DEVELOPMENT AND VALIDATION OF A SCALE TO MEASURE THERAPEUTIC MISUNDERSTANDING WITH RESPECT TO CLINICAL TRIAL RESEARCH PARTICIPATION

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ABSTRACT

Clinical trial research participants often exhibit *therapeutic misunderstanding.* Factor and item analyses of responses by 464 community-dwelling older adults (age 49+) recruited online enabled the development of the 23-item Therapeutic Misunderstanding Scale (TMU). In accord with Horn and Grady's three facets definition (2003), a three-factor structure was supported by both exploratory and confirmatory factor analyses (n = 164 & n = 300 respectively). Internal consistency of responses to the full TMU as well as the therapeutic misconception, misestimation, and optimism subscales was calculated as α = .90, α =.87, α =.79, and α =.75, respectively. Correlations between the TMU and related instruments by 37 clinical trial participants provide support for convergent and discriminant validity of responses to this scale. Test-retest reliability was found to be r = .54 over an average interval of 35 weeks. Results are discussed in context of ongoing challenges to define and measure therapeutic misunderstanding.

Keywords: Therapeutic misconception, scale development, factor analysis, informed consent, scale reliability, scale validity

Subject Terms: Factor analysis, psychometrics, clinical trials

- For my parents (Mao & Mao) -

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GLOSSARY

Clinical equipoise	A genuine uncertainty in the efficacy of an intervention being examined (Freedman, 1987).
Clinical trial	A clinical trial is a control experiment testing a medical treatment on human participants (Piantadosi, 2005).
Cognitive adaptation	Humans have a basic propensity to selectively attend to and recall positive personally relevant information. This adaptive psychological process which effects attention to, encoding, and recall of information includes phenomena such as perceived mastery of situations, undue optimism, and excessive perceptions of situational control (Taylor, 1983; Taylor, Kemeny, Reed, Bower, & Gruenewald, 2000).
Phase I clinical trial	Initial small-scale studies (usually between 20 and 80 participants) to determine the toxicities, safety, dosage, and side effects of the experimental drugs in healthy participants or patients. In oncology trials, phase 1 trial participants are often in the advance stages of their illness and have usually tried all the existing treatment available to them.
Phase II clinical trial	Medium-scale controlled clinical studies (usually about 100-500 participants) conducted primarily to further evaluate the short-term toxicities, side effects, and risks of the drug on those who have the target illness. Phase II clinical trials also seek to gather preliminary evidence of drug efficacy. A control group may be included, where these participants are given a placebo (i.e., an inactive pill) or standard treatment. Participants and physicians are blind to treatment assignment.
Phase III clinical trial	Large-scale controlled trials (1000-5000 participants) intended to evaluate and confirm the efficacy of the drug and to a lesser extent, to continue monitor its short-term side effects. Phase III trials are usually randomized with participants and physicians blind to their treatment assignment.

Phase IV clinical trial	Also known as open-label extension studies and post-marketing surveillance studies. Phase IV trials are run to obtain additional information including the drug's cost effectiveness, risks, benefits, optimal use and mode of delivery over the longer term. All participants in the extension study are given the experimental drug, and both they and their physician know this (i.e., no placebo condition).
Optimistic bias	A phenomenon where people perceive themselves as less (or more) likely than their peers to experience negative (or positive) outcomes (Weinstein, 1989)
Relative health stock	A health stock is defined as one's remaining survival time as measured in quality-adjusted years of life. Relative health stock then, is the ratio of perceived current health stock to their perceived health stock before their current diagnosis (Gaskin, Kong, Meropol, Yabroff, Weaver, & Schulman, 1998).
Socially desirable responding	A systematic tendency to present oneself positively, the most common response bias that can confound responses to self-report measures (Paulhus, 1991). This phenomenon involves both deliberate distortion (i.e., impression management) as well as an honest, but overly positive self-presentation (i.e., self deception).
Therapeutic misunderstanding	A phenomenon first described by Appelbaum, Roth, and Lidz (1982) whereby participants believe every aspect of research is intended to benefit them. In this study, it is defined as a three-facets constructs in which stakeholders: 1) conflate the goals and nature of research and treatment; 2) appraise the risks and benefits of research participation unrealistically; 3) understand both 1) and 2) but remain hopeful and excessively optimistic about their outcomes.

CHAPTER 1
THERAPEUTIC MISUNDERSTANDING: A PRIMER

1.1 Introduction

Since the formal introduction of randomized controlled trials (RCT) more than half a century ago, this methodology has become the gold standard in determining the efficacy of a wide range of clinical interventions. Medical research has subsequently been transformed by two important developments: the patient autonomy movement that challenges medical paternalism; and the doctrine of informed consent that seeks to protect and respect individual autonomy in the decision-making process. In the era of shared medical decision-making (see Frosch & Kaplan, 1999), informed consent occupies a fundamental role in both treatment and research (Faden, Beauchamp, & King, 1986; O'Neill, 2003; Tri-Council Policy, 2003; 45 Code of Federal Regulations 46 [45 CFR 46]). Whether clinical trial participants, indeed, understand and fully appreciate the information exchanged during the consent process remains less clear.

A body of research has led researchers to question how well the process of obtaining *informed consent* has achieved its goals of prompting autonomous or shared decision-making (O'Neill, 2003). Research thus far has focused almost exclusively on two dimensions: the actual consent process; and participants' understanding and comprehension. Studies on the first dimension reveal that most consent forms are written at a reading level too high for the general population to comprehend (Paasche-Orlow,

Talyor, & Brancati, 2003; Sharp, 2004) given that the current cohort of older adults has, on average, ten years of formal education (O'Rourke & Tuokko, 2000). For example, Sharp (2004) found that only 10.3% of oncology trials consent forms were written at a grade level of ten or less.

Studies on the second dimension of participant understanding and comprehension reveal prevalent misconceptions about the purpose and nature of research (Appelbaum, Roth, & Lidz, 1982; Lidz & Appelbaum, 2002) and misunderstanding of concepts such as randomization, the use of placebos, the double-blind procedure, and *clinical equipoise* (Joffe, Cook, Cleary, Clark, & Weeks, 2001b; Kerr, Robinson, Stevens, Braunholtz, Edwards, & Lilford, 2004; Robinson, Kerr, Stevens, Lilford, Braunholtz, & Edwards, 2004). *Clinical equipoise* is defined as a genuine uncertainty regarding the efficacy of the intervention being examined (Freedman, 1987).

Of particular interest and concern is what has been coined *therapeutic misconception* (Appelbaum et al., 1982), which herein refers to *therapeutic misunderstanding* to reflect Horng and Grady's (2003) elucidation of this phenomenon (a definition I adapted for this thesis and explain in due course). This construct has been defined as a phenomenon where prospective participants conflate research with treatment and believe that all aspects of the research are intended to directly benefit them (Appelbaum et al, 1982; Appelbaum, Roth, Lidz, Benson, & Winslade, 1987; Horng & Grady, 2004; Lidz & Appelbaum, 2002). This phenomenon stands in contrast to the doctrine of informed consent in which participants must understand the distinction between research and treatment (Sankar, 2004). The presence of therapeutic misunderstanding also undermines a central tenant of ethical research, that of clinical

equipoise. In Canada, the Tri-Council Policy (2003), in accord with other international documents that govern and regulate research practice, mandate clinical equipoise as a fundamental feature and a moral necessity to ensure that participants are not disadvantaged or harmed as a result of participation in clinical trial research.

Since Appelbaum and colleagues (1982) first introduced the concept, studies have shown that therapeutic misunderstanding is a robust and widespread phenomenon (see Lidz & Appelbaum, 2002 for a review). In a qualitative study on the frequency and risk factors of therapeutic misunderstanding across a wide range of trials (e.g., asthma, Attention Deficit Hyperactive Disorder, cancer, depression, heart disease, hepatitis C, and arthritis), Appelbaum, Lidz, and Grisso (2004) reported that up to 61.8% of participants made statements indicative of therapeutic misunderstanding, varying on the basis of how the construct was operationalized. Although research participation should be motivated mainly by altruistic reasons, 93% of older adults stated that improving their own health was the reason for participating in the Systolic Hypertension in the Elderly Program (SHEP; Schron, Wassertheil-Smoller, & Pressel, 1997). Similarly, oncology patients uniformly indicated that they were primarily motivated to participate in a phase I clinical trial because of possible therapeutic benefits (Daugherty et al., 1995). In addition, altruistic reasons were not evident in their responses to an open ended question. It was only when primed by a closed-end question that 33% noted that they chose to participate in order to help future patients. The only solace in Daugherty and colleagues' (1995) findings is that many patients were hesitant to say that they would receive direct therapeutic benefits, despite being motivated to enrol by such beliefs.

This problem is not restricted to clinical trial participants but extends to caregivers, substitute decision makers, and even researchers themselves. O'Hara and Neutel (2004), for example, found that substitute decision makers do not have a solid understanding of randomization nor the use of placebos in clinical trial research. Similarly, Pucci, Belardinelli, Borsetti, Rodriguez, and Signorino (2001) reported that 70% of cognitively intact caregivers failed to comprehend why and how placebos, randomization, and double-blind procedures were used or to appreciate clinical equipoise. These findings are particularly germane to research with older adults as it demonstrates that substitute decision makers may base their decisions upon faulty perceptions when deciding what is best for the persons they are representing. The centrality of this topic is underscored by the volume of research on caregivers of person with dementia (PWD) and the number of drug trials underway with this population.

Joffe and colleagues (2001b) indicated that many researchers themselves also hold erroneous beliefs. They found that less than half (46%) of researchers agreed with the statement that the main reason for participation in cancer clinical trials is likely to benefit future patients. Similarly, oncology nurses were found to have elevated expectations as to the benefits of experimental treatment (Burnett, Koczwara, Pixley, Blumenson, Hwang, & Meropol, 2001; Cheng, Hitt, Koczwara, Schulman, Burnett, & Gaskin et al., 2000).

Despite its prevalence and much discussion in the literature on its implications, there has been a paucity of empirical study to examine the antecedents and correlates of therapeutic misunderstanding (Lidz & Appelbaum, 2002). This is largely a result of the inability to measure therapeutic misunderstanding. It is clear that a valid and reliable

instrument is needed to advance our understanding of the nature of therapeutic misunderstanding, ascertain its prevalence, and to identify strategies to ameliorate its negative implications. Until recently, there has been no systematic way to measure this construct (Lidz, Appelbaum, Grisso, & Renaud, 2004). This led Appelbaum and colleagues (2004) to develop the Therapeutic Misconception Index (TMI), a semi-structure interview to assess the presence of therapeutic misconceptions-one of three facets of therapeutic misunderstanding. Their efforts also led to the subsequent development of the 6-item Therapeutic Misconception Scale (Dunn, Palmer, Keehan, Jeste, & Appelbaum, 2006). Independently, Joffe, Cook, Cleary, Clark, and Weeks (2001a) developed the Quality of Informed Consent (QuIC) questionnaire, with five questions to assess therapeutic misconception. Although these instruments represent a needed step forward, we still lack a psychometrically sound, self-report instrument to measure therapeutic misunderstanding.

The purpose of this thesis is foremost to develop a scale to measure therapeutic misunderstanding and secondarily, to advance a conceptual model of the antecedents and correlates of therapeutic misunderstanding. It is hoped that this will serve as an important, albeit small step by providing a tool to facilitate future investigation of therapeutic misunderstanding and aid practitioners in efforts to detect its presence, so that appropriate interventions can be developed to minimize, if not eradicate, the problematic aspects of this phenomenon.

CHAPTER 2
THERAPEUTIC MISUNDERSTANDING: ITS CONCEPTUALIZATION, ORIGINS, AND IMPLICATIONS

According to Lidz and Appelbaum (2002), therapeutic misunderstanding entails a failure to appreciate the different (often conflicting) nature and goals of research and treatment. This, in turn, leads to a misattribution of therapeutic benefit and intent when such benefit is far from guaranteed because of the study's research design. For example, participants in a phase I clinical drug trial may expect a cure for their condition, or amelioration of their symptoms, even though the purpose of phrase I clinical trials is to determine the toxicity and dosage of a drug.

In this section, I attempted to clarify the conceptual boundaries of therapeutic misunderstanding by: 1) reviewing what is, and what is not, therapeutic misunderstanding; 2) distinguishing therapeutic misconception from therapeutic misestimation and therapeutic optimism; 3) examining some of the problems in defining therapeutic misunderstanding; 4) proposing a 3-facets definition of therapeutic misunderstanding based on the literature; and 5) summarizing what is known about its origin and correlates. I also briefly note the implications and significance of therapeutic misunderstanding to underscore the need for a valid and reliable measure of this phenomenon. Finally, I conclude with a conceptual model of therapeutic misunderstanding to guide the development of a scale to measure this important construct.

2.1 Initial Conceptualization

More than two decades since the term therapeutic misunderstanding was first introduced, the concept has evolved to mean more than a simple misunderstanding of scientific methodology and the presumption of personal care in clinical research. More precisely, studies that examined participants' understanding of the research methodology and lack of differentiation between research and treatment predated the introduction of the term. In 1975, Gray noted that more than two-thirds (69%) of the participants did not understand the double-blind methodology of the study in which they were enrolled, and more than two-fifths (41%) were not aware that they were participating in clinical research.

It was not until 1982, however, that Appelbaum and colleagues identified the phenomenon as a unique construct. In that study, they found that participants often had strong expectations of direct personal benefits. These misconceptions were evident by their limited understanding of experimental research methodology. Most astonishing was how they rationalized their belief that participation provided them direct benefits. When descriptions of various aspects of the research methodology such as randomization were not given, participants constructed elaborate explanations to maintain the belief that their medical interests were taken into account. When explanations were provided, participants reverted to distortion or denial in order to maintain the belief that they would personally benefit from study participation.

2.2 Defining What is Therapeutic Misunderstanding

It was not until 1987 that the first definition of therapeutic misunderstanding was proposed in which this construct was defined as *participants' belief that every aspect of*

clinical trial research is to provide direct personal benefit and failure to acknowledge the disadvantages or constraints imposed by research methodology (Appelbaum et al., 1987). *Clinical trial* is defined here as a control experiment to test a medical treatment on human participants (Piantadosi, 2005). In subsequent years, addition aspects of therapeutic misunderstanding have been defined and studied. In its current form, therapeutic misunderstanding consists of three essential elements or what Appelbaum and colleagues (2004) have labelled: 1) the mistaken beliefs of personal care and its associated failure to recognize the conflicting goals between research and treatment; 2) the misattribution of therapeutic intent to research when it is implausible or unreasonable and its associated, misconstrued, or unrealistic appraisal of the benefits of research participation; and 3) the failure to appreciate the risks or disadvantages of research participation. As will become apparent, an expectancy of personal care and optimism underscore each of these elements. Moreover, an underlying assumption of these elements is recognition or acknowledgement of one's condition as opposed to mere understanding, attribution, or appreciation.

2.2.1 Element 1: The conflation of research and treatment

A fundamental element of therapeutic misunderstanding is the conflation of the goals of research and treatment. This confusion often involves the expectation of benefits by study participants. Incidentally, the delineation between research and non-research activities is also a daily challenge for institutional review boards (Amdur, Speers, & Bankert, 2006). Lidz and Appelbaum (2002) cogently state that research and treatment differ in at least two dimensions (i.e., the protocol involved and its intended audience). Whereas research strives for *standardization* of treatments to establish efficacy for *a*

group of people in the future; treatment, in contrast, entails *individualized* treatment to ensure maximal benefits for a particular *individual in the present.* As noted by the U.S. National Bioethics Advisory Commission (as cited in Joffe & Weeks, 2002), blurring the boundaries between the two could result in therapeutic misunderstanding. That is,

> ... [T]he belief that the purpose of a clinical trial is to benefit the individual patient rather than to gather data for the purpose of contributing to scientific knowledge ... It is not a misconception to believe that participants probably will received good clinical care during research. But it is a misconception to believe that the purpose of clinical trials is to administer treatment rather than to conduct research (p. 1847).

Distinguishing these conflicting goals is essential, as research participation may involve the sacrifice of personal care; failure to recognize this is said to be a form of therapeutic misunderstanding (Appelbaum et al., 2004). There is evidence that points to this failure. For instance, Appelbaum and colleagues (1987) found that only 9% of participants could see a restriction in personal care (in the form of reduced treatment options) by participating in research.

These conflicting goals also violate what Fried (1975) has called the *principle of personal care*; that is, an expectation that physicians will always have their patients' best interests at heart. It should be noted that the principle of personal care has been challenged in certain school of ethics and that clinical trial is not the only situation where conflicts with this principle arises (see Piantadosi, 2005). This and other ethical issues have been widely debated in the clinical research literature (see Lernaire, 2004; Miller & Brody, 2003a). What is of concern here is the prevalence of this belief among the general public and their resistance to disconfirming information despite attempts to improve the consent process.

Clinical trial participants often adhere to the belief of personal care even when challenged (Appelbaum et al., 1987). Indeed, many participants found the idea of random assignment so at odds with the principle of personal care that they formed elaborate alternative explanations to make sense of how treatment was assigned in randomized controlled trials (Appelbaum et al., 1982, 1987; Mills, Donovan, Smith, Jacoby, Neal, & Hamdy, 2003). In one study, participants' personal care beliefs were so strong that despite being explicitly told that they had been given a placebo, six out of fifteen or 40 % of outpatients high in the trait of neuroticism believed that they had been given active medication (Park & Covi, 1965). An extensive survey of outpatients (n=1,882) conducted by the Advisory Committee on Human Radiation Experiments (ACHRE; 1995) found that participants generally believed that clinicians had their best medical interests in mind. Most revealing, however, were the explanations they offered. Many participants believed that the experimental treatment would not be offered if it did not confer direct benefits or if it posed significant possible risks of harm. As will be later discussed, studies on lay understandings of randomization also suggest that the general public has a difficult time accepting that physicians will not ensure that they receive the best personal care in clinical trials (Appelbaum et al., 2004; Ellis et al., 1999). The general public also tends to see random assignment as an unacceptable aspect of clinical research (Kerr et al., 2004).

2.2.2 Element 2: The misattribution of unreasonable benefits

The second element of therapeutic misunderstanding centres around the misattribution of therapeutic intent when it is implausible or unreasonable. Appelbaum and colleagues (2004) called this the misconstrued or unrealistic appraisal of the benefits

of research participation. They also noted that this is a less common aspect of therapeutic misunderstanding. Indeed, the five therapeutic misconception questions in Quality of Informed Consent (QuIC; Joffe et al., 2004a) only measure the first element (i.e., therapeutic misconception) and fail to explicitly examine whether misattribution of therapeutic intent is present. This again underscores the lack of consensus on the operational definition of therapeutic misunderstanding.

Appelbaum and colleagues (2004) argued that this kind of therapeutic misunderstanding is a result of misperceptions as to the nature of research as opposed to misunderstanding of the research methodology that precludes personal care (i.e., the first element). Interestingly, the role of participant expectancies regarding the principle of personal care also contributes to this kind of therapeutic misunderstanding. The difference here is that it operates through a distorted understanding of the relative risks/benefits of study participation as opposed to ignorance of research methodology.

2.2.3 Element 3: The failure to appreciate the risks inherent in participation

Lastly, researchers have identified a third aspect of therapeutic misunderstanding, that is, the failure to appreciate the risks or disadvantages inherent in research participation (Lidz et al., 2004). It should be noted that among these three elements, risk misperception is the least studied and most contested as it seems to contradict evidence from the risk perception and risk communication literature (Sandman, 1999; Slovic, 1987). For example, experts in risk perception have argued that misconception and misunderstanding of risk information have as much to do with poor communication as misperception.

In an interesting article, Lidz and colleagues (2004) distinguished between the two types of risks inherent in clinical trial research. The first pertains to familiar risks, uncertainty, and disadvantages associated with experimental and standard treatments. These kinds of risks include side effects and inconveniences such as commuting to a hospital to receive treatment. The second type is what they call risks that stem directly from the research design, such as the disadvantages of receiving a placebo, of random assignment, and the physician being blind to their treatment condition. Interestingly, they argued that constraints upon personal care imposed by these research methods should be considered an important risk factor. Whereas the first kind of risk and its associated disadvantages are well known in studies of clinical trial participant satisfaction (e.g., Schron, Wassertheil-Smoller, & Pressel, 1997), the latter are not.

For reasons that beg further explanation, Lidz and colleagues (2004) conclude that therapeutic misunderstanding is more prevalent than previously thought based on their findings that less than 15% of participants explicitly appreciate the risks inherent in research. While these authors acknowledged some limitations of their study (e.g., absence of control in proper disclosure) and despite noting that asking participants to report risks inherent in the design of research is a daunting task, they failed to consider the possibility that the findings may be attributed to a different understanding of risk between laypersons and experts, and that they might be responding to risk questions differently (Meropol et al., 2003; Weinfurt, Sulmasy, Schulman, & Meropol, 2003). The possibility that the third element of therapeutic misunderstanding is a result of the risk perception will be explored in detail later.

Furthermore, the under-appreciation of risk also contradicts findings reported with cancer patients in which they systematically overestimated both the risks and benefits of research participation (Meropol, Weinfurt, Burnett, Balshem, Benson, & Castel, 2003). Nonetheless, Lidz and colleagues (2004) did draw attention to the possibility that perhaps one type of risk is under-appreciated by participants in clinical trials research.

2.3 Defining What is not Therapeutic Misunderstanding

Much of the confusion regarding therapeutic misunderstanding may be dispelled by clarifying what it is not. As noted by Clark and Watson (1995), establishing the operational definition of constructs is integral to scale development. Given the ambiguity concerning how therapeutic misunderstanding should be defined, approaching this topic by defining what it is not therapeutic misunderstanding provides a useful point of departure. In this section, differences between therapeutic misunderstanding and misunderstanding of research are discussed. A philosophical analysis by Weinfurt and colleagues (2003) is then reviewed to distinguish therapeutic misunderstanding from linguistic confusion.

