsors hope that results of this study will benefit clinical research endeavors through increasing interventional efficacy of subject recruitment and retention programs aimed at increasing and maintaining clinical trial participation in eligible and active patients. This knowledge also carries with it the potential for development of new educational and training programs focused on the dissemination of information relating to the applied practice of new and improved subject recruitment and retention approaches.

Introduction

Clinical trials, formal investigations of the effects of experimental interventions on people, generate evidence for decision-making in all areas of medicine and healthcare. The option of participating in a clinical trial can be particularly important for patients with serious or life-threatening health conditions who have limited treatment options. For these patients, participation in a clinical trial may offer the best chance of finding an effective treatment (United States General Accounting Office (GAO), 1999¹). However, today, only one in ten adults indicates that they have participated in a clinical trial, a number virtually unchanged since 2001 (8% in 2001, 10% in 2003, 11% in 2004, and 10% in 2005) (Harris Interactive News, 2005²).

Therefore, a clearer understanding of patients' attitudes, beliefs and perceptions towards clinical trials in general may give significant insight into increasing participation. One possible means of attaining this goal is through the development of a better understanding of the attitudinal and psychographic variables that influence an individual's decision to seek out, or alternatively avoid, clinical research opportunities via a scientifically designed investigation similar in nature to those widely performed for this purpose in recent years by physicians and clinical research personnel interested in patient participatory behavior, as well as in fields such as marketing and advertising where consumer preferences and attitudes are of paramount importance.

The published literature indicates that numerous factors influence patient participation in clinical trials. However, most of the evidence is not based on rigorous studies. Most of the available studies were not driven by any clear hypotheses and they focus on participation with respect to one particular area of investigation, i.e., disease-specific – cancer (Valentino, et. al., 1999³; Wells, et. al., 2006⁴), physician perspectives (Edwards, et. al., 1998⁵), patient-specific – pediatrics (Harth, et. al., 1992⁶; Wiley, et. al., 1999⁷; Tait, et. al., 2003⁸), elderly and (Kemeny, et. Al., 2003⁹) minorities (Advani, et. al., 2003¹⁰; Astro, et. al., 2004¹¹; Wells, et. al., 2006¹²).

To remedy this problem, two patient recruitment service providers, D. Anderson & Company (DAC) and Matthews Media Group (MMG) are conducting a primary research study designed to accept or reject hypotheses of how the clinical trial participant population can be segmented by attitudinal characteristics. This study may lead to the optimization of subject recruitment and retention methodologies in the clinical trial industry. Specifically, several distinct attitudinal clusters that allow the categorization of individuals according to their degrees of receptivity to participation in clinical research studies will be studied to determine reliability and validity.

Objectives under Study

The study will have the following objectives:

- Attempt to establish, independent of the proposed segmentation model, attitudinal clusters that appear naturally in the clinical trial population and are useful for improving recruitment methodology.
- Identify variables, if any, that can predict who will participate in clinical trials and who will not, in order to increase the efficacy of recruitment and retention programs.
- Identify any other meaningful patterns or attributes in the clinical trial participant population that relate to the decision to become involved in a clinical trial. This knowledge carries with it the potential for development of new educational and training programs aimed at the dissemination of information about, and applied practice of, new and improved methodologies.
- Publish and present results of the study in a scholarly journal for the education of healthcare professionals.

Participant Clusters: Attitudinal Segmentation Models

Data analyzed from preliminary exploration has resulted in the tentative definition of six psychographic clusters that may characterize the decision to participate in clinical trials. The six clusters can be described as follows:

1. Highly influenced by a physician's recommendation – slight trend toward less educated

2. Newly diagnosed – have a long-term disabling or life-threatening disease; primarily women and not age-specific; motivated to travel further and wait longer for treatment
3. In more advanced stages of disease – typically older; have exhausted other treatment options and are looking for alternatives
4. Advocates for their own health – often well-educated and reasonably affluent; generally women
5. Uninsured or under-insured – motivated by the high cost of treatment and lack of financial resources
6. Very risk-averse – current medical treatment is meeting most needs; therefore must believe treatment will benefit them personally

While trends in the limited amount of data collected to date appear to support these clusters as defined, they have not yet been tested empirically or independently.

Review of the Literature

Gaining an understanding of the factors influencing one's participation in clinical research trials has been the subject of investigation in numerous studies over the past decade. These studies have raised our consciousness to a variety of real, and in some cases, perhaps only perceived, contributing factors that have originated from evaluation of data provided by interested physicians, patients and other healthcare professionals.

While most of the studies undertaken to date offer evidence that observable personality traits, attitudes, and demographic and socioeconomic characteristics influence an individual's propensity to participate in a clinical trial, there is little research devoted to correlating these factors with this propensity. This gap is important since attitudes form the basis of preferences applied to decisions an individual faces. Further, in the absence of research to generate such correlative data, there can be no framework for understanding how personality and attitudes affect an individual's decision to participate in a clinical trial.