2.3.1 Therapeutic misunderstanding and misunderstanding of research

Central to the concept of therapeutic misunderstanding is that it is correlated but distinct from misunderstanding of research. As early as 1982, Appelbaum and colleagues noted that participants can express therapeutic misunderstanding even when they understand the methodological aspects of the study. Lidz and Appelbaum (2002) further noted that therapeutic misunderstanding can exist independently of participants' understanding of the nature, purpose, and method of research. More recently, Appelbaum

and colleagues (2004) further clarified that therapeutic misunderstanding is not simply misunderstanding of the different facets of research; without the misattribution of therapeutic benefits to the individual, lack of recall or comprehension of research - while problematic - is not sufficient to constitute therapeutic misunderstanding. Recently, Jansen (2006) argues even further that unless decision to take part in a clinical trial was based mainly from these misconceptions (i.e., committing a therapeutic errors), these misconceptions themselves are not problematic.

2.3.2 Therapeutic misunderstanding or linguistic confusion?

In an important conceptual article, Weinfurt and colleagues (2003) cautioned against the danger of conflating therapeutic misunderstanding with linguistic confusion. Their analysis was particularly germane in setting the conceptual boundaries of one aspect of therapeutic misunderstanding, that is, the unrealistic appraisal of the benefits of research participation (also known as *therapeutic misestimation*). They argued that this unrealistic expectation of personal benefit should be considered in light of not only what participants are told, but also how they were told, and the intent of participants' answers when questioned. Sankar (2004) came to the same conclusion in her analysis of participant consent transcripts. She argued that in order to understand therapeutic misunderstanding, one needs to examine how and by whom critical information is conveyed during the process of obtaining participant consent.

Weinfurt and colleagues (2003) noted that before determining that participants have misconstrued the intent of clinical trials research (i.e., therapeutic misunderstanding), we need to exclude three potential sources of linguistic confusion, namely: 1) the multiple speaker problem; 2) the semantic ambiguity problem; and 3) the

pragmatic problem (see Table 2.1). It should be noted that the multiple speaker problem also pertains to an issue separate from therapeutic misunderstanding (i.e., assessing patient's decision making capacity; Searight & Russell, 1998). This problem also points to the more general issue of inadequate and inconsistent disclosure in the consent process. Taken together, these findings suggest that researchers play a central role in fostering and dispelling therapeutic misunderstanding. This issue will be discussed in detail when sources of therapeutic misunderstanding are later discussed.

Table 2.1: Three source of linguistic confusion with examples

Sources of Confusion	Descriptions	Examples
The Multiple Speaker Problem	When individuals receive multiple and conflicting messages from more than one sources (e.g., investigator, physician, friends, medical journal, newspaper, Internet).	When the benefits of a clinical trial are inconsistently described in the same consent form
The Semantic Ambiguity Problem	When individuals and researchers are not asking or answering the same question because of the different frameworks or paradigms they implicitly use (i.e., multivocality).	When frequency type format (e.g., 1in 100) was used to convey probabilistic information and belief-type format (e.g., 1%) was used to assess understanding.
The Pragmatic Problem	When individuals' communication goals, or speech act, differ from those of researcher.	When study participants' unrealistic appraisal of benefits was intented to convey confidence in recovery to reassure their love one rather than as their understanding of the actual benefits.

Adapted from Weinfurt and colleagues, by permission (2003).

2.4 Distinguishing Therapeutic Misconception, Therapeutic Misestimation, and Therapeutic Optimism

In their landmark conceptual paper, Horng and Grady (2003) argue that there is more than one form of misunderstanding in research. To this end, they distinguish therapeutic misconception from therapeutic misestimation and therapeutic optimism (see

Table 2.2), and arrive at conclusions similar to those of Appelbaum and colleagues (2004).

Table 2.2: Therapeutic misconception, therapeutic misestimation, and therapeutic optimism

Concept	Definition	Ethical Significance	Example
Therapeutic misconception	The research participant conflates research with clinical care	Rarely tolerable because understanding of the nature of research is necessary for an informed decision to participate in research.	Mark believes that the purpose of a Phase I cancer trial is to help him personally.
Therapeutic misestimation	The research participant underestimates the risk, overestimates benefit, or both	Sometimes tolerable because understanding the exact probability of harm and benefit may not be necessary for an informed decision to participate in research.	Susan estimates that she has a 30% chance of benefit in a Phase I cancer trial. Previous studies suggest that benefits accrue to 5% of participants.
Therapeutic optimism	The research participants hope for the best personal outcome	Always tolerable because hope does not compromise the autonomy of a decision to participate in research.	Thomas hopes that he will be one of the 5% who benefit from a Phase I clinical trial.

2.4.1 Therapeutic misconception

According to Horng and Grady (2003), therapeutic misconception occurs when participants conflated research with treatment. This represents what has been called the core element of therapeutic misunderstanding, where failure to grasp that the goals of research and treatment are not always compatible (Appelbaum et al., 2004), and misattribution of therapeutic intent to research (Lidz & Appelbaum, 2002). Appelbaum

and colleagues called this *the mistaken belief of individualized care*. According to Horng and Grady (2003), such misconceptions stem from a misunderstanding of the nature or goals of research. This is in contrast to conflation due to poor understanding of the research methodology as initially conceived by Appelbaum and colleagues (1982). As Sankar (2004) explained, the goals of clinical care and research are inherently different. Whereas the former strives to treat patients with the best available interventions, the latter aims to determine the efficacy of a new intervention that might become a recommended treatment for future patients. Miller and Brody (2003a) not only underscore the competing goals of the two but argue that because of these fundamental distinctions, a different ethical framework should be used to justify clinical research. The implications of this argument are significant and an extended discussion of this topic will be covered in a later section.

2.4.1.1 What does random assignment mean?

A related and more focused area of research regarding therapeutic misconception is the lay understanding of randomization. While there are at least four types of misunderstanding in research methodology that can comprise individualized clinical care (i.e., clinical equipoise, double-blind, placebo, & randomization), failure to appreciate these suggests the presence of therapeutic misconception. Random assignment has received the most attention.

Understanding of randomization could be considered the first element of therapeutic misunderstanding (according to the Appelbaum group), that is, the misunderstanding of research methodology. As such, I will focus primarily on research in this domain to illustrate the first type of therapeutic misunderstanding.

Research in this area suggests that the process of randomization in clinical research is not well understood (Appelbaum et al., 1982; Featherstone & Donovan, 2002; Kodish et al., 2004), that the use of random assignment in general is perceived as unacceptable (Kerr et al., 2004), and that even if random assignment is understood, participants often struggle to accept that such a procedure will determine the treatment they receive (Appelbaum et al., 1982). Moreover, participants and non-participants alike often form alternative explanations to make sense of why randomization is used and why they should participate (Featherstone & Donovan, 2002). This misunderstanding is most salient when explicit knowledge of what randomization means is examined. Wagoner and Mayo (1995), for instance, found that 78% of the general public did not understand what the word 'randomly' means. Similarly, in a pediatric clinical trial to treat leukaemia in children, half of the parents could not explain what randomization meant despite being informed by physicians during the consent process (Kodish et al., 2004).

But most notable is not how participants struggle to understand random assignment but rather, the low acceptability of this aspect of clinical research. In fact, when participants' working understanding of randomization is studied, they tend to do relatively well and recall the major principles of this research methodology (Kerr et al., 2004; Mills et al., 2003). As Kerr and colleagues (2004) documented, most people were able to correctly identify computer, coin toss, and draw out of a hat as methods of randomization, suggesting that laypersons have a working understanding of the basic concept. What was alarming in their findings, however, was the low acceptability of random assignment relative to non-experimental methods. Only 37.7% found the use of computers for assignment to treatment conditions acceptable compared to 75% when

asked which they preferred (Kerr et al., 2004). In actuality, as Senn (2003) illustrated, it is very difficult to produce alternatives as a group that is ethically superior to random assignment.

Mills and colleagues (2003) obtained similar results in a qualitative study of middle aged and older cancer patients in terms of their recall, understanding, and perception of clinical equipoise, randomization, and trial enrolment. The majority understood random assignment but had more difficulty describing its importance. Most notable, they reported that agreeing to random assignment was dependent to a large extent on one's acceptability of clinical equipoise. Thus, it appears that randomization is considered acceptable only if participants found that physicians were genuinely uncertain about the effectiveness of each available treatment (Mills et al., 2003). Trust may also come into play, as this may also depends on the confidence patients have on the competence of their physician.

2.4.2 Therapeutic misestimation

Horng and Grady (2003) have defined therapeutic misestimation as misunderstanding of the likelihood of benefits and harm to research participants. Compared to concern for misconception about *the nature and goals* of research as with therapeutic misconception, the problem here entails a misunderstanding of the *probability* of benefits and risks in research participation. This has been called the least known and appreciated aspect of therapeutic misunderstanding by Appelbaum and colleagues (2004).

At this point, it should be noted that the operational definitions espoused by Horng and Grady (2003; hereafter called the *three facets definition*) and Appelbaum and

colleagues (2004; hereafter called the *three elements definition*) are not synonymous. One might be tempted to pair the Appelbaum group's first element with Horng and Grady's therapeutic misconception and to equate Appelbaum group's second and third elements with Horng and Grady's therapeutic misestimation. Closer inspection, however, reveals subtle differences as to the underlying factors believed to be at the core of these phenomena. For example, the three elements definition considers the conflation of research and treatment to result from a misunderstanding of research *methodology*, rather than a misunderstanding of the *nature and intent* of clinical research as held by the three facets definition. Similarly, the three elements definition considers the unrealistic appraisal of benefits a result of a misunderstanding of the *purpose* of research rather than a misunderstanding of the *probability* of benefits and harm as held by the three facets definition. Indeed, in a recent article, Appelbaum and colleagues (2004) noted that their second element is a special case of therapeutic misestimation, that is, misestimation of benefits due to a misconception about the nature of research itself.

It is important to keep in mind that, according to the three elements definition, understanding and perception of risks and benefits, including both their magnitude and likelihood, are not sufficient to avoid therapeutic misunderstanding (Lidz & Appelbaum, 2002). So long as participants misattribute therapeutic intent when there is none, regardless of their understanding of the nature, purpose, and method of research, therapeutic misunderstanding is said to exist.

2.4.3 Therapeutic optimism

The most important clarification on a conceptual level proposed by Horng and Grady (2003) is the distinction between the two forms of 'misunderstanding' and what

they have termed *therapeutic optimism*. They defined this construct as the expression and maintenance of inordinate hope despite having an accurate understanding of both the nature and intent of research and the potential benefits and risks of clinical research participation.

Research examining the relationship between optimism and therapeutic misunderstanding has been sparse. Among the few studies, it appears that optimism, at least situational optimism about one's medical condition in the short term (i.e., within a year), was related to therapeutic misunderstanding as measured by the Therapeutic Misconception Index (TMI; Appelbaum et al., 2004). Research on cancer patients' perceptions of the intent of phase I clinical trials also suggests that optimism plays a key role. Patients who failed standard treatment tended to have high expectations for a new experimental therapy. They were also more optimistic than their physicians about the likely outcomes of experimental treatment (Cheng et al., 2000; Meropol, Weinfurt et al., 2003). For example, Cheng and colleagues (2000) reported that phase I trial cancer patients systematically overestimated the prospective benefits of experimental treatment compared to both physicians' and nurses' perceived benefits. Interestingly, these patients also overestimated the benefits of standard treatment. Indeed, the authors found a positive correlation between perceived benefits from experimental and standard treatments. This suggested that, overall, patients were optimistic about their treatment. Findings that these patients overestimated the benefits of standard treatment are surprising, given that they (as in the case of phase I oncology patients) were unresponsive to standard treatment. A more recent study by this same group of researchers (Meropol, Weinfurt et al., 2003) replicated their earlier findings and found that clinical trial participants, in particular

those who chose to enrol (acceptors as opposed to decliners) were: 1) more likely to perceive benefits from an experimental treatment; 2) expected to live longer than taking a standard treatment; and 3) felt confident that they would be among those who would benefit from participation in the trial. Although these findings might not generalize to participants in other phases of clinical trials or to participants with other illnesses (Cheng et al., 2000), they nonetheless draw attention to the important role of optimism among clinical trial participants as a contributing factor to therapeutic misunderstanding.

In a sense, the Appelbaum group has acknowledged such a distinction but have yet to classify this phenomenon as a distinct construct. As recently as 2004, Lidz and colleagues reiterated the distinction between understanding and misattribution of therapeutic intent. They were adamant in noting that therapeutic misunderstanding can occur with or without understanding of research, and accompanied by or not by misattribution of therapeutic intent. What they neglected to specify are instances when both misunderstanding and misattribution are absent (i.e., when participants understand and do not misattribute therapeutic intent to research), that is, the occurrence of therapeutic optimism. That it took more than two decades for this distinction to be made should not be surprising given both the paucity of research and lack of attention on therapeutic misunderstanding until the last decade and, most importantly, difficultly in distinguishing between the two in a systematic way (Horng & Grady, 2003).

2.4.4 Implications for scale development

Advances by Horng and Grady (2003) underscore two important points related to the development of a measure for therapeutic misunderstanding. First, by redefining the operational definition first proposed by the Appelbaum group, it illustrates that

therapeutic misunderstanding is comprised of at least two forms of misunderstanding (i.e., therapeutic misconception and therapeutic misestimation) that should be assessed as well as a form of optimism that need not be discouraged (see Jansen, 2006 for a different perspective). It also suggests that theoretically, therapeutic misconception might coexist (or exist without) therapeutic misestimation and vice versa, though this remains to be demonstrated in empirical research. For example, participants could have an accurate understanding of the purpose of research, distinguish it from individualized treatment, but still overestimate the benefits of participation, underestimate the risks associated with the experimental treatment, expect unlikely benefits, or fail to appreciate or recognize the risks to themselves.

Second, by defining therapeutic misestimation as the misunderstanding of risks and benefits, it connects research in therapeutic misunderstanding to research in risk perception and comprehension of probabilistic information. Understanding how laypersons perceive risk is important and carries significant implications for medical decision making. For example, it has been shown that patients' choice between treatments with minimal survival differences is associated with patients' preferences as to the way in which treatment risks are communicated (i.e., numerical or verbal; Mazur, Hickman, & Mazur, 1999). Despite the centrality of risk perception and therapeutic misestimation, surprisingly, there has yet been no combined study of these related constructs.

2.5 Confusion Within: The Roots of Problematic Definition

Why is there such confusion regarding the conceptualization of therapeutic misunderstanding? Moreover, why does uncertainty regarding its operational definition

persist? To answer these questions, it is necessary to examine the key components or facets of therapeutic misunderstanding more closely. It is my belief that this confusion is a result of multiple interpretations of key terms within each element or facet of therapeutic misunderstanding as well as the ambiguous usage of such terms (Kopelamn, 2002; Resnik, 2005). The problem can be attributed to disagreement among researchers and ethicists as to how key concepts in the research and the consent process should be defined, and deep divisions as to the appropriate ethical and moral foundations of clinical research (Miller & Brody, 2003a).

This problem is best exemplified by examining different views of key components of therapeutic misunderstanding, the perception of risk and benefits of research participation. What constitutes minimal risk in research involving human research participant has been rigorously debated by ethicists (Kopelman, 2000; Resnik, 2005). Although federal regulation in both Canada and the United States define minimal risk to mean that the probability of harm or discomfort should not be greater than would occur in the daily life or during routine physical or psychological assessments, there is confusion as to whether the referent should always be healthy normal individuals or those in similar situations/conditions relative to the participants (Oki & Zaia, 2006).

This lack of agreement is further complicated by differing perceptions of risk between experts and laypersons (Horng & Brody, 2003a; Sandman, 1999; Slovic, 1987), opposing views among experts on the possible cognitive mechanisms underlying judgements of risk frequency (Hertwig, Pachur, & Kurenhäuser, 2005), and the influence of the presentation format on participants' ability to understand and integrate probabilistic information in their decision-making processes (Edwards, Elwyn, Covey,

Matthews, & Pill, 2001; Edwards, Elwyn, & Mulley, 2002; Gigerenzer, 2002; Gurmankin, Baron, & Armstrong, 2004; Kim, Goldstein, Hasher, & Zacks, 2005; Schwartz & Hasnain, 2002). To further complicate matters, outcome measures used to evaluate the effectiveness of communicating risk information at both the individual and public health levels vary considerably (Edwards & Elwyn, 1999). The problem extends to how benefits are assessed as the use of imprecise, unfamiliar and ambiguous terms used to describe potential benefits in research participation may actually foster therapeutic misunderstanding (Churchill, Nelson, Henderson, King, Davis, & Leahey et al., 2003).

2.6 Operational Definition of Therapeutic Misunderstanding

Based upon the conceptual literature regarding therapeutic misunderstanding, a revised operational definition is proposed for this study. Following both the pioneering work of the Appelbaum group and the related writings of Horng and Grady (2003), a definition that integrates both is advanced. Therapeutic misunderstanding is believed to be composed of three-facets or constructs where stakeholders: 1) conflate the goals and nature of research and treatment (i.e., therapeutic misconception) because of either a mistaken belief of personal care, a failure to appreciate the purpose of research, or a misunderstanding of the research methodology involved; 2) appraise the risks and benefits of research participation unrealistically (i.e., therapeutic misestimation) because of either a misattribution of therapeutic intent or a different conceptualization of probabilistic information; and 3) understand both 1) and 2) but remain hopeful and excessively optimistic about their outcomes (i.e., therapeutic optimism). The word stakeholders is used deliberately to reflect that therapeutic misunderstanding is not restricted to research participants. Unlike the common usage of stakeholders in health

promotion literature (i.e., those who have a stake in the initiative), the word stakeholders here is meant to describe all involved both directly and indirectly in clinical trials research (e.g., patients, physicians, nurses, caregivers).

2.7 The Origins of Therapeutic Misunderstanding

Research to date suggests a wide range of antecedents of therapeutic misunderstanding with little consensus at this juncture. However, factors can be organized into two types: those within the person (intrapersonal factors; e.g., misconception and possible cognitive distortions) and those external to the person (non-participant factors; e.g., description, disclosure, and the content of consent form). Research thus far has focused almost exclusively on intrapersonal factors and this has led to criticism (see Sankar, 2004). Recently, emphasis has shifted to non-participant factors. This is perhaps most eloquently summarized by Appelbaum (2002) who stated that, "confused investigators generate confused subjects; the latter then enrol in studies, seeking therapeutic benefits that are almost certain not to accrue" (p. 23).

Before proceeding, there are several caveats that should be kept in mind. First, although I reviewed the intrapersonal and non-participant factors separately for conceptual purposes, the two often interact to produce therapeutic misunderstanding. Second, the factors reviewed below consist of what I later call 'task independent' factors. That is, factors that are not specific to the research project and therefore, their influences on therapeutic misunderstanding are not contingent on the risk/benefit ratio of a specific clinical trial. Factors that are task dependent or contingent on the facets of the specific clinical trial such as comprehension of the research methodology, risk perception, and probability have been previously reviewed, though not explicitly discussed as such.

2.7.1 Intrapersonal factors

A factor is classified as intrapersonal when it is mainly, but not exclusively, attributable to the individual as opposed to interpersonally or socially determined. Under the rubric of intrapersonal factors, there are at least four person-level factors of note: 1) the expectancy of personal care; 2) optimistic bias; 3) the notion of relative health stock; and 4) the by-product of risk perception. Together, these provide the basis for an array of testable hypotheses regarding the origins of therapeutic misunderstanding. Intrapersonal factors can manifest in one of three ways: confusion; misconception; or cognitive adaptation (i.e., selective attention and information possessing leading to positive self-deception; O'Rourke, 2002). These, in turn, colour the meaning ascribed to task dependent variables. It is likely that there might be affective or personality dimensions that are equally important. Given the paucity of research in this area, however, with the exception of the risk perception explanation, the present discussion is limited to cognitive processes to avoid undue speculation.

2.7.1.1 The expectancy of personal care

A primary example of an intrapersonally determined therapeutic misunderstanding is the expectancy of personal care. The notion of personal care was first defined by Fried (1974), who stated that research participants generally presume that medical decisions are made solely for their benefit. The basis of this erroneous perception is yet unknown, but it has been suggested that it may stem from previous life experience with the medical and healthcare systems (Appelbaum, 2002). Lidz and Appelbaum (2002) contend that the basis of such expectancies stems from many sources, including the 'glorification' of medical research in the mass media. The fact that similar clinical

tests are used in both settings and physicians often play the dual role of investigator and clinician further bluring the boundaries between research and treatment (Sharp & Orr, 2004). In perhaps the sole empirical study on this subject, Stone, Kerr, Jacobson, Conboy, and Kaptchuk (2005) found that past experiences of ineffective treatment, the experience of other participants (i.e., vicarious learning), and medication side-effects had a significant impact upon participants' expectations. Moreover, these expectations were found to change over the course of their participation in the clinical trial.

What we do know is that such expectancies are widespread among research participants (Appelbaum, Roth, & Lidz, 1982; Appelbaum, Roth, & Lidz et al., 1987; Appelbaum, Lidz, & Grisso, 2004; Ellis et al., 1999; Mills et al., 2003). Regardless of the origins of such expectancies, they play a role in both the misunderstanding of individualized care and misattribution of therapeutic intent. Perhaps this phenomenon is best epitomized by findings specific to the relationship between acceptability of randomization and the decision to participate in clinical trials. For instance, the results of a recent qualitative study by Appelbaum and colleagues (2004) suggest that participants in a randomized clinical trial had difficulty accepting that physicians are not allowed to select their treatment based of their personal medical needs. In a related study that examined patients' attitudes toward randomized controlled trials, 74% of participants thought that their physicians would ensure that they received the best possible treatment (Ellis et al., 1999). The low acceptability of randomization may partially explain the prevalence of therapeutic misunderstanding. If participants are reluctant to accept random assignment and/or clinical equipoise, they are more likely to misconstrue the purpose and intent of research and therefore misattribute therapeutic intent to research participation.