These findings are underscored by comments often found in the conclusions of published articles and research papers that additional research is needed to elucidate the presently obscure factors contributing to an individual's decision to participate in a clinical trial (AHRQ, 2005¹³; Ellis, P.M., 2000¹⁴; Giuliano, et. al., 2000¹⁵).

While the body of previous research into attitudinal phenomena associated with clinical trial participation has resulted in a rudimentary understanding of participatory dynamics for certain diagnoses within certain therapeutic areas, the comprehensive model needed by the many clinical research practitioners in our industry describing participatory behavior in terms of the more deeply entrenched elements of human nature, and which transcends specific diagnoses, is even farther from realization. It should be noted that this lack of comprehensiveness is not the result of a lack of forethought or merit in research to date, but simply a result of the very interest-specific nature of these previous studies as well as the lack of a coordinated effort to include multiple patient types and therapeutic areas in the quest to formulate a broad-based model of patient participation dynamics.

Because studies are often designed with very specific objectives in mind and often closely mirror the investigator's chosen field, specialty, or immediate informational need, it cannot be assumed that conclusions reached through such research are applicable across all therapeutic areas and subject recruitment scenarios.

Common categories of participation research interest include: (a) investigator therapeutic area of interest – overwhelmingly oncology, (b) gender-related patterns of participation, (c) participation by race or specific to minorities and "underserved" populations, (d) child and/or parent participation dynamics, (e) geriatric/elderly participation trends, (f)

uninsured/under-insured patient participation trends, (g) physician/patient perspective comparisons and (h) informed consent-related participation phenomena.

The literature reviewed primarily relied on the use of patient demographic information, information about observable behaviors, stated preferences, and clinical study data, either alone or in combination, to gain insight into patient participation. The findings reported by investigators highlight important trends, which, when considered together, provide encouraging support for the existence of an underlying attitudinal framework that, if understood through the application of future research, could be used to describe, or even predict, patient propensity to enroll in a clinical trial.

The literature review identified commonly recurring concepts such as:

Physician Influence. Many of those who have participated in a clinical trial rely heavily on the advice of their regular physician. According to Comis et. al. (2000¹⁶), the role of the physician is key in getting patients to participate, and most of those who do participate say that a doctor had a great deal of influence on their decision to do so. Further, in a study conducted by ERCI (2002¹⁷), random-effects calculations were used to combine the studies and estimate the typical percentages of patients who cited reasons for participation in three general categories, with one of the categories being physician influence (27%). Moreover, trends in the last few years indicate an increase in individuals who cite their doctor's recommendation as a reason they decided to participate in a clinical research study (31% in 2005 compared to 21% in 2004) (Harris Interactive Inc., 2005¹⁸).

Financial Considerations. Limited insurance reimbursement, possible denial of insurance coverage, and increased out-of-pocket expenses for medical care are all important negative factors positively influencing patient decision-making in favor of clinical trial participation. In fact, lack of insurance coverage, or fear that they will not have coverage, has been found to be a significant problem perceived by patients in general (Schilsky, 2005¹⁹). In a report by the U.S. General Accounting Office, Health, Education and Human Services Division (1999)²⁰, it was found that insurance coverage practices profoundly influence patient participation.

Severity of Disease. Individuals who are faced with a serious, terminal and/or life-threatening illness, are in desperation, or have a chronic condition, are more willing to participate in a clinical trial because of the feeling that they have nothing to lose. In fact, eight out of ten members of the general public state they would consider a clinical trial if faced with cancer (Comis et. al., 2000²¹). Further, findings suggest that for some patients, clinical trials fulfill a need to try "everything" in their fight against a disease or illness.

In a survey analyzed by Nurgat et. al. (2005)²², 38 phase I and phase II cancer chemotherapy trial participants completed a survey exploring motivations surrounding clinical trial participation. 71% strongly agreed that "surviving for as long a time as possible was the most important thing (for them)."

Early Access to New Treatments. In a study conducted by Lee et. al. (2005)²³, investigators found that early access to new therapy was an important factor in participation. In addition, one study also found that eligible patients may choose not to participate in clinical trials due to their "personal preferences for certain types of care" (United States General Accounting Office, 1999²⁴).

These examples are a small but representative fraction of the literature. While most of the literature supports the notion that attitudinal factors influence patients' willingness to participate in clinical research activities, some investigators are skeptical. A small number of studies did not uncover sufficiently convincing evidence to support the influential effect of patient attitudes. For example, Comis et. al. (2003)²⁵ concluded that the primary problem with accrual is not the attitudes of patients, but rather, the loss of potential participants due

to the unavailability of an appropriate clinical trial, the disqualification of large numbers of patients, and the reluctance of physicians to engage in accrual. Ferguson (2001)²⁶ stated that over half of the patients surveyed did not believe that doctors knew best about whether or not they should participate in clinical trials.

Also in dispute is the perception that adults often participate in clinical research trials for financial gain. A recent study by Harris Interactive (2005)²⁷ reported that fewer adults participate or plan to participate in trials for financial benefits (36% in 2005 compared to 50% in 2004). To further substantiate this claim, there were indications that patients enrolled in clinical trials were significantly less likely to be uninsured, i.e., assumed to be swayed toward participation for financial benefit (Sateren, et. al., 2002²⁸).

Standardization of Study Questionnaires

The body of literature reviewed does not reveal the existence of a standardized or traditional structure for attitudinal clustering studies, nor does it reveal any questionnaires specific to the precise topic proposed for study, although questionnaires on related topics such as that associated with the work of Cassileth (1982) investigating the effect of recent and damaging media attention on attitudes with respect to clinical trials do exist. Results of that survey, completed anonymously by 104 patients with cancer, 84 cardiology patients, and 107 members of the general public, indicated that most respondents believed patients should serve as research subjects regardless of medical status, and that participation helps future patients and increases medical knowledge while providing superior care in an ethical setting. However, responses concerning potential personal participation revealed more self-concern and less altruism.

Other examples include a quantitative survey of public attitudes towards cancer clinical trials (Comis, et. al., 2000²⁹). The survey further supports the notion that physician involvement is key and states that most patients who participate say that a doctor had a great deal of influence on their decision to do so ("highly influenced by a physician's recommendations"). The study also found that patients who did not participate cite possible denial of insurance coverage and increased out-of-pocket expenses for medical care as important negative factors influencing their decision to participate. Also, a large majority of patients said they believed trials would benefit themselves and others, that they would receive newer or better treatments in a trial, and that they would receive more care or attention. In addition, Matthews Media Group (MMG) undertook a study, "Formative Research into Attitudes Toward and Perceptions of Clinical Trials Participation," (December 2001)³⁰, which presented details of a psychographic profile questionnaire utilized to collect preference, attitude and belief data necessary to perform a cluster analysis on 54 breast cancer survivors and members of the general public participating in the survey, but again as mentioned previously, this endeavor was therapeutically specific to the area of oncology.

Another related example is the use of The Health Belief Model as a guide in structuring questions related to influences that affect participation in clinical trials (Verheggen, et. al., 1998³¹). In addition to The Health Belief Model, another study utilized a social/ecological perspective to suggest there are intrapersonal barriers (attitudes, beliefs about the illness/disease) that influence individual perceptions regarding participation (Wells & Zebrack 2006³²). Another study gauged patient attitudes and personality traits through personality evaluations derived from various psychometric tests such as the Gordon Survey of Interpersonal Values Questionnaire, the Coopersmith Self-Esteem Inventory and the Cattell Sixteen Personality Factor Questionnaire (Harth, et al., 1992³³).

Regardless of which personality assessment instrument is developed or adopted for the proposed study, no studies identified to date have attempted to utilize a three-dimensional approach to identifying attitudinal patterns through the concurrent analysis of (a)

socioeconomic and demographic data, (b) scientifically identified personality traits using psychometric evaluation, and (c) self-reported preference information relating to various aspects of clinical trial participation. In short, the proposed study will be the first to investigate the existence of attitudinal clusters that can be utilized to describe, and possibly predict, participatory behavior of prospective clinical trial subjects based on the scientific evaluation of individual data and information gathered via widely accepted methods of psychometric analysis.

Summary

Current and recent literature includes evidence that there are various attitudes, beliefs, barriers and factors that affect clinical trial participation. However, most of the evidence is not based on rigorous or robust studies encompassing a broad-based prospective patient population. Nor do these studies attempt to take into account personality-linked traits that may be characteristic of certain patient populations or categories. In addition, most previous studies emphasized respondent preferences rather than the attitudes which collectively form the basis for individualized preferences. In doing so, the origin of these preferences was never sufficiently investigated for the purpose of gaining a more thorough understanding of decision-making dynamics in the potential clinical research participant.

The literature clearly supports the notion that there are factors and attitudes affecting one's decision to participate in a clinical trial. However, while many studies have sought to identify factors playing into this decision, no study has attempted to identify and scientifically establish attitudinal clusters that allow for the categorization of prospective research participants based on their attitudinal profiles to understand their motivations and more effectively provide clinical trial-related information to them. Previous attitudinal and motivational research studies tend to be limited to very specific patient populations.

While conclusions derived from the literature are helpful in understanding participatory behavior, very little meaningful data addresses the basis for these behaviors. In short, the literature does not lend itself to the support of any assertions concerning the existence or nature of attitudinal clustering in prospective clinical trial participants. A literature review shows a strong interest in understanding patient motivations and attitudes leading to clinical trial participation, but no data thus far has been published that employs a three-dimensional assessment of patient attributes to identify broad categories corresponding to patterns of attitudinal clustering. In consideration of the fact that there has been no research of a similar nature yet conducted to date, the proposed study will focus on establishing validation and reliability of these clusters.

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