It is likely that the expectancy of personal care interacts with other factors to foster therapeutic misunderstanding. For example, the expectancy of personal care may contribute to an overly optimistic outlook expressed by cancer patients enrolled in phase I trials (Meropol, Weinfurt et al., 2003). This false expectancy of personal care may also reinforce the erroneous expectation that physicians would not encourage them to enrol in a trial unless direct benefits would accrue to them.

2.7.1.2 Optimistic bias

Previously, it was mentioned a primary assumption of therapeutic misunderstanding is a failure to recognize or acknowledge one's condition as opposed to mere understanding, attribution, or appreciation. When reviewing the literature, Horng and Grady (2003) noted that while participants understood random assignment and what a placebo is, but they did not apply these concepts to themselves. This failure of recognition is a prime example of optimistic bias. Unlike other factors, optimistic bias can have positive implications (similar to therapeutic optimism) as it can reflect adaptive cognitive functioning. The *theory of cognitive adaptation* maintains that humans have a basic propensity to selectively attend to and recall positive personally-relevant information. This adaptive psychological process which affects attention to, encoding, and recall of information includes phenomena such as perceived mastery of situations, undue optimism, and excessive perceptions of situational control (Taylor, 1983; Taylor et al., 2000). Particularly at times of adversity and loss, adaptive cognitive functioning has been shown to predict both the mental and physical health of older adults (O'Rourke, 2002a, 2004).

That selective information processing plays a role in therapeutic misunderstanding has been noted by researchers (e.g., Arkin et al., 2005). Precisely what type of information they filter out has not been well established. What we do know is that participants' beliefs of personal care may lead to distorted beliefs regarding research methodology, and subsequently a biased risk/benefit assessment (Appelbaum et al., 1982, 1987). Researchers have speculated that severely ill patients are more likely to selectively filter information (known as the *vulnerability hypothesis*; Lidz & Appelbaum, 2002). Indeed, Schaeffer and colleagues (1996) reported that healthy volunteers could recall more risk and side effect related information compared to severely ill phase I participants. On the other hand, recent research has questioned the vulnerability hypothesis (see King & Henderson, 2003). Moreover, results from optimism research also suggested that optimistic individuals do not ignore health risk information or selectively attend to positive information (Aspinwall & Brunhart, 2000).

Optimistic bias has been well documented in the research literature. This phenomenon is evident when people perceive themselves as less (or more) likely than their peers to experience negative (or positive) outcomes (Weinstein, 1989). However, this construct has yet to be examined specific to research regarding therapeutic misunderstanding (see Jansen, 2006). This is surprising as optimistic bias provides the basis for testable hypotheses regarding the second and third elements of the operational definition of therapeutic misunderstanding. By extrapolation, this hypothesis might take the following form: if an unrealistic appraisal of the benefits and risks of an experimental treatment is the result of an optimistic bias, one would expect to find a significant difference between the perceived benefits (higher) and risks (lower) for oneself vis-à-vis

other study participants. This, however, has yet to be determined though prior research would support this hypothesis.

One finding to support this hypothesis is found in an initial study of attitudes toward clinical trials. Cassileth, Luck, Miller, and Hurwitz (1982) found that when asked why prospective participants might enroll in research, 69% made reference to potential benefits to society whereas only 5% sited personal benefits. When asked, however, why they might participate, 52% stated it would be for their personal benefit and only 23% sited the advancement of science. Although not specifically labelled as optimistic bias, Appelbaum and colleagues cited this finding in 1987 to illustrate therapeutic misunderstanding. The results of his study provide a clear example of the discrepancy between general knowledge and self-specific beliefs.

2.7.1.3 Relative health stock

The notion of *relative health stock* and its ability to explain medical decisions was first advanced by researchers examining risk-taking decisions made by cancer patients (Gaskin, Kong, Meropol, Yabroff, Weaver, & Schulman, 1998). As a health economic index, health stock is defined as "patients' remaining survival time as measured in quality-adjusted life years" (p. 85). Relative health stock then, is the ratio of patients' perceived current health stock to their perceived health stock before their current diagnosis. In the Health Stock Risk Adjustment Model proposed by Gaskin and colleagues (1998), they suggested that patients' perceptions of treatment benefits are dependent on their relative health stock. The model hypothesizes that as a patient's relative health stock declines, s/he is more likely to change the risk/benefit calculus so as

to overvalue potential benefits and undervalue potential risks when deciding whether to undergo an experimental treatment.

While the model has yet to be fully assessed, the notion of relative health stock holds promise as a potential explanation for therapeutic misunderstanding, in particular, therapeutic misestimation. Preliminary support for the model comes from empirical research that applied the model to examine patients' and physicians' perceptions regarding phase I oncology trials (see Cheng et al., 2000; Meropol, Weinfurt et al., 2003). The results of these studies suggest that patients systematically overestimate the benefits of experimental treatment and associated risks. Furthermore, participants estimated a greater likelihood of benefits and lower chances of adverse events than those who declined to participate in the trial. Interestingly, this tendency to overestimate both risks and benefits were independently reported in a study that examined risks and benefits perceived by surgical patients (Lloyd, Hayes, Bell, & Naylor, 2001). More recently, Gaskin and colleagues (2004) reported findings that support relative health stock as a construct distinct from optimism and preference for quality or quantity of life. In addition, cancer patients with low relative health stock were more likely to participate in clinical trial research as predicted by the model. Together, these findings support the hypothesis that patients overestimate the benefits and discount the risks of clinical trial participation. In part, the strength of this model can be ascribed to its parsimony although the authors have yet to define the precise cognitive and affective mechanisms by which therapeutic misunderstanding results.

2.7.1.4 The by-product of risk perception?

There is yet another explanation at the intrapersonal level that could explain the second and third aspects of therapeutic misunderstanding. Once again, research thus far has failed to test this explanation (or even acknowledge it), let alone rule it out as a possibility. This neglected possible explanation is that inflated estimates of benefits and certain types of risk are simply a by-product of a well-known phenomenon in risk perception, that is, the tendency to overestimate small probabilities and underestimate large probabilities (Slovic, 1987). This bias in judgements of risk frequencies is well documented in the literature, though pinpointing the mechanisms responsible remains an elusive goal (see Hertwig et al., 2005).

The finding that risk is more than the product of the magnitude of harm and its likelihood has been consistently supported in the literature (Sandman, 1999; Slovic, 1987). Precisely why this awareness has evaded the attention of medical decision-making researchers is therefore somewhat surprising. Ropeik and Slovic (2003) contend that risk perception is attributable to objective and emotion-based factors. According to Sandman (1999), experts tend to think in terms of *hazard* when asking about risk (i.e., the objective aspect) whereas laypersons tend to think in terms of *outrage* (i.e., both objective and subjective aspects), in particular, emotions such as fear, worry, and anxiety. As a result, when laypersons are asked to estimate risk, they tend to overestimate the risk of rare events (e.g., Severe Acute Respiratory Syndrome or SARS) but underestimate the risk of prevalent ones (e.g., cancer; Slovic, 1987). Risk perception is also dependent on other subjective factors, including emotions (see Peters, Burrstone, & Mertz, 2004). Slovic (1987) argued that individuals base their judgments on an array of factors such as

whether or not the risk is perceived as controllable, how dreadful it is, how global and catastrophic its potential impact, whether it was chosen or imposed, and whether the risk is observable, known and novel in contrast to thinking of it only in terms of numbers of fatalities. Using factor analysis, Slovic (1987) was able to distill this construct into three factors: 1) how dreadful the risk; 2) whether the risk is unknown; 3) the number of people exposed to the risk.

As with optimistic bias, this explanation provides a basis for testable hypotheses, thus making it a viable topic for future study. The hypothesis might take the following form: if, in fact, a by-product of risk perception, then participants should overestimate the probability of both benefits and risks that occur infrequently irrespective of their potential positive and negative effects on the participant. Once again, there is no direct evidence but ironically, research conducted with cancer patients in which the health stock risk adjustment model was tested has provided supported for this assertion. In one study, Cheng and colleagues (2000) reported a rather peculiar finding; patients not only overestimated the probability of the benefits, but also the toxicity. Meropol, Weinfurt, and colleagues (2003) replicated this finding in a subsequent study, as did Lloyd and colleagues (2001) independently.

2.7.2 Non-participant factors

Recently, research has begun to examine the role of non-participant factors relative to therapeutic misunderstanding. Non-participant factors encompass a broad range of constructs at both the interpersonal and societal levels of explanation. Included within the interpersonal domain are problematic disclosure, inadequate disclosure in the consent process, observer bias, and imposition of investigators' own therapeutic

misunderstanding. At the societal level are government policies, mass media, and the marketing efforts of the pharmaceutical industry. The end result of these factors is misattribution of study participation benefits and distorted understanding due to miscommunication or distorted and inconsistent messages.

2.7.2.1 Disclosure

Research to date has failed to rule out poor patient-physician communication or inadequate disclosure as the cause of therapeutic misunderstanding. Studies that have looked at what physicians say and what participants recall or understand have shown discrepancies between the two in terms of the content of discussion (Meropol et al., 2003) as well as perceptions of risk and benefit (Gurmankin et al., 2004; Lloyd, Hayes, Bell, & Naylor, 2001).

With respect to communication content, Meropol and colleagues (2003) reported that patients' recall of various topics, including change in quality of life, life expectancy, side-effects as well as benefits and risks, were significantly lower than the corresponding recollections of their physicians. Whether this reflects inadequate communication or difficulties in information encoding and recall remains to be determined. Regardless, it is unlikely that without controlling for disclosure of information to patients, clarification as to whether therapeutic misunderstanding is the result of selective attention/retention or due to poor physician communication has yet to be determined.

In terms of risk perception, Gurmankin and colleagues (2004) concluded in their analogue study of physician risk communication concerning cancer risks that messages tended to be lost during the communication process. Irrespective of the presentation

format (numerical vs. verbal), they found that participants overestimated their risk of cancer compared to that stated by their physicians.

Sometimes, misunderstanding and miscommunication stem from physician discomfort when discussing the uncertainty of experimental treatments and related details. According to Appelbaum and colleagues (1987), physicians often feel ill at ease acknowledging uncertainty regarding which treatments are best for their patients. This may be attributable to physicians' difficulty in these instances reconciling their roles as both clinicians and researchers (Lidz & Appelbaum, 2002; Miller & Brody, 2003a).

It is also possible that some deliberately avoid full disclosure and fail to fully delineate the difference between research and treatment for the fear that this might discourage participation in clinical research, thereby fostering therapeutic misunderstanding. This ambivalence between what is ethically mandated and what one believes has been documented in a study of investigators' perspectives and communication of benefits in gene transfer trials (Henderson et al., 2004). These authors reported that principle investigators (PIs) tend to have high expectations of gene transfer therapy but refrain from communicating this expectation to clinical trial participants because they are methodologically disinclined from fully disclosing therapeutic intent. The distinction between hope and expectation is indeed imprecise; and without uniform standards as to how possible benefits should be communicated to study participants, investigators will continue to resort to inconsistent, vague, and ambiguous language. One PI cogently summarized investigators' therapeutic optimism,

> Expecting it and hoping for it are two different things. If we've done our job right, they [participants] don't expect it, but they hope for it. But I think they hope for it because we tell them that it's possible (Henderson et al., 2004; p. 228).

Miscommunication can also occur when the physician/researcher (i.e., expert) and patient/participant (i.e., layperson) use different criteria to arrive at a decision, and rely on different paradigms when judging the sufficiency of communication. This assertion, however, represents a minority view in literature. Sankar (2004) has argued that implicit reliance of the transmission model of informed consent is a potential yet overlooked factor in therapeutic misunderstanding. A central though dated premise of the transmission model is that sender and receiver share the same goals, expectations and decision making criteria, and that successful communication means that the information has been sufficiently conveyed rather than understood. The transmission model also stands in contrast to contemporary thought in risk communication as conveyance of information alone is no longer deemed sufficient for meeting the standards/goals of good practice in risk communication (Fischhoff, 1995).

On a more philosophical level, Weinfurt (2004) warns of the risk of engineering erroneous bioethical crises by adopting non-applicable frameworks when considering this issue. He argues that laypersons' reports of perceived study benefits and their associated expectations of clinical trial participation entail more than simply their understanding of the relative pros and cons of participation. In order to disentangle the issue, one needs to examine at the specific context more closely in which decisions are made in order to understand subtle communication goals. In the end, Weinfurt (2004) concludes that misunderstanding might be more accurately described as a by-product of applying

erroneous information processing frameworks rather than discursive perspectives in the analysis of the specific context in which decisions are made.

2.7.2.2 Obtaining participant consent

Difficulty studying the actual process of disclosure has led many researchers to pursue an alternate, albeit imperfect route. Instead of examining the process whereby investigators explain the research protocol to prospective participants, researchers have examined consent forms used in clinical trials. As such, consent forms are probably the most scrutinized of the non-participant factors.

There are two general problems with consent forms. The first is inconsistency of the message and language, and the second is a lack of precision in the choice of words. The proper use of words is important as inconsistent and conflicting messages lead to confusion (i.e., the multiple speaker problem; Weinfurt et al., 2003). Furthermore, inaccurate use of words to convey therapeutic intent likely fosters therapeutic misunderstanding among prospective participants (Sankar, 2004). As previously mentioned, a significant percentage of the general public does not understand terms frequently used in clinical trial research such as placebo (23%), double-blind (83%) and randomly (78%; Wagoner & Mayo, 1995).

Do consent forms adequately address the issue of precision of words and message consistency? Consent form studies thus far have produced mixed results. On the negative side, Hochhauser (2002) argued that with the use of acronyms (e.g., ALIVE for Adenosine Lidocaine Infarct zone Viability Enhancement trial, BEST for Beta-blocker Evaluation of Survival Trial, and MAGIC for MAGnesium In Coronaries), nebulous terms to denote clinical trials (e.g., study, medical research trial, clinical research

program), and questionable advertising claims to which prospective participants and physicians are subjected, it should come as no surprise that consent is not fully informed and that therapeutic misunderstanding occurs. Qualitative analyses of consent forms used in gene transfer research found overly optimistic descriptions of the potential benefits of gene transfer trials (Kimmelman & Palmour, 2005) and use of confusing and inconsistent language to describe the possible benefits of paticipation (Churchill et al., 2003; Henderson, Davis, King, Easter, Zimmer, & Rothschild et al., 2004), participants, investigators, and the intervention (King, Henderson, Churchill, Davis, Hull, & Nelson et al., 2005). In addition, conflicting information to describe potential study benefits even within the same consent form has been found (King et al., 2005). Labelled the *multiple speakers problem*, the existence of conflicting written content can lead prospective participants to arrive at a skewed understanding of potential study risks and benefits as compared to the corresponding understanding of these risks and benefits as held by study researchers (Weinfurt et al., 2003). The impact of word choices has been demonstrated by Sugarman and colleagues (1998), where respondents assigned greater risk and uncertainty when the research is described as a 'medical experiment' compared to 'medical research' or 'medical study'.

On the other hand, some have argued that the problem lies not with consistency and clarity of content (Sankar, 2004; Weinfurt, 2004). Citing the review by Horng, Emanuel, Wilfond, Rackoff, Martz, and Grady (2002), critics concluded that no substantial problems arise from the consent form itself with respect to appraisal of risks and benefits of phase I cancer trials. However, we currently do not have comprehensive comparative research examining consent forms used with other populations or the

treatment of other illnesses/disorders. According to King and colleagues (2005), it would appear that other disciplines have yet to apply the same level of consistency and rigour as required to obtain consent in oncological research, though there is evidence that overly optimistic descriptions, at least in gene transfer trials, has declined over the past decade (Kimmelman & Palmour, 2005).

In order for decision-making to be influenced by the consent form content, participants need to read and reflect upon what is written. There is evidence, however, that this may not be the case. For instance, Lavelle-Jones, Byrne, Rice, and Cuschieri (1993) found that 69% of surgical patients admitted that they signed the consent form without reading it. These rarely documented findings should not surprise us as others have repeatedly pointed out the complexity (e.g., reading level required and length) of consent forms used in clinical trials research (Sharp, 2004). Indeed, it has been found that even the templates provided by Institution Review Boards (IRBs) do not meet their own readability standards (Paasche-Orlow et al., 2003).

2.7.2.3 Observer bias and investigators' own therapeutic misunderstanding

At first glance, it would seem tautological to suggest that investigators' own therapeutic misunderstanding cause those of participants. Closer inspection, however, reveals that this might be the case. As previously noted, there is evidence that caregivers (O'Hara & Neutel, 2004; Pucci et al., 2001), physicians (Daugherty et al., 1995; Joffe et al., 2001b), and nurses (Burnett et al, 2001; Cheng et al., 2000) also hold therapeutic misunderstanding with regard to clinical trials. This is most evident in their unrealistic appraisal of direct benefits accrue to study participants. Daugherty and colleagues (1995) noted that participants' beliefs might be influenced by those held by the physicians who

provide the trial information. How these misconceptions are communicated to participants is unknown; however, it is plausible that they are conveyed by use of nebulous terms and inadequate/incomplete disclosure as previously discussed.

Here, we can apply findings from the unblinding of double-blind procedures to illustrate the subtle but non-trivial influence of investigator and physician biases on participant comprehension. The topic of unblinding pertains to disclosure of the study condition to which participants had been assigned. Research over the years has demonstrated that blinding is more difficult to achieve than previously perceived in both pharmacological and non-pharmacological clinical trials (Basoglu, Marks, Livanou, & Swinson, 1997; Bourton, Tubach, Giraudeau, & Ravaud, 2004). Moscucci, Byrne, Weintraub and Cox (1987), for example, reported that 74% and 45% of participants in the placebo group and treatment group respectively correctly guessed their treatment assignments. In an unpublished review of 27 studies (n = 13,082), Shapiro and Shapiro (1997) reported that assignment condition was guessed correctly by 67% of clinicians, by 65% of patients, and 71% of relatives and other staff. It is conceivable that the side-effects of the medications might reveal their assignment. While the association between physician/investigator and patient/participant assumptions has yet to be directly assessed, it remains to be empirically discounted that patients' knowledge of treatment assignment is not influenced by communication and other physician behaviours.

2.7.2.4 Government policy, the pharmaceutical industry, and the media

The most controversial hypothesis regarding the origins of therapeutic misunderstanding comes from Dresser (2002), who has argued that government policies and pharmaceutical advertising (particularly advertising directly to consumers) play an

ever increasing role in fostering therapeutic misunderstandings. Hawthorne (2005) noted the pharmaceutical industry spent over $3 billion U.S. dollars to market their drugs, and up to one-third of some pharmaceutical companies' budgets were spent on advertising and lobbying (see also National Institute for Health Care Management, 2001 on advertising spending). While the former increases drug revenue, the latter can translate into powerful influence on government policy and regulation, as demonstrated in the dispute regarding the re-importation of prescription drugs from Canada into the United States. Dresser (2002) stated that a series of policies by the U.S. Food and Drug Administration (FDA) and National Institutes of Health to shorten the duration of clinical trials prior to approval of new medications have created an unduly positive image of clinical research. But the most significant changes that could affect participant expectations and beliefs is a new U.S. law that requires insurers to cover routine care costs for those enrolled in clinical trials, further blurring the boundary between research and treatment and, as a result, indirectly promoting therapeutic misunderstanding (Sharp & Orr, 2004). Hochhauser (2002) echoed Dresser concerns, also cautioning against the significant influence of pharmaceutical industry marketing campaigns (see also Brody, 2007; Hawthorne, 2005). In England, for instance, concerns about the influence of pharmaceutical industry have prompted a report by the House of Common's Health Select Committee on this issue and the lack of transparency in the regulatory system (Kennedy, 2005).

In terms of therapeutic misunderstanding, the influence of pharmaceutical industry is probably most problematic with respect to conflict of interests in the form of financial incentives paid to physicians who recruit their own patients (see Brody, 2007;

Yessian, 2006 for example). The ethics of these financial incentives has been hotly debated. Many have argued that the suggestion that physicians will alter their practices because of such incentives is naïve; nonetheless, the concern primarily pertains to having physicians who treat patients be the persons who recruit, inform, and monitor these same patients enrolled in clinical trials. Some have argued that this fosters therapeutic misunderstanding among patients/participants by blurring the distinction between treatment and research, arguing that a third party should explain the research protocol and methodology (Dresser, 2002; Horng & Grady, 2003; Lidz & Appelbaum, 2002; Sales & Lavin, 2000). This problem may be particularly problematic in open label extension studies as participants are often blind to their treatment assignments and the efficacy of the drug has yet to be determined (Taylor & Wainwright, 2005). Even when asked by a third party within clinical settings, it may be perceived as mildly coercive as the power and status of the physician may transfer to those identified as his/her proxy (e.g., research nurse). The intricate relationship between pharmaceutical industries and drug discoveries is unlikely to go away given the huge capital investment and liabilities forbade the non-profit approach to clinical trials. With so few unique distinct chemical entities available, the market driven and 'me-too' drug approach to drug discovery is also unlikely to be replaced in the near future (Bartfai & Lees, 2006),

Closely related to pharmaceutical advertising is how the media portrays clinical research. Lidz and Appelbaum (2002) noted that positive images of the benefits of clinical research in the mass media reinforce the expectancy of personal care. At the same time, journalists and health reporters perpetuate such misconceptions by reporting preliminary medical discoveries that promise to cure all forms of illness (Dresser, 2002).

Such misconceptions are further reinforced by lobbying and fundraising efforts by patients and advocacy organizations hoping to lead to cures for Parkinson's, Alzheimer disease (AD), and cancer among others. These organizations, in turn, obtain a substantive amount of funds from the pharmaceutical industry (Hawthorne, 2005). Not to discount the good intentions of these groups, the unintended effects of this reporting may be pronounced though yet to be fully assessed or understood. A panel of Canadian clinical bioethicists also noted that the media disproportionably reports certain ethics challenges, while paying comparatively little attention to other equally important ones (e.g., ethical issues related to research participation; Breslin, MacRae, Bell, Singer & The University of Toronto Joint Centre for Bioethics Clinical Ethics Group, 2005).

2.8 Implications and Significance

The significance of therapeutic misunderstanding may be broad and pervasive. Three of the most important implications pertain to: 1) the doctrine of informed consent; 2) the debate on public versus personal health goals; and 3) the ethics of clinical trial/clinical equipoise.

2.8.1 The doctrine of informed consent

The notion of therapeutic misunderstanding stands in contrast to the doctrine of informed consent (Appelbaum, 2002; Sankar, 2004) in which a central tenet is to protect and respect individual autonomy in medical decision-making (Faden et al., 1986). Precisely how well the consent process fulfils this role has been the subject of considerable debate (see O'Neill, 2003). Of particular relevance to the current study is how therapeutic misunderstanding undermines the requirements for *voluntary* and

informed consent. Before proceeding, it is worth reviewing the general requirements of informed consent set forth in different jurisdictions.

2.8.1.1 Informed consent: An overview

The legal and moral foundations of informed consent have been prescribed in several important documents. First established in the Nuremberg Code through the Declaration of Helsinki (World Medical Association, 2004; see Carlson, Boyd, & Webb, 2004 for a brief review), developed countries have since adopted these documents as part of their own guidelines that govern the research process involving human participants.

In Canada, ethical conduct for research involving human participants is governed by the Tri-Council Policy Statement (2003), issue by the (former) Medical Research Council of Canada, the Natural Sciences and Engineering Research Council of Canada, and the Social Sciences and Humanities Research Council of Canada. Free and informed consent are among the guiding ethical principles of this document. In section 2, article 2.1 (d), the policy states that free and informed consent is at the heart of ethical research involving human participants, noting that it is a *process* of dialogue and that information sharing occurs throughout the entire process, as opposed to one point in time (i.e., initial recruitment).

In order for consent to be valid, it must be given voluntarily by an informed and competent individual (Tri-Council Policy, 2003). Similar requirements exist in the United States, where federal guidelines require that informed consent must be voluntary, informed, and rational (Fischman, 2000; Kuther, 1999). These three criteria of voluntariness, being informed, and competency can be said to be universal requirements of valid and informed consent (Grisso & Appelbaum, 1998).

Of these criteria, the first two have particular relevance to therapeutic misunderstanding. Competency, though germane to research with older adults, will not be discussed as it relates primarily to those impediments to thought and decision making ability (e.g., Alzheimer disease). In contrast, therapeutic misunderstanding entails no loss of cognitive capacity.

Article 2.4 of the Tri-Council Policy (2003) outlines five general conditions for proper information disclosure (see Table 2.3). The so-called Common Rule in the United States stipulates similar requirements with at least eight elements (see Table 2.3; 45 C.F.R. 46).

2.8.1.2 Why is therapeutic misunderstanding a threat to informed consent?

Having discussed the general requirements of informed consent, we are now in a position to examine why therapeutic misunderstanding is a threat to this fundamental aspect of ethical research practice. It should be noted that while the above requirements pertain to disclosure of information rather than how it has been received, it is implied that an understanding of these elements is required. On the basis of this assumption, therapeutic misunderstanding undermines general conditions (A) and (C) under the Tri-Council Policy (2003).

Table 2.3: General disclosure requirements relevant to free and informed consent in Canada and their corresponding requirements in the United States.

Tri-Council Policy *	US Common Rule **
a) A statement that the individual is being invited in to take part a research project b) A statement of research purpose, the identity of the researcher, the expected duration and nature of participation, and a description of research procedures	1) A description of the nature, purpose, expected duration, and procedures of the study, including a clear statement that recruitment is sought for participants in a research study.
c) A comprehensible description of reasonably foreseeable harms and benefits that may arise from research participation as well as the likely consequences of non-action	2) A description of reasonably foreseeable risks 3) A description of the foreseeable benefits 4) A disclosure of appropriate alternatives
d) An assurance that prospective participants are free not to participate, have the right to withdraw at any time without prejudice to pre-existing entitlements, and will be given continuing and meaningful opportunities for deciding whether or not to continue to participate (i.e., longitudinal research)	8) A statement that participation is voluntary and that the participant can withdraw at any time without penalty or loss of benefits
Covered in Section 3	5) A statement of how confidentiality of information will be maintained
Covered in additional information required under Section 2	6) An explanation of any compensation available to study participants with more than minimal risk 7) An explanation of how the participant can get pertinent questions answered

* Based on Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.* 1998 (with 2000, 2002 and 2005 amendments).

** Based on 45 C. F. R. 46.

Violation of general condition (A) occurs as a result of the first element of therapeutic misunderstanding (i.e., the conflation of research and treatment). To satisfy this ethical requirement, individuals need to understand that they are participating in a

research project, not merely an alternative form of treatment. As Sankar (2004) noted, for consent to be informed, participants need to understand that they are enrolling in research and, more importantly, appreciate the distinction between research and treatment. Thus, therapeutic misunderstanding, at least conflation between research and treatment, is antithetical to general condition (A) of the Tri-Council Policy and compromises the principle of autonomy through distortion of the nature of research (Horng & Grady, 2003).

Violation of general condition C results due to the second and third elements of therapeutic misunderstanding (i.e., the misattribution of benefits and the failure to appreciate the risk inherent in participation, respectively). If one accepts that a failure to accurately report the expected benefits and risks of an experimental treatment entails a failure to inform, then it follows that these participants may well hold therapeutic misunderstanding. As noted, the second and third elements of therapeutic misunderstanding pertain to the expectation of personal care in clinical research. Appelbaum (2002) has argued that clinical research cannot be justified and informed consent does not exist without the understanding that the principle of personal care does not necessarily apply. Thus, when research has a high risk/benefit ratio, overestimation of benefits and underestimation of risks constitutes an ethical issue that undermines the guiding principles of the Tri-Council Policy and the US Common Rule.

2.8.2 Conflicts between public and personal health goals

Whereas the implications of therapeutic misunderstanding for informed consent have been discussed at length, how the existence and amelioration of therapeutic misunderstanding might affect participants' satisfaction with clinical research, their

decision whether or not to enrol, and participant attrition have only attracted researchers' attention as of late (Lidz & Appelbaum, 2002; Glannon, 2006; Miller & Brody, 2003a). Although sparse, there is evidence to suggest that increased understanding can reduce rates of participation. For instance, Mills and colleagues (2003) found that people who have a clear understanding of random assignment tend to decline participation. The idea that increased understanding and reduced misconceptions might decrease participation in clinical research is not exclusive to the study of therapeutic misunderstanding. Similar concerns have been raised in the risk communication literature, where decision-making with full understanding of treatment procedures appears to reduce prospective participants' willingness to undergo routine screening procedures (e.g., mammography; Edwards, 2004).

Conflict between personal (i.e., to foster informed decision making) and public health goals (i.e., to improve the health of the population) raises interesting but complex issues. For physicians, balancing these conflicting roles is not unique to clinical trial research, it merely sharpens the issue; indeed, there are ample examples in everyday medical practice that require balancing dual or multiple roles (see Piantadosi, 2005). Vaccination programs are a classic example (Piantadosi, 2005; Senn, 2003). From the perspective of the individual, the ideal scenario would be for him to be not vaccinated in a world where everybody else is. This of course is unattainable and a compromise has to be made to balance the risk benefit ratios between the public and individual.

Those who espouse the deontological perspective argue that individual autonomy should take precedence because it is 'unethical' to balance the cost to participants against the uncertain benefits to society, utilitarians would contend that individual choices and

actions should be viewed in light of their societal consequences (Smith, 2000). As Salovey and Rothman (2003) noted in their discussion of risk communication, even though one might accept and respect the rights of individuals to put themselves at risk, the aggregate cost to society can be unacceptable. Similarly in clinical research, it might be argued that one should protect and respect individual autonomy and promote informed and shared decision making even if doing so might impede scientific progress to the detriment of future patients.

2.8.3 Therapeutic misunderstanding and clinical equipoise

Tension between personal and population health goals underscores a more fundamental issue in bioethics. This clash between the disparate goals of research and treatment lies at the heart of the first element of therapeutic misunderstanding as well as clinical equipoise. As it turns out, it appears that therapeutic misconception does not only exist in the minds of participants, investigators and caregivers, but also among ethicists themselves (Miller & Brody, 2003a). The relationship between therapeutic misconception and clinical equipoise is not self-evident but has significant implications for ethical research, in particular, the use of placebos in clinical trials.

Miller and Brody (2003a) diverge from the dominant view (known as the 'similarity' position, which, incidentally, is also the dominant view in the European Union; Lernaire, 2004) that the same ethical framework in clinical care should be applied in experimental settings. In particular, they examined whether clinical equipoise is a solution to 'the RCT dilemma' or a misguided effort to divert attention away from the real issues inherent in research ethics and participant protection. They argue that by applying the same ethical framework for treatment to clinical research conflates the

discrepant goals of the two (see also Brody, 2007). Unknown to ethicists and investigators who extrapolate the therapeutic obligation in treatment to research, it actually may foster therapeutic misunderstanding among participants because researchers themselves view research through a therapeutic lens (see also Lernaire, 2004). By challenging the merits of the 'similarity' position, Miller and Brody (2003a) counter the need to apply clinical equipoise as an ethical and moral justification for scientifically valid but potentially disadvantagous procedures in clinical trial research (e.g., randomization and the use of placebos). Instead, they advocate for the adoption of an alternate ethical framework that clearly distinguishes research from treatment by fully acknowledging their distinct and divergent goals. This framework, the so-called 'different' position was originally espoused in the Belmont Report by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1979.

In other words, Miller and Brody (2003a; see also Appelbaum, 2002; Lernaire, 2004; Sharp & Orr, 2004) argue that the blurring of clinician and investigator roles inevitably fosters therapeutic misunderstanding among study participants (maybe even among clinicians/researchers themselves). Therefore, given that the adoption of clinical equipoise and the 'similarity' position conflate the boundaries and different ethical obligations required for treatment and research, these positions should be abandoned. Instead, the 'different' position that explicitly acknowledges these distinct ethical obligations should be adopted (Miller & Brody, 2003a).

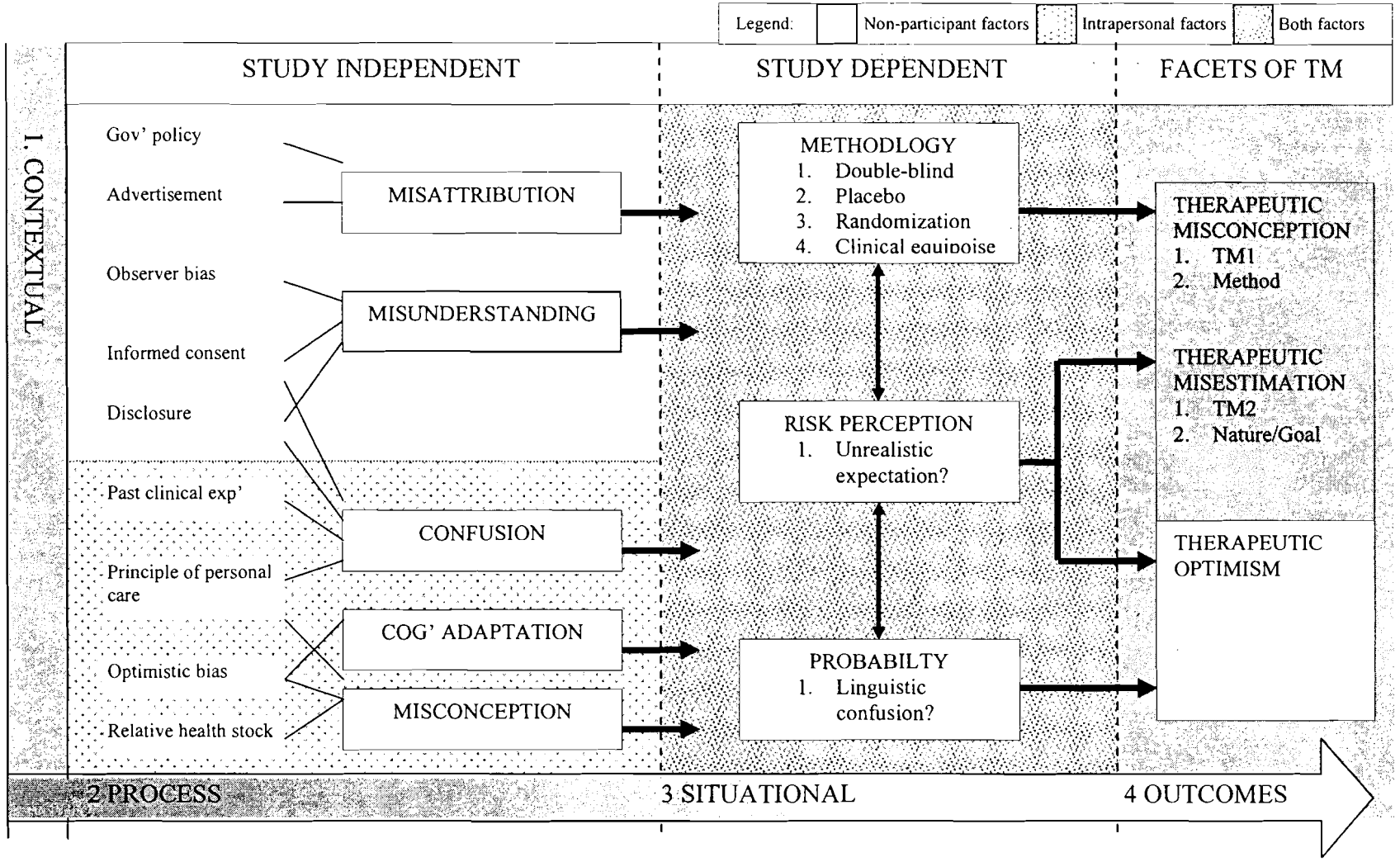
This controversial position advocated by Miller and Brody (2003a) has stimulated a lively debate as to how the interests of patients/participants can best be served (cf.

Mann & Dijulbegovic, 2003; Glass, 2003; and Miller & Brody, 2003b, 2003c). What is clear is that the implications of therapeutic misunderstanding are complex and have yet to be fully appreciated in relation to research ethics.

2.9 A Conceptual Model of Therapeutic Misunderstanding

An important first step in scale development is to articulate a clear conceptualization of the construct to be measured and the theoretical context in which it is embedded (Clark & Watson, 1995; DeVellis, 2003). While a well-formulated theory is not necessary for instrument development, thorough consideration of theoretical issues will increase the likelihood of establishing psychometrically sound scales (Clark & Watson, 1995). A clear conceptual foundation is also an integral element when assessing construct validity of scale responses. Unfortunately, there does not yet exist a comprehensive theory or a conceptual model of therapeutic misunderstanding. Therefore, having established an operational definition of therapeutic misunderstanding, having examined its implications and significance, and after reviewing factors that are believed to be related or contribute to this construct, I will conclude this section with a conceptual model to guide the development of the proposed scale (see Figure 2.1). This conceptual model is by no means exhaustive nor has it yet received direct empirical support. Future research is required to attain these goals.

Figure 2.1: A proposed conceptual model of therapeutic misunderstanding.



There are several caveats that need to be acknowledged before presenting the proposed model. With few exceptions, specific components of the model have been discussed previously and will not be repeated here. Therefore, discussion will be restricted to an analysis of how these components are assumed to interact to produce the various types of therapeutic misunderstanding. Notice that many pathways have not been specified. This is due to the absence of empirical research and theoretical guidance on these complex phenomena. Also absent are indices of the direction of relationship between different constructs. It should be stressed that this conceptual model is not a path diagram or structural equation model regarding the antecedents or components of therapeutic misunderstanding. A path diagram to inform scale development is presented in the methods section.

2.9.1 Grouping of constructs

Constructs are placed in groupings with the use of margins and three distinct pattern backgrounds. The two margins (one at the top and another on the left but extended to the bottom) of the model convey important information on how different constructs (discussed as contributors earlier) are believed to be related to therapeutic misunderstanding. The top margin (moving from left to right) distinguishes between study independent and study dependent contributing factors whereas the final column delineates the three hypothesized components of therapeutic misunderstanding. Participants' beliefs and perceptions (e.g., prior clinical experience) or study independent variables are in place prior to study dependent variables thereby signifying the temporal sequence among constructs. In other words, pre-existing study independent contributors

are hypothesized to exert influence on study dependent contributors lending to therapeutic misunderstanding.

2.9.2 The chrono-arrow

To further reflect the hypothesized temporal relationship among constructs, the second margin labelled the 'chrono-arrow', places these contributors within context of the consent process. The arrow begins at the top left corner and ends on the bottom right, distinguishing points in the process during the consent process potentially leading to therapeutic misunderstanding (i.e., contextual factors, process factors, situational factors, outcomes). A secondary purpose of the chrono-arrow is to highlight points of possible intervention to prevent, reduce, eliminate, or redress the occurrence of therapeutic misunderstanding.

The placement of sequential points is also important as each has been strategically positioned in relation to various contributing factors most salient at various points in the process. This is intended to highlight specific factors at specific points in the process. For example, point 1 (contextual factors) indicates that particular attention should be paid to misattributions and misunderstandings that result from an array of interpersonal and societal factors (e.g., incomplete disclosure). Point 2 (process) encompasses intrapersonal factors such as the expectancy of personal care, optimistic bias, perceived relative health stock, and risk perceptions that can create confusion, misconception, or cognitive adaptation which, in turn, colour understanding and appreciation of research. At point 3 (situational factors), specific and proximal factors leading to the emergence of therapeutic misunderstanding are listed. Finally, at point 4 (outcomes), therapeutic misunderstandings are listed resulting from the extent and content of information

provided to participants and the intrapersonal processes by which these participants filter, encode, and recall this information.

2.10 Study Goals and Hypotheses

To summarize, the goal of this thesis is to develop a psychometric instrument to measure therapeutic misunderstanding for use with clinical trial participants. Based on the reviewed literature, it is known that therapeutic misunderstanding is widespread among study participants, investigators, health professionals, and substitute decision makers. Moreover, the existence of therapeutic misunderstanding has important implications for the doctrine of informed consent, the conflict between personal and public health goals, and the principle of clinical equipoise. Without a valid and reliable measure of therapeutic misunderstanding, it is unlikely that the prevalence of this phenomenon can be effectively documented nor interventions developed or tested. Furthermore, the number of clinical trials conducted with older adults will only increase in coming years. This is because of illnesses specific to older adults (e.g., AD) and the different risk/benefit ratios of treatments for this population preclude extrapolation of results with young adults (Le Quintrec, Bussy, Golmard, Herve, Baulon, & Piette, 2005). Taken together, the development and validation of a measure of therapeutic misunderstanding is both necessary and timely.

A three facet definitions of therapeutic misunderstanding is advanced and a conceptual model is proposed to explain the relationships among therapeutic misunderstanding and associated constructs. Therapeutic misunderstanding is believed to be composed of three facets in which stakeholders: 1) conflate the goal and nature of research and treatment (i.e., therapeutic misconception) because of a mistaken belief of

personal care, a failure to appreciate the purpose of research, or a misunderstanding of the research methodology; 2) appraise the risks and benefits of research participation unrealistically (i.e., therapeutic misestimation) because of either a misattribution of therapeutic intent or a different conceptualization of probabilistic information; and 3) understand both 1) and 2) but remain hopeful and excessively optimistic about their outcomes (i.e., therapeutic optimism).

The research question I addressed in thesis was how we can objectively measure a person level of therapeutic misunderstanding. These led to four specific research questions: 1) what are the good indicators for measuring the three facets; 2) how are these facets related to each other; 3) is the resulting scale measuring what it is purport to measure; 4) is the scale a reliable measure over time. To further investigate question 2, I translated the question into 5 hypotheses, representing the hypothesized factor structure of therapeutic misunderstanding based on the 3 facets definition.

Hypothesis 1: Based on an integrative review of the literature, it is hypothesized that therapeutic misunderstanding can be best measured as a 3 factor construct. More specifically, 1.1) therapeutic misunderstanding can be effectively measured by three factors labelled as therapeutic misconception, therapeutic misestimation, and therapeutic optimism; 1.2); resulting items from an extended item pool will significantly contribute to measurement of their respective factors (i.e., simple structure); 1.3) items will load on one and only one factor (i.e., no cross loading); 1.4) these factors will be significantly inter-correlated; and 1.5) these factors will be subsumed by a higher-order, second-level general latent factor labelled therapeutic misunderstanding.

Theses hypotheses were tested and the psychometric properties of responses to the proposed scale were established in two studies. Study 1 established item content and ascertained the reliability of responses to this new scale with community dwelling older adults using a web-based survey. The factor structure of the proposed instrument as well as the content validity of responses were also be examined in this study.

Study 2 examined the validity of responses to the scale with a clinical sample of participants. Specifically, validation is used here in a sense that is similar to the one espoused by the program evaluation standards of the Joint Committee on Standards for Educational Evaluation (as cited in Thompson & Daniel, 1996); that is, validation as a process of compiling evidence to support the interpretations of, and inferences draw from responses to the proposed instrument. This was achieved by an examination of the reliability and the criterion validity of responses to the scale with participants currently or previously enrolled in a clinical trial.

CHAPTER 3 METHOD

3.1 A Two Studies Approach

This thesis consisted of two studies with analyses performed on separate datasets from two separate populations. Study 1 was a web-based survey of 464 self-selected, community-dwelling older adults recruited for the purposes of scale construction. The primary objective of Study 1 was to obtain participant responses to an initial pool of items to arrive at a working version of the scale. This was accomplished by item-analyses of responses from the 464 participants as well as separate analyses of 164 randomly selected responses sets using exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) on the remaining 300. Responses to the proposed instrument were subsequently validated with the assistance of a separate sample of 37 self-identified clinical trial participants over 49 years of age (i.e., inference validation study).

The rationale for two studies is empirical whereas a two sub-samples approach is both practical and conceptual. First, with respect to a two studies approach, it is customary in scale construction to first develop a working scale, and then validate responses to the instrument using a separate sample (e.g., O'Rourke & Cappeliez, 2002). Second, a two sub-samples approach was needed due to logistical constrains as well as the limitations of developing a scale based solely on responses by clinical trial participants.

Large sample sizes are required for scale development procedures such as exploratory and confirmation factor analyses (Comrey, 1988; Kline, 2005). Clark and Watson (1995), for instance, recommend that a minimum sample of 300 be used for the purpose of scale construction. Given the timeframe of a master's thesis, it was simply not feasible to recruit 300 or more clinical trial participants within a reasonable time. A decision was therefore made to split the scale development process into two studies with separate sub-samples.

More importantly, ensuring that the results were based on a sample of older adults comparable to the one in which the proposed instrument is intended is essential to establishing the reliability and validity of responses. This is because reliability of responses is affected by sample composition and variability (Dawis, 1987), and validity is dependent on the sample from which inferences are drawn (Streiner & Norman, 2003; Thompson & Daniel, 1996). Moreover, overly homogeneous samples can attenuate correlations among variables, which can result in findings that have poor replicability across samples (Fabrigar, Wegener, MacCallum, & Strahan, 1999; Reise, Waller, & Comrey, 2000).

Notwithstanding the appeal of developing the instruments from a sample of older adults enrolled in a clinical trial, it was assumed that this approach might produce biased results due to exclusion of non-consenters. More precisely, older adults enrolled in clinical trials are a defined population which, by definition, excludes those who declined to enrol, or for other reasons, did not choose to participate. Indeed, Meropol, Weinfurt and colleagues (2003) found statistically significant differences between those who enrolled and those who declined to participate in phase I oncology clinical trial research.

For instance, study consenters were more likely to expect benefits, were more confident of being among those who would benefit, and had higher likelihood of benefit ratings for both experimental and standard therapies than non-consenters. Furthermore, controlled clinical trial are conducted to make comparative inference among treatment groups and not to draw representative inference about the population of interests (Senn, 2003). Basing item inclusion decisions solely on responses by clinical trial participants, therefore, would have invited uncertainty as to the validity and reliability of responses and, more importantly, have led to the development of a less than ideal measure.

3.1.1 Internet data collection

Internet based recruitment is believed to enable recruitment of less circumscribed samples. The heterogeneity of such samples also increases covariation among variables resulting in a higher internal consistency of responses. Given that older adults often cope with at least one chronic condition or suffer from one life threatening disease (Newbold & Filice, 2006; Statistics Canada, 1999), it can be inferred that their experiences are a sufficient approximation to most clinical trial participants. In other words, it is within the realm of possibility that many if not most older adults might be approached or deemed eligible at some point to take part in a clinical research study.

Internet data collection has been effectively employed in a variety of research contexts, including studies with general older adult samples (e.g., O'Rourke, 2005) and physician risk communications studies (e.g., Gurmankin et al., 2004). The following section will review the advantages of this mode of data collection, refute misperceptions regarding Internet-based data collection, and outline strategies to address some limitations.

In terms of the objectives of this thesis, Internet-based data collection conferred unique advantages (see Reips, 2006 for a review). Most notably, it provided a solution to the aforementioned problems (i.e., exclusion of non-participants). With respect to logistical challenges, web-based recruitment and data collection is comparatively inexpensive and provides rapid responses. Also of note, Internet-based data collection allows researchers to recruit more geographically diverse samples as compared to more traditional methods of recruitment (e.g., O'Rourke, 2005; Reips, 2006). As Granello and Wheaton (2004) noted, web-based data collection enables researchers to access participants that are not necessarily in contact with the healthcare system, therefore improving the generalizability of findings to non-clinical populations.

Despite the common preconception that Internet-derived study participants are demographically distinct, prior research with older adults has found that such samples are comparable to those recruited by means of more traditional self-selection methodologies with respect to age, sex, level of education, and socioeconomic status (O'Rourke, 2003; O'Rourke & Cappeliez, 2002). These findings are in accord with those reached in a large-scale comparative study by Gosling, Vazire, Srivastava, and John (2004). In fact, Internet samples were found by these authors to be more diverse in their composition.

It should be noted that sample comparability is contingent on the type of research and its purposes. In research where representative samples are crucial to the validity of results as in the case of marketing and polling (i.e., where generalizability to populations is integral to answering the research question), Internet-based data collection may not be ideal (Granello & Wheaton, 2004). Moreover, in contrast to positive results obtained from comparative studies in social psychological research, studies in business and

marketing have found significant demographic differences between the two methods (Roster, Rogers, Albaum, & Klein, 2004).

Perhaps more important than sample compatibility is the finding that substantive variables of interest do not differ markedly between samples (Roster et al., 2004). The results of available research have been favourable. In particular, Gosling and colleagues (2004) reported that web-based participants do not appear to differ with respect to well-being and personality constructs compared to those recruited by more traditional means. Hiskey and Tropp (2002) also found in longitudinal studies, results obtained from web-based survey are comparable with those collected from traditional survey.

Steps were taken to minimize limitations inherent in conducting web-based research. In particular, sampling biases, low response rates, higher rates of item omission and multiple submissions (also known as *protocol validity*; see Johnson, 2005) pose a significant challenge for self-report web-based studies (Birnbaum, 2004; Granello & Wheaton, 2004; Roster et al., 2004).

Of note, web-based research tends to have lower response rates then telephone and mail surveys (Granello & Wheaton, 2004; Roster et al., 2004). For examples, Harewood, Wiersema, and de Groen (2003) reported lower responses to a web-based survey (34%) as compared to the telephone responses (78%) and standard mail (67%) for a patient satisfaction survey. Similar results have been found in non-health related research. For instance, Sills and Songs (2002) obtained a 22% response rate after three reminders for their international student survey. A comparative study by Roster and colleagues (2004) in a corporate organization found lower response rates to a web-based survey (32.6%) compared to a telephone survey (40.5%). Of note, response incentives

have been used in web-based studies to increase participation with good results (O'Rourke, 2004; Tuten, Galesic, & Bosnjak, 2004). Inclusion in a $500 dollar lottery draw was made available to participants who provided usable questionnaire responses in order to increase response rates for this study and to speed data collection.

Item omission or missing data is not unique to web-based research but has been found to be more prevalent with this method of data collection. For instance, Johnson (2005) reported that missing responses in web-based personality research were two to eight times higher than rates found with paper-based inventories. Irrespective of the method of data collection, managing missing data is important prior to statistical analysis. This is particularly germane in this instance as missing data are common in research with community dwelling older adults (Mazaux et al., 1995; Vance, DeLaine, Washington, & Kirby-Gatto, 2003). Missing data are also a common problem in the analysis of covariance structures (e.g., confirmatory factor analysis; Allison, 2003; McDonald & Ho, 2002) and can negatively impact reliability estimates (Enders, 2004). Moreover, a different strategy is needed depending on the proportion of missing data and whether data are missing at random or systematically (Kline, 2005; McDonald & Ho, 2002). Details on how missing data were handled are discussed in greater detail in the data screening and missing data sections.

Multiple submissions are another possible problem with web-based research. In online personality research, estimates of multiple submissions ranged from 3.5% to 4% of responses (Gosling et al., 2004; Johnson, 2005). Birnbaum (2004) provided a list of reasons for multiple submissions and strategies to address this problem. Following his recommendations, participants were asked not to participate more than once and

reminded that they had only one chance in the lottery irrespective of number of submissions made. Identifiers such as email addresses are commonly requested from participants to detect duplicates (e.g., O'Rourke & Cappeliez, 2002). For this study, the Internet Protocol (IP) address of participants was logged using common gateway interface (cgi) script (Birnbaum, 2004; Fraley, 2004), though it could not distinguish multiple submissions from the same participant from multiple entries or from different participants within the same household. Building on the suggestion by Johnson (2005), duplicate records were identified using the Duplicate Record Finder in SPSS.

3.2 Study Participants (Studies I & II)

A total of 530 participants returned usable results. Data were collected from a website specifically constructed for this thesis (http://www.sfu.ca/~phchou; see Appendix A & B). Participants were recruited through websites and bulletin broads targeted to older adults (e.g., American Association of Retired Persons, SeniorNet, 50+ Net, Age of Reason) as well as an online social psychological research website (e.g., Psychological Research on the Net; http://psych.hanover.edu/research/exponnet.html). The vast majority of the participants were from Canada (89.8%). Those from the United States comprised the second largest group of respondents (6.0%), with remaining response originating from other English speaking countries including Australia, New Zealand, and England. As previously mentioned, a $500 lottery prize was awarded to one randomly selected participant as a response incentive to facilitate data collection. Participants were also asked to indicate whether they would be willing to take part in a follow-up study to enable calculation of test-retest reliability of responses to the proposed instrument.

Details on how duplicate cases and missing data were dealt with can be found in the results section.

The average age of participants was 60 years (SD = 6.24, range 50 to 84). Slightly more females participated in the survey (57.5% vs. 42.1% respectively). This sample is quite well educated, with an average of 14.0 years of education (SD = 3.96, range 0 to 25). The majority were married (72.3%), of White/European origin (93.4%), and reported English as their first language (92.3%). Slightly over half of the participants had retired from the paid workforce (54.9%), though a significant minority continued to work on either a full-time (26.0%) or part-time basis (11.9%).

With respect to health, participants on average reported that they had four chronic conditions (SD = 2.63, range 0 to 13). The top three reported were trouble falling or staying asleep (n = 271), followed by arthritis/rheumatism (n = 253) and allergies (n = 195). Over half (56.3%) reported their health to be good (25.7%), very good (23.4%), or excellent (7.2%). Closed to two-thirds (65.1%) reported their health to be just as good as others their age, and 43.8% indicated that their health is about the same as last year. The majority indicated that health conditions have little impact on their lives (52.6%), followed by not at all (30.0%) and a great deal (16.2%).

It is important to examine sample composition and variability because reliability and validity of responses are influenced by these two factors. Therefore, I also tabulated the same descriptive information between those who were current or past clinical trial participants and those that were not (see Appendix C for details). It was found that clinical trial participants were significantly older (M = 61.82 vs. 59.76 years, t[528] = 2.52, p = .01) and, on average, reported one additional chronic health condition (M = 4.73

vs. 3.90, (t[528] = 2.41, $p < .05$) than their non-trial counterparts. With respect to specific chronic conditions, a higher proportion of the clinical trial participants reported having arthritis (χ^2 [1, N = 505] = 5.18, $p < .05$), undergoing surgery (χ^2 [1, N = 498] = 4.53, $p <$ .05), and vision problems (χ^2 [1, N = 490] = 4.31, $p < .05$). A higher percentage of clinical trial participants had retired from the paid workforce (χ^2 [1, N = 522] = 8.12, $p =$ .04). No differences were found with respect to years of education (t[514] = 1.62, *ns*), religious service attendance (t[475] = -.20, *ns*), and time required to provide responses (t[528] = .05, *ns*). Also of note, the sex, marital status, ethnicity, and first language were statistically indistinguishable between groups.

Of the 66 self-reported clinical trial participants approached to participate in Study 2, 23 did not take part. Participants and non-participants were largely comparable with respect to demographic characteristics. However, non-participants reported fewer years of education (M = 13.2 vs. 15.6 years, t[29] = 2.19, $p < .05$; equality of variance not assumed). They were also more likely to report that their health had worsen over the past year (χ^2 [2, N = 66] = 8.12, $p < .05$) and that their health status impacted their life a great deal (χ^2 [2, N = 66] = 8.67, $p = .01$).

3.3 Item Generation

3.3.1 Number of items

Item generation was guided by the operational definition of the construct measured (i.e., the three facets definition of therapeutic misunderstanding) established on the basis of the existing literature and theory. In addition to newly written items, existing items from related scales (e.g., Life Orientation Test-Revised) informed the development

of the initial item pool. Clark and Watson (1995) explain that the goal of item generation is to create a sample of items that sufficiently cover all relevant content of a construct. To ensure that an adequate number of items assess each major dimension so that each content area was sufficiently represented in the final scale (i.e., each factor or subscale), 127 items were generated based on each of the three facets of therapeutic misunderstanding (Horng & Grady, 2003; see Appendix D for details). Redundancy at this stage was tolerable, in fact, desired because psychometric analyses can only determine what should be included among the existing items but cannot identify others that might have been in the item pool (Clark & Watson, 1995; DeVellis, 2003; Noar, 2003). Redundancy of items is also advantageous when conducting exploratory and confirmatory factor analyses for item selection (Reise et al., 2000).

3.3.2 Readability of scale items

The reading level required to understand items was examined using the Flesch-Kincaid readability scale (grade-level range, 0-12) available in Microsoft Word. For the initial 127 items, Flesch-Kincaid Grade Level of the therapeutic misconception sub-scale, therapeutic misestimation subscale, and therapeutic optimism subscale were 8.8, 10.8, and 6.7 years respectively.

3.3.3 Item format

Although there is no consensus as to which item format is most optimal (Clark & Watson, 1995), choosing a proper item response format is important because it can influence the variability of scale responses. As DeVellis (2003) explains, "a measure cannot covary if it does not vary" (p. 75); as such, a scale with limited variability (i.e.,

true/false response format) can lead to erroneous conclusions as to the relationship between its responses and other constructs (Comrey, 1988; Streiner & Norman, 2003). Estimation methods used in factor analysis further assume that variables are measured on interval or ratio scales (Byrne, 2001). The use of ordinal scales with too few categories (e.g., less than five) can therefore lead to distorted findings (Reise et al., 2000). Aside from increasing the number of items in the scale, adopting a response format that has a higher number of scale response categories will increase variability (DeVellis, 2003; Reise et al., 2000). For this reason, a 5-point Likert-type format was adopted for this scale. Another reason for the 5-point Likert-type format pertains to the nature of the phenomenon. Conceptually, therapeutic misunderstanding as a latent construct is believed to be continuous rather than discrete. Likert-type response formats are widely assumed to provide greater sensitivity of measurement than a dichotomous response format.

To guard against yeah saying or nay-saying biases, efforts were made to develop items that were negatively worded and reverse keyed. This is an important feature in test construction because, if not employed, it can produce ceiling effects for responses to a scale (Streiner & Norman, 2003). Having both positive and negatively worded items also has the benefit of maintaining respondent's attention and enables identification of contradictory responses. Following the recommendations of Comrey (1988) and Clark and Watson (1995), double negative, complex, and double-barrelled items were excluded from the scale.

3.3.4 Content validity

Content validity describes a scale's ability to reflect the content of the construct measured (Streiner & Norman, 2003), in this case, therapeutic misunderstanding. Unlike more quantitatively oriented forms of validity, content validity is not mathematically determined; instead, it is commonly assessed with aid of topic area authorities.

A panel of experts reviewed the initial item pool and suggested others to provide full coverage of the construct. Items were reviewed by researchers familiar with therapeutic misunderstanding, ethicists, and clinicians. They included Drs. Paul Appelbaum, Charles Lidz, and Thomas Grisso, who are the principle researchers of the therapeutic misunderstanding as well as Drs. Sam Horng and Christine Grady, the authors who first conceptually distinguished the three forms of therapeutic misunderstanding. Each of the experts was provided with the prospective item pool and the operational definition of therapeutic misunderstanding. The general feedback from the panel was positive, most agreed that items provided adequate content coverage, depth, and relevance for therapeutic misunderstanding. There were, however, some concerns with respect to the applicability of certain items to real world clinical trials research (discussed more fully in the limitations section in Chapter 5).

3.4 Scale Construction: Study 1

The primary objective of Study 1 was to obtain participant responses to the initial pool of items in order to develop and refine the proposed instrument. Study 1 addresses the following research questions. First, what are some good questions to ask if you want to know a person level of therapeutic misunderstanding? Second, how are these 3 types of errors related to each other? This was accomplished via an evaluation of item

distribution scores and correlation coefficients as well as an examination of the factor structure and various psychometric properties of responses of the proposed scale (e.g., reliability and validity of responses). This process also enabled a direct test of the hypothesized factor structure in hypothesis one (i.e., factorial validity of the three facets model).

3.4.1 Procedure

Study 1 participants were selected on the basis of not being enrolled in a past or current clinical trial research study. An *analogue study* design commonly used in decision making research, was adopted for Study 1. In analogue studies, participants are asked to imagine that they are faced with a particular decision in a specific situation (Reynolds & Streiner, 1998). For this study, participants were given the following introductory text:

> Imagine you are suffering from a chronic illness or other serious disease. After discussing your condition with your family physician and/or specialist, you have been told that there is a new experimental treatment for your condition. It is not known whether or not this new treatment would provide any benefits to you above and beyond currently available treatments. A physician or clinical nurse has asked you to consider enrolling in this randomized controlled trial. Depending on the group to which you would be assigned, you may receive an inactive medication (i.e., placebo) or the experimental treatment. The likelihood of being assigned to these two groups is equal (i.e., 50/50). With this in mind, please answer the following questions as if you were faced with this decision (Flesch-Kincaid Grade Level = 12.0).

It is acknowledged that analogue studies can have questionable external validity (see Reynolds & Streiner, 1998). This is exemplified in depression research in which self-reported distress from college students has been considered to be an *analogue* for clinical depression (Coyne, 1994; Vredenburg, Flett, & Krames, 1993). Hypothetical

studies, the economic counterpart of analogue studies, have also been questioned with respect to their utility in health measurement (see Gurmankin et al., 2004 for an application of analogue study in physician risk communications). Streiner and Norman (2003), for instance, noted that econometric methods such as time trade-off and analogue studies are not completely value free as in contrast to what their proponents have claimed. It appears that real patients ascribe higher (more positive) utilities to states of ill health than do healthy individuals imagining themselves to be in that state. Moreover, such studies also require higher participant reading levels. Nonetheless, analogue studies have the advantage of rapid participant recruitment in scale development (Reynolds & Striener, 1998).

With respect to this thesis, however, the question remains as to the extent of threat this poses to the accuracy of findings. Reports on prevalence of chronic illness among older adults suggest that it is not unrealistic to ask participants to consider whether or not they would enrol in a clinical trial given that 82% of older Canadians suffer from at least one chronic illness (Statistics Canada, 1999) and that they are considerably more likely to die from a life-threatening disease compared to younger age groups. Moreover, a considerable amount of clinical trial research has been conducted on common chronic conditions such as arthritis and life threatening diseases such as cancer (Hawthorne, 2005). As previously noted, the sample recruited for study 1 reported to have an average of four chronic conditions; Only 32 participants (7.1%) responded that they do not have any chronic condition and 50.1% indicated that they had arthritis, a condition that topped the list of most advertised prescription drugs (National Institute of Health Care

Management, 2001). Taken together, the analogue context of this study, albeit contrived, was believed to be a sufficient approximation to yield preliminary results.

3.4.2 Analytical techniques

3.4.2.1 Psychometric evaluation

Item selection was aided by several considerations. The distribution of item responses was first examined to assess the psychometric properties of responses using the full non-clinical trial sample (n = 464; i.e., univariate item-level analyses). This entailed examination of the mean, standard deviation, skewness, kurtosis, item total correlation (ITC), and square multiple correlation values for each item according to *a prior* criteria. This was followed by dividing the non-clinical trial participants into two sub-samples: 164 and 300 for exploratory factor analysis and confirmatory factor analysis respectively, a practice customary in scale construction studies (see Noar, 2003; O'Rourke & Cappeliez, 2002). Pre-analytic issues such as sample size requirements and the assumptions of various statistical techniques can be found in the result sections.

3.4.2.2 Factor structure and construct validity of responses:

Construct validity pertains to an instrument's ability to effectively measure the target construct (see DeVellis, 2003 for an alternative definition) and to consist of at least three components-substantive, structural, and external (Clark & Watson, 1995). Construct validity is suggested when responses to an instrument are significantly associated with concrete indicators of the target construct. To examine the factor structure of responses, exploratory factory analysis (EFA) was performed with SPSS Factor on 164 randomly selected web-based participants. To establish the multi-dimensionality and construct

validity of responses to the proposed scale, confirmatory factor analysis was subsequently performed on remaining data (n = 300) in an attempt to replicate the structure observed with EFA. Factor analysis is suitable to assess construct validity (Schmidt & Embretson, 2003) and is used frequently to examine multi-dimensional constructs (Clark & Watson, 1995).

3.4.2.3 Validating the factor structure (model specification)

Confirmatory factor analysis was used to replicate the factor structure identified based on the EFA solution. Based on the literature and the proposed operational definition of therapeutic misunderstanding, it was expected that a three factor solution should be supported by the data, each representing a subscale or facet of therapeutic misunderstanding. Furthermore, conceptual associations among therapeutic misconception, therapeutic misestimation, and therapeutic optimism led to the assumption that the factors would be moderately correlated ($.3 \leq r \leq .5$).

Although second order models are not commonly assessed, it is prudent to rule out this possibility in the absence of a prior justification for the superiority of a first order model. As Chen, Sousa, and West (2005) noted, second order models might be suitable when the lower order factors are inter-correlated (as assumed here) and there is a higher order factor hypothesized to explain these associations. Conceptually, it can be argued that the three facets of therapeutic misunderstanding are subsumed by a general second order factor given their conceptual relatedness. A second order factor model also has the advantage of being more parsimonious (Rindskopf & Rose, 1988 as cited in Chen et al., 2005) and providing addition information on measurement error associated with the three facets measured by first order factors (Chen et al., 2005).

Given these considerations, two competing models were tested using confirmatory factor analysis in AMOS: a first order model (i.e., three correlated factors/subscales, see Figure 3.1); and a second order model with each of the three factors hypothesized to contribute significantly to measurement of an overarching latent therapeutic misunderstanding construct (see Figure 3.2).

3.4.3 Item analyses on responses to the revised scale

The psychometric properties of responses to the revised scale were summarized after revisions had been made on the basis of results of the EFA and CFA. As with the initial item analyses, the mean and standard deviation of each item are reported along with reliability indices. The latter includes item the total correlation, SMC values, item-level alpha, alpha of each subscale and the entire scale, as well as test-retest reliability.

3.4.4 Reliability of responses

The reliability of scale responses is defined as the proportion of the true score variance to the total score variance (DeVellis, 2003; Schmidt & Embretson, 2003; Streiner, 2003). During pilot testing, internal consistency was examined and computed as Cronbach's alpha. The goal was to obtain an alpha within the range of .80 and .90 for each subscale and overall scale responses (O'Rourke, Hatcher, & Stepanski, 2005). It should be noted that internal consistency, as with other forms of reliability, is not sufficient to establish the uni-dimensionality or validity of the scale. Although internal consistency is a measure of the homogeneity of items within a scale (DeVellis, 2003), statistics such as Cronbach's alpha can be confounded by other factors (e.g., the number

Figure 3.1 First-order, correlated three factors model of therapeutic misunderstanding.

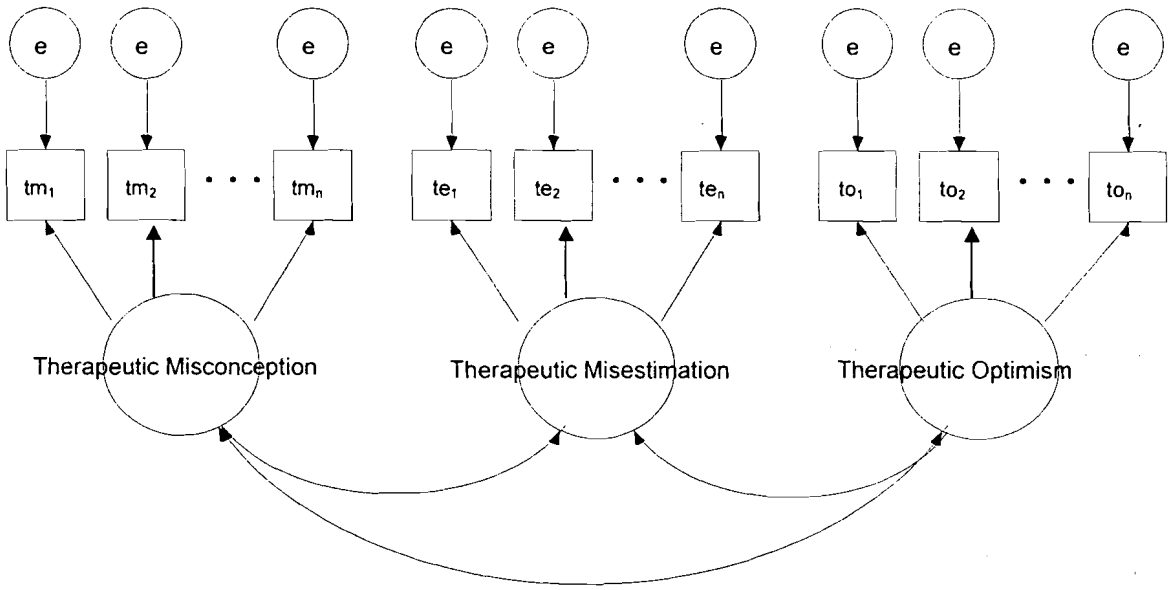
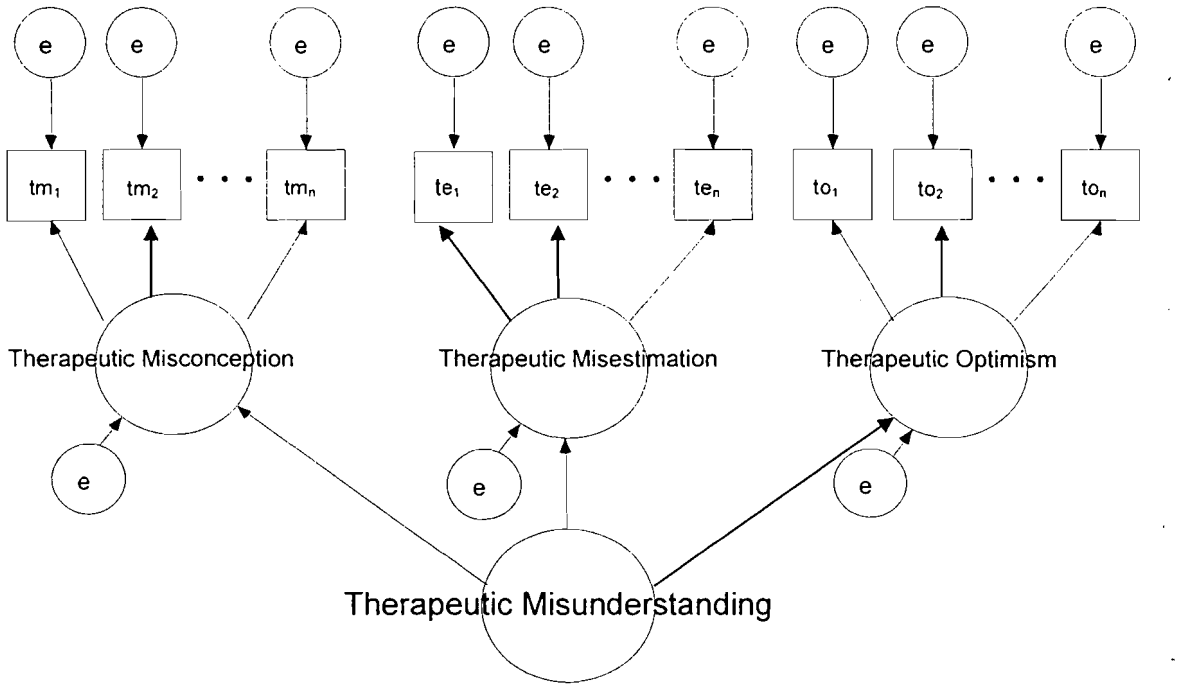


Figure 3.2 Second-order, three-factor model of therapeutic misunderstanding.



of items, see for example Streiner, 2003). As stated by Clark and Watson (1995), internal consistency merely indicates the degree of inter-correlation among items whereas uni-dimensionality indicates whether or not items measure a single underlying construct.

3.5 Inference Validation-Study 2

Because the nature of therapeutic misunderstanding might differ between clinical and non-clinical samples, a sub-sample consisting of older adults who were identified as current/past clinical trial participants (n = 66) was approached to respond to the proposed instrument. Of those, 44 completed the final scale and other related measures. The objectives of this second study were to assess whether responses to the proposed scale obtained from a community sample of older adults were applicable to a clinical sample. At the heart of study 2 lies two research questions. First, does the resulting instrument-Therapeutic Misunderstanding Scale (TMU) measuring what it is purport to measure? (i.e., construct validity of responses). Second, is TMU a reliable measure over time? (i.e., test-retest).

3.5.1 Procedure

Participants were identified based on their responses to two of the background questions. Those endorsing the statements "Are you currently enrolled in a clinical drug trial?" [yes/no] or "Have you ever been in a clinical drug trial?" [yes/no] were included. On this basis, 66 self-reported clinical trial participants were identified. These 66 participants were invited to complete a second online questionnaire constructed specifically for this thesis (see Appendix B). As an incentive, respondents were sent a $10 Starbucks gift card. A total of three rounds of email messages (one initial invitation

and two reminders) were sent out in September, 2006. During that period, 44 completed the final scale and other related measures, representing a respond rate of 66.6%.

3.5.2 Psychometric evaluation

Psychometric evaluation for the second study proceeded similarly to study one and will not be repeated here. The following section will briefly describe new and different procedures or elements that are unique to Study 2 data analyses.

3.5.3 Test-Retest reliability of responses

To examine the test-retest reliability of responses, the self-identified clinical trial participants were asked to complete the proposed scale a second time two to nine months after receiving initial responses. Ideally, this correlation should fall within the range of .7 $\leq r \leq .8$.

3.5.4 Convergent and discriminant validity of responses

The evaluation of convergent and discriminate validity of responses is specific to Study 2. Convergent and discriminant validity were assessed by examining whether responses to the proposed new scale and other related and distinct constructs emerged as predicted (Foster & Cone, 1995). A number of related measures, selected from the proposed conceptual model, were administered to clinical trial participants. These included measures of therapeutic misunderstanding, understanding of informed consent, optimism, risk perception, and relative health stock. Correlation coefficients between these measures and the proposed scale were examined to ideally provide data in support of the measure of as well as criterion-related validity of responses. Support for construct validity was sought by examining simple bi-variate correlations between these measures.

Table 3.1 outlines the expected direction and magnitude of associations between these related measures and the proposed measure of therapeutic misunderstanding.

Table 3.1: Expected correlation between facets of therapeutic misunderstanding and related measures.

Measures	Expected Correlation
TM – TMI	$.36 \leq r \leq .80$
tm – QuIC	$-.36 \geq r \geq -.80$
te – Risk Perception	$-.36 \geq r \geq -.80$
to – LOT-R	$.36 \leq r \leq .80$
TM – Relative Health Stock	+

Note: TM – Proposed instruments total scores; tm – proposed instruments subscale scores for the therapeutic misconception facet; te – proposed instruments subscale scores for the therapeutic misestimation facet; to – proposed instruments subscale scores for the therapeutic optimism facet; TMI – Therapeutic Misconception Index; QuIC – Qualify of Informed Consent Questionnaire; LOT-R – The Life Orientation Test-Revised

The addition of the Therapeutic Misconception Scale afforded an opportunity to further evaluate the construct validity of responses to the proposed instrument because this scale is purported to measure the same construct. As noted by various authors (e.g., Foster & Cone, 1995; Streiner & Norman, 2003), convergent validity of responses to a measure should be tested by methods that are maximally different. Although two scales cannot be said to be maximally different, assessing convergent validity vis-à-vis the correlation between the proposed scale and Therapeutic Misconception Scale nonetheless provided preliminary information. To the extent that the two correlate moderately to strongly (i.e., $.36 \leq r \leq .80$), this would provide evidence that responses to the scale possess convergent validity, not due to shared-method variance (i.e., different response

keys). Of note, the use of different response formats also increase one's confidence in the association found between measures.

3.6 Measures

In addition to the proposed measure, other instruments that are hypothesized to be related to therapeutic misunderstanding were administered to Study 2 participants (see Appendix B). Participants from Study 2 were asked to complete the proposed scale or the TMS first, followed by the other theoretically related measures in one of two randomly counterbalanced forms. At the beginning of the online survey, participants were asked to provide socio-demographic information and describe their experiences with clinical trials (see Appendix A & B). Information on the latter was collected because prior research has demonstrated a negative association between excessive perceived benefits and experiences with clinical trials (King & Henderson, 2003). It should be noted that many of these measures have not been extensively validated, thus caution is warranted when examining the psychometric properties of these measures and their associations with the proposed new measure. Unfortunately, these appear to be the only available measures.

3.6.1 Measure of therapeutic misunderstanding

3.6.1.1 Therapeutic Misconception Scale (2)

The Therapeutic Misconception Scale (TMS; Dunn, Palmer, Keehan, Jeste, & Appelbaum, 2006) is a 6-item measure developed for use with research participants. The items gauge participants' perceptions of individualization of care and blinding. The scale is scored dichotomously (True/False) and each item has a correct answer corresponding to a hypothetical clinical trial (e.g., "The researcher won't know exactly which

medication I am receiving"). Internal consistency of responses by 87 persons with schizophrenia has been reported as $\alpha = 0.75$.

3.6.2 Measure of understanding

3.6.2.1 Quality of Informed Consent (2)

The Quality of Informed Consent scale (QuIC; Joffe et al., 2001a) is a brief questionnaire that measures participants' objective and subjective understanding of the eight basic elements of informed consent as outlined in the Common Rule (45. C.R.F. 46) for clinical trial research. The current version consists of 20 questions assessing objective understanding and 14 assessing subjective understanding. Participants were asked to indicate their extent of agreement on a 3-point Likert-type scale (i.e., Disagree, Unsure, Agree) on the objective scale. Responses for the subjective scale were scored on a 5-point Likert-type scale ranging from "*I didn't understand this at all*" to "*I understood this very well*". Test-retest reliability over a mean interval of 15.4 days has been reported as $r = .66$ and $r = .77$ for tests of objective and subjective understanding, respectively (Joffe et al., 2001a). Importantly, internal consistency and validity (other than content validity) of responses to the QuIC have yet to be determined.

3.6.3 Measure of optimism

3.6.3.1 The Life Orientation Test - Revised (LOT-R) (2)

The Life Orientation Test - Revised (LOT-R; Scheier, Carver, & Bridges, 1994) is a measure of dispositional optimism. The scale consists of six core items (three positively worded and three negatively worded) and four filler items not used in scoring. These filler items were not administered in this study to minimize participant burden. Responses

are scored on a 5-point Likert-type scale, ranging from *strongly disagree* to *strongly agree*. Total scores range from 0 to 24 with higher totals suggestive of greater optimism.

Internal consistency of responses to LOT-R, as measured by Cronbach's alpha has been reported as α=.78 (Scheier et al., 1994) and α=.85 with older adults (O'Rourke, 2004). Test-retest reliability has been reported as r=.68, r=.60, r=.56, and r=.79 for four months, 12 months, 24 months, and 28 months respectively (Scheier et al., 1994). Existing research by Scheier and colleagues suggests the convergent validity of responses (r = .48 with self-mastery scale and r = .50 with Rosenberg's Self-Esteem Scale) and discriminant validity (r = -.53 with Trait version of the State-Trait Anxiety Inventory and $-.43 \leq r \leq -.36$ with measures of neuroticism) of responses to the LOT-R.

3.6.4 Measure of risk perception (2)

Four questions, adopted from Gaskin and colleagues (2004) were used to measure participants' risk perception as to the benefits and potential harm of both the experimental and standard treatments in the clinical trial research for dementia. Dementia was chosen as a target condition because none of the participants recruited for this study are/were in a dementia related clinical trial (i.e., responses not confounded by current/past clinical trial experiences), and secondarily, to have a single reference condition to anchor risk perceptions. A visual analogue scale was used as the response format based on the assumption that people interpret verbal descriptions of probability estimates differently (Streiner & Norman, 2003; Woloshin, Ruffin, Gorenflo, 1994). It is acknowledged that the use of visual analogue response scales have their own disadvantages (e.g., respondents usually provide responses in multiples of 5 or 10 rather

than using the entire scale); however, the risk perception literature remains equivocal on what is the best method to measure respondents' risk perception.

The use of multiple modes of responding to measures is a strength of this study. When an association is found, it lends confidences that the relationship is not simply a by-product of shared response method. Following the recommendation of Streiner and Norman (2003), the visual analog scale was presented vertically similar to a 'thermometer' instead of a horizontal line to facilitate older adults' responds to the scale.

3.6.5 Measure of relative health stock (2)

Relative health stock was measured by asking participants to select one of nine pies that best represents the loss of 'fullness' in their lives due to their diagnosis or change in health condition (Gaskin et al., 2004 see Appendix B for actual question). As reported by Gaskin and colleagues (2004), this measure of relative health stock was found to be distinct from dispositional optimism, monetary risk preference or preferences for quality versus quantity of life, and participants' perceived probabilities of benefit and toxicity of therapy. In the same study, relative health stock was found to predict cancer patients' decision to enrol or decline clinical trial participation.

3.6.6 Demographics questionnaire (1 & 2)

A demographics questionnaire (see Appendix A) was constructed to gather participant socio-demographic information, perceived health, and previous clinical trial experience. Socio-demographic information included age, sex, years of education, income, and ethnicity. Additional questions were included to assess Study 2 participants' previous clinical trial experience, such as clinical trial phase (e.g., open label) and

satisfaction with participation (see Appendix B). Perceived health was measured using four questions adopted from the Canadian Study of Health and Aging (Canadian Study of Health and Aging, 1994).

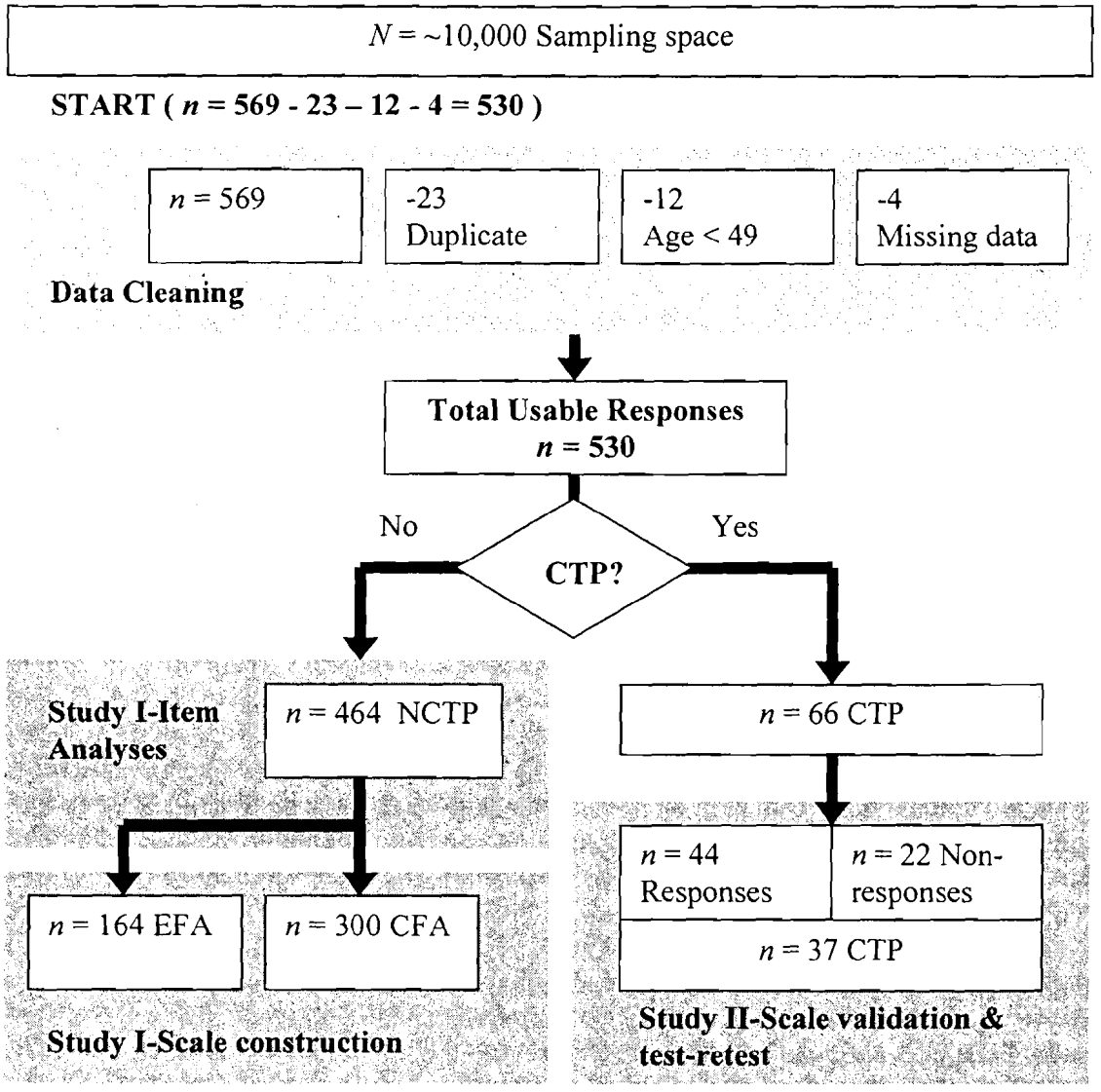
CHAPTER 4 RESULTS

Results based on the instrument development phase of this thesis (Study 1) and instrument validation study (Study 2) were conducted and analyzed separately. For clarity of presentation, findings from these two are summarized in separate sections. Overall implications and limitations of both studies are then presented and discussed jointly in the final chapter (i.e., Discussion).

4.1 Study I

Requests for participation were sent to 10,000 member of the Canadian Association of Retired Person. These data were collected in two waves between December, 2005 and February, 2006 at which point 555 participants completed the online survey. An additional 14 responses were received in June, 2006 to further increase sample size. This yielded an initial sample of 569 participants, representing a maximum possible response rate of 5.6% (see Figure 4.1). Prior to analyses, missing data were assessed and data were screened for duplicate cases, non-normality, and outliers.

Figure 4.1: Flowchart of initial sample to final sample for data analyses.



Note: NCTP-Non-clinical trial participant; CTP-Clinical trial participant; EFA-Exploratory factor analysis; CFA-Confirmatory factor analysis.

4.1.1 Data cleaning

4.1.1.1 Duplicate cases

I used SPSS duplicate analyses to identify duplicate entries. Using IP addresses, dates, and time of submission, 23 of the 555 responses were flagged as duplicate (4.1% of all cases). A further six and three participants response sets were excluded because they

were too young (<49 of age) or they didn't report their age respectively. Four others were removed because over 50% of their responses were missing. This revised total resulted in a working sample of 530 participants.

4.1.1.2 Missing data

It was anticipated that missing data might be an issue because of higher reported omission rates in web-based research (see Section 3.1.1) and studies with older adults in general (Vance et al., 2003). The SPSS missing data analysis module was used to identify patterns of missing data for the initial set of responses. Missing value analyses were conducted only with the 127 working scale items as other background variables (e.g., age, education, number of chronic condition) were used for descriptive purposes only.

I first assessed the type of missingness (e.g., missing completely at random). Results of the Little's MCAR test was statistically significant ($p < 0.01$), suggesting that the missing data were not missing completely at random. The magnitude of missing data, however, is small with 12/127 items having about one percent missing responses.

To investigate further, I ran separate variance *t* tests on the item "there is no known risk to participants in this study" because it had over 1% of missing data to identify any patterns. Results showed that the question did not have different non-random pattern of missing data with respect to age, years of education, number of chronic conditions, and completion time. I did find different percentages of missing data between this and other scale items. Cross-tabulation of the missing indicator variable with other categorical background variables revealed that a higher percentage of mixed ethnicity participants did not answer that question. Together, this supports the observation that the data are not missing completely at random.

Of the 520 initially recruited participants derived at Time 1, eighteen did not answer one or more scale questions. Four had more than 50% (range 52% to 100%) of their responses missing and were deleted from further analyses. Comparison between these four participants and the rest of the sample on key demographic variables indicated that they spent considerably less or more time answering the scale items and that they are all female (see Appendix E).

Given the non-random nature of missing data, traditional methods (e.g., listwise deletion, mean value substitution) were not used because of known problems such as underestimation of standard errors and distortion of correlations and covariance among variables (Allison, 2003; Byrne, 2001; Kline, 2005; Schafer & Graham, 2002). If one assumes missing data are unlikely to depend on participants' scores on therapeutic misunderstanding, it could reasonably be asserted that data are missing at random (MAR). Assuming that data are MAR, normal model maximum likelihood (ML) provides relatively unbiased parameters and standard errors estimates (see Schafer & Graham, 2002). The hock-deck imputation method, which imputed data based on like responses, available in PRELIS was used to impute the missing data (< 2% of total cases).

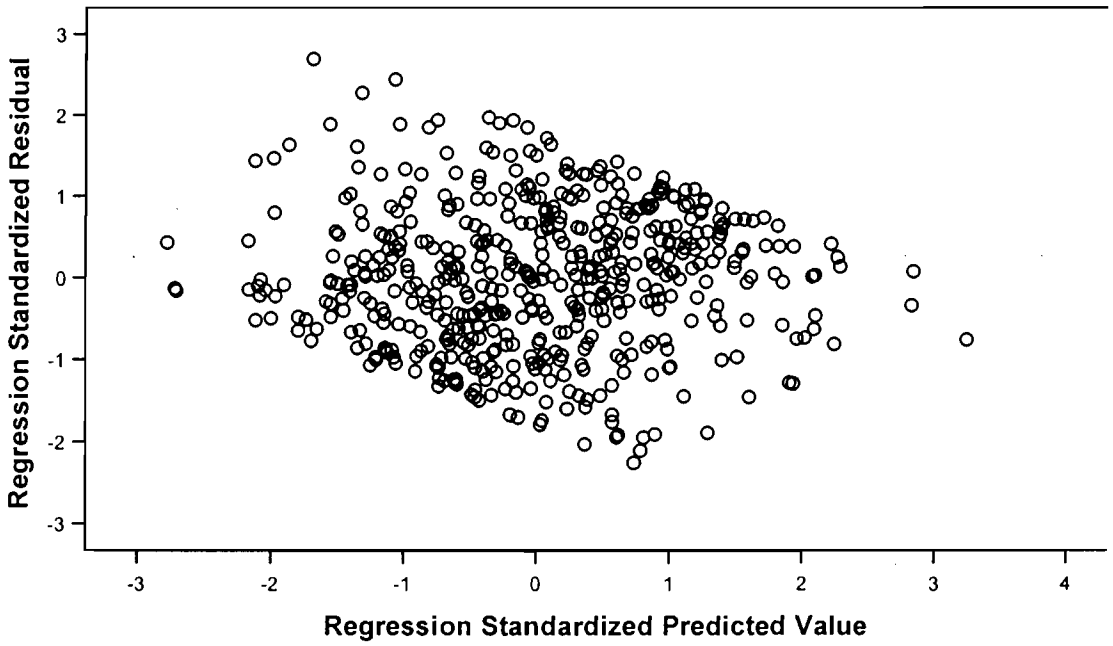
4.1.1.3 Normality and outliers

How data are distributed affect many analytic decisions. This principle applies equally to all stages, from item analyses to both exploratory and confirmatory factor analysis. For instance, Maximum likelihood (ML) estimation, the most common estimation method in the analysis of covariance structures, assumes multivariate normality (Byrne, 2001, 2005; Crowley & Fan, 1997; Kline, 2005; McDonald & Ho,

2002; Schumacker & Lomax, 2004; Tabachnick & Fidell, 2001). Therefore, it is essential to screen data to ascertain whether or not assumptions of statistical techniques are met.

Multivariate non-normality is difficult to assess, but in many instances, it can be estimated by inspecting the univariate distributions of variables, skewness, kurtosis and residual scores. Histograms showed that the distribution of most items appeared relatively normal. Given the 5-point Likert scale of the proposed measure, it is not surprising that none of the items were excessively skewed (skewness > |2.8|). However, a few items from the therapeutic misconception and therapeutic optimism subscales were leptokurtic based on the criterion of kurtosis > |2.8|. With the exception of the item "I would enrol in this study to advance the researchers knowledge of my illness", these overly peaked items were deleted. Following the guidelines of Wilkinson and APA Task force on Statistical Inference (1999), residuals of the data from a mock regression were examined to supplement the above methods in identifying distribution irregularities and non-linearity (see Figure 4.2). The residual scatterplot suggests that the data are relatively normal, linear, and homoscedastic.

Figure 4.2: Residual scatterplot from mock regression with case ID as dependent variable and scale items as independent variables.



Outliers, another source of non-normal data, were assessed by examining the frequency of distribution of z scores (a score greater than three standard deviations above or below the mean is commonly considered an outlier; Tabachnick & Fidell, 2001) and using Mahalanobis distance (Kline, 2005; Tabachnick & Fidell, 2001). No out of range responses were observed in the histogram depicting responses to scale items. Z scores indicated that 36 and 12 items had extreme values (i.e., z scores > |3.29|) on both sides of the mean respectively. These results are not surprising given the relatively large sample size. The z scores result also suggested that the lower and upper ends of the response format were under-utilized with some questions. A mock regression using case ID as dependent variable and scale items as independent variable (entered as one block) was run to identify multivariate outliers. The average Malhalanobis distance was 126.75 (*SD*

= 44.50). The ten most extreme cases exceed the critical value for Malhalanobis distance (χ^2 = 182.00, *df* = 127), suggesting the presence of multivariate outliers. This is in contrast with results from standardized residuals, where none exceed the critical value of 3.29.

4.1.2 Item analyses

Each item was examined according to the following *a priori* criteria. First, items were required to have mean values greater than their standard deviations. All 127 items met this criterion. Second, following the recommendations of Clark and Watson (1995), items with a broad distribution of responses are desirable (e.g., responses provided at each of the 5 response points). As shown in Appendix E, except for 4 items (tmisc014, tmisc119, to097, to107), all of the response formats were chosen, although the lower ended of the range tended to be relatively under-utilized. Items with skewness and kurtosis values greater than 2.8 (or less than -2.8) were considered problematic and were subsequently deleted. As discussed in section 4.1.1.3, none of the items were overly skewed.

Third, items were considered only for subsequent factor analyses if their item-total correlation (ITC) exceeded 0.3 as per convention. ITC values indicate the content saturation of an item. In classical test theory, the higher the ITC, the more discriminating that item relative to the target construct. Items with ITC values of .3 or above were initially retained. As noted by Floyd and Widaman (1995), items that do not correlate moderately with the total score are poor candidates for factor analysis.

Where possible, square multiple correlation (SMC) values were also consulted to aid the item selection process. In keeping with the procedure described by O'Rourke and Cappeliez (2002), items with SMC values greater or equal to .50 were retained. SMC values were not available for items from the therapeutic misconception and therapeutic optimism subscales because the determinant of the covariance matrix was zero or approximately zero. This indicated that some items are multicolinear/singular or are linear dependent of other items, suggesting some item redundancy.

These selection criteria resulted in a total of 55 candidate items for exploratory factor analysis: 30, 10, and 15 items from the therapeutic misconception, therapeutic misestimation, and therapeutic optimism subscales respectively. Table 4.1 shows a stratification of items into their respective sub-domains according to the selection criteria (see Appendix F for complete details).

Table 4.1: Selection criteria of variables for inclusion of exploratory factor analysis.

Item	Dist'	Mean > SD	S <|2.8|	K <|2.8|	ITC >|.3|	SMC >.5
Therapeutic Misconception [30]						
1) Reason (6 out of 9)						
1, 6, 26, 28. 31	Y	Y	Y	Y	Y	N/A
29	Y	Y	Y	N	Y	N/A
(17, 27, 30)	Y	Y	Y	Y	N	N/A
2) Personal care (11 out of 13)						
10, 18, 19, 20, 21, 25, 37, 42, 43, 44, 112	Y	Y	Y	Y	Y	N/A
(4, 8)	Y	Y	Y	Y	N	N/A
3) Blinding (3 out of 6)						
3, 23, 45	Y	Y	Y	Y	Y	N/A
(5, 22, 24)	Y	Y	Y	Y	N	N/A
4) Purpose (3 out of 9)						
7, 115, 116	Y	Y	Y	Y	Y	N/A
(9, 14, 15, 16, 118)	Y	Y	Y	Y	N	N/A
(13)	Y	Y	Y	N	N	N/A
5) Research method (6 out of 17)						
12, 34, 38, 39, 40, 47	Y	Y	Y	Y	Y	N/A
(33, 46, 117, 119, 120, 126, 127)	Y	Y	Y	Y	N	N/A
(32, 35, 36, 41)	Y	Y	Y	N	N	N/A
Therapeutic Misestimation [10]						
1) Endpoint (7 out of 10)						
50, 54, 55, 56, 57, 58, 124	Y	Y	Y	Y	Y	N
(48, 51, 53)	Y	Y	Y	Y	N	N
2) Benefit (2 out of 8)						
62, 124	Y	Y	Y	Y	Y	N
(49. 52, 63, 66, 121, 125)	Y	Y	Y	Y	N	N
3) Risk (1 out of 7)						
64	Y	Y	Y	Y	Y	N
(59-61, 65, 122, 123)	Y	Y	Y	Y	N	N
Therapeutic Optimism [15]						
1) Dispositional optimism (12 out of 38)						
70, 71, 72, 77, 81, 91, 92, 93, 94, 97, 102, 110	Y	Y	Y	Y	Y	N/A
(75, 78-80, 82, 83, 86-90, 95, 96, 98-101, 103, 107-109, 111-114)	Y	Y	Y	Y	N	N/A
(96)	Y	Y	Y	N	N	N/A
2) Optimistic bias (4 out of 6)						
67, 68, 69, 84	Y	Y	Y	Y	Y	N/A
(74, 76)	Y	Y	Y	Y	N	N/A
3) Hope (0 out of 6)						
(73, 76, 85, 105, 106)	Y	Y	Y	Y	N	N/A
(104)	Y	Y	Y	N	N	N/A
Total = 55 items						

Note: **Bold item numbers** were selected as candidates for EFA; (numbers in brackets) indicate the total number of candidate from each subscale. Y = Yes; N = No, N/A = Not Available.

4.1.3 Internal consistency of responses of working scale item

The internal consistency of responses of the 55 working items was found to be α = .95. This alpha value is high, suggesting redundancy of items (O'Rourke, Hatcher, & Stepanski, 2005). The Cronbach's alpha values for the therapeutic misconception subscale, therapeutic misestimation subscale, and therapeutic optimism subscales were α = .91, α = .80, and α = .89 respectively.

4.1.4 Exploratory factor analysis

Exploratory Factor Analysis (EFA) was performed on 164 randomly selected cases from the 464 non clinical trial participants. All analyses were performed using SPSS Factor. In total, two rounds of EFA were done to arrive at a refined item pool. Prior to the analyses, several steps were taken to determine the appropriateness of the dataset (Tabachnick & Fidell, 2001).

4.1.4.1 Sample size

It is generally agreed that larger sample sizes provide more stable factor solutions. Beyond that, however, there is little agreement on the minimum number of participants needed for exploratory factor analysis. Until recently, two explicit guidelines had been espoused. The first frames sample size requirements in terms of absolute minimums, with recommendations ranging from 100 to 250 participants (Comrey, 1988; Hogarty et al., 2005). The second is the participants-to-variables ratio, with recommendations ranging from 3:1 to 20:1 (Floyd & Widaman, 1995; Hogarty et al., 2005; Thomspon, 2004).

These rules of thumbs have been questioned, however, based on results from simulation study findings which indicate that necessary sample sizes vary as a function of

the ratio of number of indicators per factor, and communalities of the variables (Hogarty et al., 2005; MacCallum, Widaman, Zhang, & Hong, 1999; Mundfrom, Shaw, & Ke, 2005). In general, the higher the ratio of indicators per factor and communalities, the smaller the minimum sample size required. Under these conditions, it has been suggested that samples as small as 100 may be sufficient to obtain accurate estimates of factor loadings for single factor constructs (Fabrigar et al., 1999; MacCallum et al., 1999; Reise et al., 2000; Russell, 2002).

Given these considerations, it was believed that the proposed EFA sample size (n = 164) was sufficient to meet both sample size and the participants-to-variables requirements (assuming that approximately 10 items per each of the three sub-scales will be retained). Incidentally, meeting the latter requirement also simultaneously satisfies the over determination of factors condition. Although communalities for the working items were rather low (see Table 4.6 & 4.7), simulation study results suggest that communalities play a diminishing role in sample size requirements as the number of indicators per factor increases beyond seven (Mundfrom et al., 2005), which lends further support to the assertion that the sample size of 164 was sufficiently large to obtain a stable factor solution.

4.1.4.2 Pre-analyses

Prior to factor analyses, several steps were taken to determine the appropriateness of the dataset (Tabachnick & Fidell, 2001). Although factor analysis is relatively robust to violation of the normality assumption, multivariate normality was first assessed by determining that responses to items were at least univariate normal (Floyd & Widaman, 1995). Using 'mock regression' (see Kline, 2005), data were screened to assess whether

assumptions of normality, linearity, absence of outliers, multicollinearity and singularity had been met. Outliers were screened again for the 55 items using mock regression. No outliers were found and examination of the residuals normal probability plot (P-P Plot) confirmed that these items are normally distributed.

Second, the Kaiser-Meyer-Olkin measure of sampling adequacy was computed; a value of .6 or above is required for factor analysis. The Kaiser-Meyer-Olkin Measure of sampling adequacy value (KMO = .87) indicated sufficient common variance among variables for factor analysis. The interrelatedness of the items is corroborated by the finding that numerous correlations coefficients among the 55 items were in excess of .30 and most of the values in the anti-image correlation matrix were relatively small.

4.1.4.3 Factor extraction and rotation

I used principle axis factoring as the extraction method for all analyses. In keeping with the three facets operational definition of therapeutic misunderstanding, a 3-factor structure was sought to determine whether or not a 3-factor solution was viable. Based on the literature, it was assumed that there would be a moderate correlation between these three facets of therapeutic misunderstanding (i.e., the three factors were not assumed to be orthogonal). Following the recommendations of various authors (Fabrigar et al., 1999; Reise et al., 2000; Russell, 2002), factor analysis with oblique rotation (direct oblimin) was used in order to reflect the theoretically expected association between the three facets of therapeutic misunderstanding. Additionally, oblique rotation was selected because, compared to orthogonal methods of rotation, it meets the simple structure criterion better and it will also produce orthogonal solutions if the three factors

are, in fact, uncorrelated (Reise et al., 2000). To facilitate selection of items, orthogonal rotation using the varimax method was also computed and interpreted.

4.1.4.4 Number of factors

The viability of a 3-factor solution was assessed using three criteria: the eigenvalue rule; the scree test; and parallel analysis. More weight was assigned to results from the latter two given that the eigenvalue rule has been widely criticized by methodologists in terms of over factor extraction, its inappropriateness when conducting a principal axis factor analysis, and its arbitrariness (Fabrigar et al., 1999; Floyd & Widaman, 1995; Reise et al., 2000; Russel, 2002).

Among procedures available for factor extraction in EFA, parallel analysis appears to be increasingly popular (Pohlmann, 2004; Russell, 2002; Thompson & Daniel, 1996). This procedure is an extension of the scree plot test; instead of subjectively interpreting the elbow or substantial drop in eigenvalues, the number of factors is determined by comparing the plots of eigenvalues from the sample data and the plots of eigenvalues from a random dataset of the same size (Fabrigar et al., 1999; Reise et al., 2000). Its unavailability in common statistical packages probably explains its under-usage (Russell, 2002).

According to the eigenvalue rule (i.e., Kasier-Guttmann rule; DeVellis, 2003; Tabachnick & Fidell, 2001), factors with eigenvalues less than one should not be retained. Results from the eigenvalue rules suggested a 13 factor solution. However, only the first accounted for more than 10 percent of the variance (27%). In contrast, both the scree-test and parallel analysis supported a 2 to 5 factor solution (see Figure 4.3 & 4.4). The eigenvalues, as shown in the scree plot, levelled off significantly after factor 5,

suggesting that any solution beyond 5 factors would be over inclusive. I used the SPSS syntax code by O'Connor (2000) to perform a parallel analysis (see Thompson & Daniel, 1996, Kaufman & Dunlap, 2000, O'Connor, 2000, Pohlmann, 2004, Reise et al., 2000, and for similar procedures in SPSS, a standalone program, SAS, excel, and R statistical packages, respectively). Results from parallel analysis are in accord with those obtained from scree-test, only the first five factors had eigenvalues which exceeded their counterparts from a random dataset. Together, theses support the hypothesized three factors solution as viable.

Figure 4.3: Scree plot

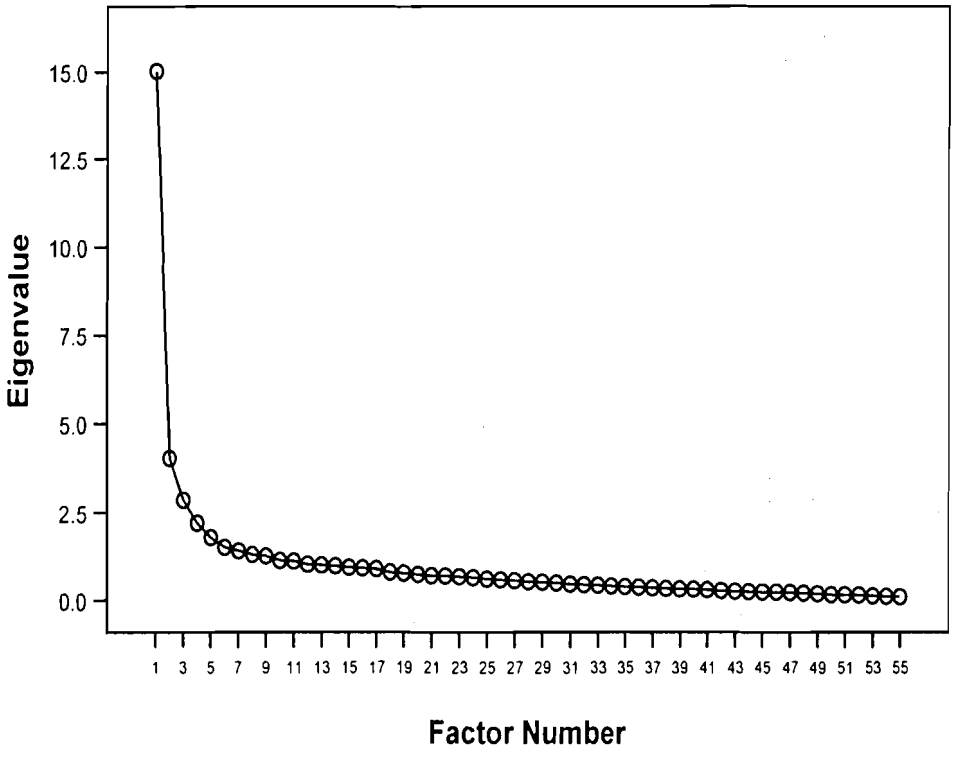
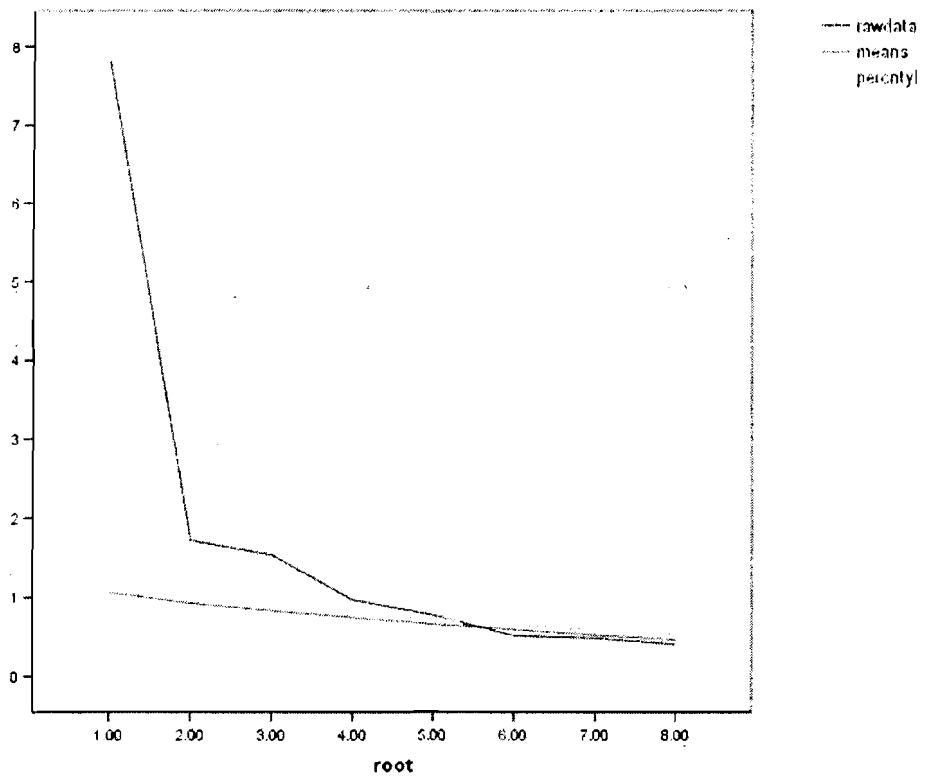


Figure 4.4: Plot of parallel analysis.



4.1.4.5 Initial exploratory factor analytic model: Round 1

I then instructed SPSS Factor to compute two 3 factor solutions, the first using principle axis factoring with varimax rotation, and the second using principle axis factoring with direct oblimin rotation. As expected, the total amount of variance was re-distributed across the three factors after rotation. For varimax rotation, the first factor accounted for 14.73 % of the variance, with the second and third explaining 11.24% and 10.57% of variance respectively. Percentage of variance explained was not available for oblique rotation because correlated factors were extracted. Of the total 20.10 units of eigenvalues, the first three factors accounted for 11.96, 5.31, and 10.46 units of eigenvalues respectively.

The three factors were low to moderately correlated with coefficients ranging from $r = .20$ between Factors 1 and 2 and $r = .54$ between Factors 1 and 3. The correlation between Factors 2 and 3 was $r = .18$. The magnitude of these correlation coefficients suggests that the 3 factors are related but not redundant constructs; suggesting that our multi-dimensional definition of therapeutic misunderstanding is viable and in accord with existing theory as well as my conceptual model.

Each item was assessed with respect to whether or not the pattern coefficient, structure coefficient, and communalities met the following *a priori* criteria. The two rotation extractions resulted in three sets of coefficients to evaluate. They are the pattern coefficients, structure coefficients for the oblique rotation solution, and the pattern/structure coefficients for the orthogonal rotation solution. Items with factor loadings less than .3 and those that did not load any of the three factors were deleted. According to Tabachnick and Fidell (2001; also see Floyd & Widaman, 1995; Hogarty et al., 2005; Pohlmann, 2004), items with loadings below of .32 should not be retained. Furthermore, items that did not load on their hypothesized factors were not retained. Finally, items that loaded across factors for the orthogonal solution (i.e., loading on more than one factors) were deleted (i.e., complex items).

With few exceptions, an item was retained if two of three of their pattern/structure coefficients were greater than .3 on the item's hypothesized factor. A total of 29 items (17, 7, and 5 items from each subscale) met all or most of the pre-established criteria (see Table 4.2). Cross-loading emerged as the most common reason for exclusion (orthogonal solution). For instance, 21 out of 30 therapeutic misconception items cross-loaded on more than one factor. A similar percentage of cross-loading items was found with the

other subscales. In the context of moderately correlated factors, the presence of complex items was expected, especially with oblique rotation solutions. The second reasonfor exclusion occurred when items failed to load on their hypothesized factors; this was most common for therapeutic misconception and therapeutic optimism items. Four items did not load on any factors and were deleted. Certain selected items also had low communalities but were included to provide adequate coverage of all factors (i.e., minimum of 5 per factor).

Factor labels

Based on the pattern of loadings and item content, I labelled the first factor *therapeutic misconception*, the second factor *therapeutic optimism*, and the third factor *therapeutic misestimation* from the oblique rotation solution; for the orthogonal rotations solution, however the labels for the second and third factors were reversed.

Table 4.2: Pattern coefficient, structure coefficient, and rotated pattern/structure coefficients, and communalities (h^2) for principle axis factoring on round 1 items.

Item		Criteria*	Pattern coefficient			Structure coefficient			Rotated P/S Matrix			h^2
			1[a]	2	3	1	2	3	1[b]	2	3	
TMc	**1**	+cc	.624			.703		.488	.627	.315		.512
	2	+c+	.490			.537		.339	.477			.295
	3	+++	.568			.516			.514			.274
	6	+cc	.392			.494		.454	.443	.405		.377
	7	+cc	.368			.413	.367		.340		.372	.256
	10	+c+	.696			.706		.369	.648			.514
	11	+c+	.579			.585		.334	.553			.347
	12	+++	-.569			-.490			-.498			.255
	18	ccc	.397	.364		.563	.474	.456	.418		.495	.476
	19	+cc	.300			.439		.383	.329		.313	.261
	20	+cc	.539			.579	.314	.326	.507		.324	.377
	21	+c+	.700			.705		.366	.651			.509
	23	+c+	.606			.595		.344	.583			.397
	25	+c+	.673			.729		.462	.657			.539
	26	www			.500	.385		.564		.494		.328
	28	www		.502			.500				.491	.259
	29	www		.619			.613				.608	.377

Item		Criteria*	Pattern coefficient			Structure coefficient			Rotated P/S Matrix			h^2
			1[a]	2	3	1	2	3	1[b]	2	3	
	31	+c+	.317			.416		.344	.339			.197
	34	+c+	.667			.714		.427	.640			.521
	37	+c+	.595			.577		.300	.558			.338
	38	+++	.425			.464			.414			.220
	39	+cc	.595			.701		.544	.622	.404		.553
	40	www			.471	.393		.556		.458		.336
	42	+++	.490			.448			.438			.207
	43	xcw				.432	.377	.408			.398	.308
	44	+c+	.705			.683		.323	.646			.475
	45	+c+	.479			.557		.403	.487			.325
	47	+cc	.514			.576		.432	.533	.340		.404
	115	+++	.375			.412			.365			.174
	116	xcw				.351		.376			.318	.217
TMe	**50**	+++			.703			.630		.639		.418
	54	+c+			.647	.404		.671		.628		.459
	55	+cc			.701	.313		.672		.629		.457
	56	+cc			.496	.502	.348	.640	.306	.494	.391	.491
	57	+++			.464			.439		.445		.212
	58	+c+			.672	.467		.726		.659		.537
	62	c++		-.357	.417			.427		.456		.310
	64	wxx		-.358								.160
	124	+++			.424			.443		.388		.204
TO	67	+cc			.574	.515	.309	.698	.308	.565	.358	.543
	68	+cc			.520	.445		.603	.301	.539		.391
	69	ccc	.382		.389	.540		.547	.456	.485		.448
	70	ccc		.421	.394	.419	.518	.538		.363	.550	.482
	71	ccc		.314	.509	.412	.423	.608		.467	.464	.474
	72	ccc	.310		.388	.514		.551	.389	.445		.371
	77	ccc		.488	.469	.425	.589	.600		.415	.627	.602
	81	+c+		.398			.462	.396			.486	.316
	84	wwx			.346			.339				.132
	91	cc+		.521	.301	.313	.586	.423			.609	.448
	92	ccc		.464	.401		.520	.440		.311	.549	.399
	93	ccc	.378	.326		.476	.412	.326	.372		.424	.335
	94	+++		.417			.453				.456	.234
	97	+c+		.606		.313	.662	.383			.680	.512
	102	+++		.627			.661				.664	.463
	110	xxx										.071

Note: Retained items appear **bolded** on the table;

* The criteria labels denote whether the pattern coefficient, the structure coefficient of the oblique solution and the pattern/structure coefficient of the orthogonal solution meet or fail the pre-established criteria.

Criteria labels are: +, good item, c cross-loading, w loaded on the wrong factors, x did not load on any factor;

[a] Factor labels: 1 Therapeutic Misconception, 2 Therapeutic Optimism, 3 Therapeutic Misestimation.

[b] Factor labels: 1 Therapeutic Misconception, 2 Therapeutic Misestimation, 3 Therapeutic Optimism.

4.1.4.6 Revised exploratory factor analytic model: Round 2

The 29 items retained from round 1 were reanalyzed using SPSS Factor. Principle axis factoring was used to extract 3 factors with both varimax and direct oblimin rotation. The three factors remained moderately correlated, with the relationship between Factors 1 and Factor 3 being the strongest (r = .44). Correlation between Factors 1 and 2 and between Factors 2 and 3 were r = .36 and r = .25 respectively. The pattern coefficients, structure coefficients, pattern/structure coefficients and communalities are presented in Table 4.3. With the exception of item 1, the pattern coefficients of every item exceeded the .3 threshold (on their hypothesized factor only). The structure coefficients, however, indicated the presence of 10 cross-loading items. Overall, simple structure was largely attained after revision. The fact that now almost every item contributed adequately to measurement of their hypothesized factors is also suggestive of an acceptable factor solution.

Table 4.3: **Pattern coefficient, structure coefficient, and rotated pattern/structure coefficients, communalities (h^2), and percents of variance for principle axis factoring on round 2 items.**

Item		Criteria*	Pattern Matrix			Structure Matrix			Rotated P/S Matrix			h^2
			1[a]	2	3	1	2	3	1[b]	2	3	
TMc	1	+cc	**.644**			**.716**		**.469**	**.653**	**.327**		.543
	2	+++	**.475**			**.535**			**.484**			.301
	3	+++	**.559**			**.521**			**.518**			.276
	10	+c+	**.650**			**.713**	**.377**	**.350**	**.653**			.526
	11	+++	**.551**			**.554**			**.530**			.307
	12	+++	**-.566**			**-.510**			**-.516**			.271
	21	+c+	**.679**			**.710**	**.356**	**.301**	**.665**			.518
	23	+++	**.601**			**.584**			**.569**			.358
	25	+c+	**.677**			**.739**	**.315**	**.412**	**.679**			.558
	31	+++	**.338**			**.423**			**.364**			.203
	34	+c+	**.657**			**.725**	**.374**	**.373**	**.662**			.544
	37	+++	**.604**			**.570**			**.563**			.331
	38	+++	**.415**			**.455**			**.417**			.212
	42	+++	**.426**			**.411**			**.400**			.181
	44	+++	**.714**			**.699**			**.677**			.490
	45	+c+	**.498**			**.569**		**.371**	**.512**			.343
	115	+++	**.405**			**.425**			**.398**			.184
TMe	50	+++			**.705**			**.674**		**.669**		.459
	54	+c+			**.585**	**.415**		**.660**		**.604**		.458
	55	+++			**.578**			**.608**		**.573**		.383
	57	+++			**.471**			**.473**		**.459**		.225
	58	+c+			**.684**	**.463**	**.308**	**.764**		**.702**		.611
	62	+++			**.476**			**.487**		**.472**		.271
	124	+c+			**.425**		**.342**	**.466**		**.427**		.274
TO	81	+++		**.479**			**.533**				**.496**	.312
	91	+c+		**.571**		**.312**	**.619**				**.584**	.402
	94	+++		**.494**			**.503**				**.490**	.258
	97	+++		**.722**			**.743**				**.719**	.556
	102	+++		**.743**			**.732**				**.724**	.542
% VAR (initial)			26.67	5.725	5.181							
Eigenvalue (oblique)						7.021	3.433	4.259				
% VAR (orthogonal)									19.24	9.853	8.481	

Note: Items with coefficients >.3 appear in **bolded** on the table;

* The criteria labels denote whether the pattern coefficient, the structure coefficient of the oblique solution and the pattern/structure coefficient of the orthogonal solution meet or fail the pre-established criteria.

Criteria labels are: +, good item, c cross-loading, w loaded on the wrong factors, x did not load on any factor;

[a] Factor labels: 1 Therapeutic Misconception, 2 Therapeutic Optimism, 3 Therapeutic Misestimation.

[b] Factor labels: 1 Therapeutic Misconception, 2 Therapeutic Misestimation, 3 Therapeutic Optimism.

4.1.5 Confirmatory factor analysis

The remaining 300 randomly selected participants responses were assigned to confirmatory factor analysis (CFA). The goal of CFA was to provide further evidence of

the viability of the hypothesized 3-factor solution. This procedure made it possible to ascertain whether or not the initial EFA solution provided adequate fit of data to the hypothesized 3-factor model. More importantly, the procedure allow me to test whether or not the three facets are similar enough that they can be grouped under a more global construct labelled as therapeutic misunderstanding (i.e., higher order factor model). All analyses were performed with the AMOS statistical program using Maximum Likelihood estimation. Prior to model estimation, the assumptions of multivariate normality and outliers were again assessed.

4.1.5.1 Sample size

As with its exploratory counterpart (EFA), confirmatory factor analysis (CFA) is a large sample statistical technique. As previously noted, sample size requirements are not invariant across different conditions in EFA (e.g., communalities) and a multitude of sample size recommendations have been proposed. Similarity, the required sample size for CFA depends on conditions such as model degrees of freedom, model complexity, distribution of variables, number of observations per parameter, and magnitude of parameters (Crowley & Fan, 1997; Klem, 2000; Russell, 2002). Although some have recommended that there should be at least 200 to 300 participants for adequate power (Kline, 2005; Jackson, 2003; Russell, 2002; Thompson, 2000), the most commonly used sample size guideline for CFA is probably the participants-to-variables ratio, with suggested values of 5 to10 being the norm (Floyd & Widaman, 1995), though more recent guidelines have suggested a higher ratio of at least 10:1 or 15:1 (Thompson, 2000).

However, large sample sizes are a double edge sword. As Crowley and Fan (1997) noted, "[a] large sample size increases the power of the test [model fit indices],

and consequently, minor discrepancies between sample data and theoretical model will tend to be declared statistically significant" (p. 527). This has led some to suggest that under certain circumstances, more participants are not necessarily better in CFA. Floyd and Widaman (1995), instead, suggest that it would be more advantageous to divide very large samples into halves, one for replication and cross-validation purposes.

Given that approximately 300 randomly selected web-based participants from the initial 464 participant pool were assigned to CFA, it is believe this sample size was sufficient to provide a sufficiently stable solution (Floyd & Widaman, 1995). Whether or not the sample size, in fact, met the minimum requirement was assessed using procedures developed by MacCallum, Browne, and Sugawara (1996). Following their SAS script, it was calculated that my final model (n = 300, df = 218) had a power of .99. This is well in excess of the minimum recommended power level of .80 (Cohen, 1992).

4.1.5.2 Model identification and estimation

Model identification is an important first step in the analysis of covariance structures such as CFA. If a model is not identified, unique estimates for parameters cannot be found, and therefore, the model is not testable (Byrne, 2001; Ullman, 2006b). Fortunately, there are various rules of thumbs closely related to the model degrees of freedom as well as ratio of indicators per factor (Kline, 2005) and therefore, these concepts will be briefly reviewed.

Whether a model is identified is a function of its degrees of freedom (*df*). A model's degrees of freedom equal the difference between the number of free parameters and the number of observations (i.e., data points). The number of observations in any given model can be derived from the equation: $v\ (v+1)/2$, where v equals the number of

observed variables (Byrne, 2001; Kline, 2005; Ullman, 2006b). According to Kline (2005), the number of parameters in a CFA model can be determined as follows:

> The total number of variances and covariances (i.e., unanalyzed associations) of the exogenous variables (the factors and measurement errors) plus direct effects of the factors on the indicators (i.e., the loadings) equals the number of parameters (p. 170).

In the analysis of covariance structures, a model can be said to be *under-identified, just-identified,* or *over-identified.* In short, an under-identified model (i.e., model $df < 0$) cannot be tested because it lacks sufficient information whereas a just-identified model (model $df = 0$) cannot be rejected (Byrne, 2001). In contrast, an over-identified model (model $df > 0$) provides sufficient information for the model to be both tested and rejected.

With this information, let us proceed to discuss the necessary and sufficient conditions for model identification. As Kline (2005) explained, in the case of measurement model identification, a model must meet two necessary conditions in order for it to be identified. First, the number of free parameters to be estimated must be less than, or equal to, the number of observations (known as the order condition). The second condition requires that every latent variable must have a scale. It must be stressed that meeting the above conditions is not sufficient for a model to be identified. To guarantee model identification, it must also satisfy the 2-indicators rule. "If a standard CFA model with a single factor has at least three indicators, the model is identified. If a standard model with two or more factors has at least two indicators per factor, the model is identified" (Kline, 2005, p. 172). As previously discussed, the number of indicators per factor for my models (i.e., between 5 and 12), ensured an over identification.

4.1.5.3 Pre-analytic issues

As mentioned, maximum likelihood (ML) estimation, the most common estimation method in the analysis of covariance structures, assumes multivariate normality (Byrne, 2001, 2005; Crowley & Fan, 1997; Kline, 2005; McDonald & Ho, 2002; Schumacker & Lomax, 2004; Tabachnick & Fidell, 2001). Although simulation studies have found that ML parameters estimates are quite robust to non-normal data, estimates of standard errors tend to be negatively biased (Kline, 2005; McDonald & Ho, 2002; Thompson, 2004). As such, it is essential to screen data to ascertain whether or not assumptions of this estimation method have been met.

At the univariate level, there was no evidence of significantly skewed or kurtotic responses to items. In contrast, results from Mardia's Kurtosis test indicated that the data were multivariate kurtotic (Mardia coefficient = 128.531; exceeding the 1.96 cutoff). Additionally, 43 cases were classified as multivariate outliers using Mahalanobis distance. They were included in the analysis with the awareness that it may adversely impact CFA results.

One might argue that an alternative estimation method such as bootstrapping (Byrne, 2001), use of ADF estimators, or the Satorra-Bentler scale chi-square (Ullman, 2006a, 2006b) should be used given that the data appeared to be multivariate non-normal. However, alternative estimation methods such as the ADF are not without their problems with small sample sizes (Ullman, 2006b), and Satorra-Bentler scale chi-square is not available in AMOS. In light of this, I proceeded with the awareness that non-normality may impact CFA results (to be latter revisit in the discussion section as a possible limitation).

Another assumption of ML estimation is that observed variables are measured as interval scale variables (Byrne, 2001). As stated by McDonald and Ho (2002), non-normality can result with the use of nominal and ordinal variables. Although SEM programs for factor analyzing categorical data are available (e.g., LISREL; see Reise et al., 2000), they require very large sample sizes, generally in excess of 1,000 observations. Furthermore, Byrne (2001) noted that the assumptions underlying these techniques also make analyses based on use of polychloric and tetrachloric matrices inappropriate in many contexts, in part, because distortion is possible when dichotomous items are analyzed. When a variable has five response points (as with this proposed instrument) and is approximately normally distributed, ML estimation is generally deemed to be appropriate (see also Dolan, 1994).

4.1.5.4 Model evaluation

In keeping with the literature, several methods were used to assess the fit of the CFA model to data. First, commonly used goodness-of-fit indices were computed to evaluate global model fit. Second, the relative fit between a first-order and a second-order model was tested using the chi-square difference calculations. Third, residual correlations (also known as standardized discrepancies) were examined to augment goodness-of-fit indices as the latter may mask misfit in a specific part of the model (McDonald & Ho 2002; Kline 2005). Finally, estimates of individual parameters were examined.

It is well accepted that many competing fit indices exist, each examining different aspects of model fit (see Kline, 2005; Sun, 2005). As McDonald and Ho (2002) noted, there is no overriding mathematical foundation on which to choose one index over another, in part, because (with the exception of Root Mean Square Error of

Approximation; RMSEA), the sampling distribution of these indices is unknown (Kline, 2005).

With this in mind, four commonly reported criteria for goodness of fit, the model chi-square (χ^2), the comparative fit index (CFI), the adjusted goodness-of-fit index (AGFI), and the RMSEA were computed to evaluate the fit of confirmatory factor models (Byrne, 2001; Floyd & Widaman, 1995; Kline, 2005; Martens, 2005; Sun, 2005; Tabachnick & Fidell, 2001; Thompson, 2004). The Expected Cross-Validation Index (ECVI) and Relative Normed-Fit index (RNFI) were also computed for comparison of first and second order models.

Most fit indices assess model fit by evaluating whether the sample covariance matrix (S) and reproduced or estimated covariance matrix (Σ) are equal. Among them, the model chi-square or likelihood ratio is the most commonly reported fit index. This statistic tests for significance between the actual covariance matrix and the estimated covariance matrix implied by the model. In contrast to traditional null hypothesis testing procedures, good model fit is suggested by a non-statistically significance model chi-square value. This criterion, however, is rarely met because of sample size sensitivity (Byrne, 2001). Nonetheless, the model chi-square value is traditionally reported in analysis of covariance structures as a matter of convention.

The CFI has been recommended as the index of choice for analysis of covariance structures (Bentler as cited in Byrne, 2001). This index measures the relative fit between a specified model and a baseline null model. Because of its comparative nature, the CFI has been referred to as an incremental or relative fit index (Kline, 2005). According to Hu and Bentler (1999), CFI values greater than .94 reflect good model fit.

The AGFI is an absolute index that penalizes for model complexity by taking degrees of freedom into account. This index measures the amount of variance and covariance in the sample covariance matrix that is predicted by the population matrix (Byrne, 2001; Schumacker & Lomax, 2004). With the AGFI, values approaching unity (i.e., 1.0) reflect a better fit; values greater than .89 are suggestive of good model fit (Byrne, 2001; McDonald & Ho, 2002)

The RMSEA is a population-based absolute fit index (Jun, 2005) that has recently been recognized as one of the most informative of available indices computed in analysis of covariance structures. The RMSEA is a discrepancy index that considers the overall error in the population (i.e., it estimates the error of approximation in the population; Byrne, 2001; Kline, 2005). Similar to other parsimony indices, it adjusts for degrees of freedom, and thus penalizes for model complexity. For the RMSEA, values approaching zero indicate better fit, with values less than .5 and .8 reflecting good and adequate fit respectively (Browne & Cudeck as cited in Byrne, 2001; Hu & Bentler, 1999).

Unlike other indices, the ECVI and the RNFI are used to compare two or more competing models. The ECVI assess the likelihood that a model cross-validates across similar-sized samples from the sample population (Brown & Cudeck as cited in Byrne, 2001). That is, it is a generalizability index. The ECVI does not have a specific cut-off point; instead, smaller values are suggestive of better generalizability across different samples within the same population (Byrne, 2001).

The RNFI has been used in previous research to compare first and second order models (e.g., Cappeliez & O'Rourke, 2006; Hertzog, Alstine, Usala, Hultsch, & Dixon, 1990) as it assesses the fit of the structural model independently of the fit of the

measurement model (Mulaik, James, Van Alstine, Bennett, Lind, & Stilwell, 1989). With respect to the RNFI, values approaching unity indicate better fit, with values greater than .94 indicate good fit of the model to data (Hatcher, 1994).

Table 4.4 summarizes details regarding cut-off thresholds derived from the literature. Together, these indices cover sample and population based approaches as well as absolute and relative fit indices (Sun, 2005).

Following the recommendations of Thompson (2004), a first-order correlated factor model and a second-order factor model were next computed. As Thompson (2004) noted, "the fit of a preferred model is more impressive when that fit occurs in the context of testing several rival models" (p. 115). Third, the merit of the three subscales of therapeutic misunderstanding were further empirically verified by examining intra-subscale correlations and inter-subscale correlations. If the subscale is defensible, the inter-subscale correlation should be significantly greater than zero but less than the average intra-subscale correlation (Clark & Watson, 1995).

Residual correlations were inspected to locate the source of misfit or good fit of data to the model. Residual correlations represent the discrepancy between the observed and predicted correlations (Byrne, 2001). According to Kline (2005), absolute values greater than .10 provide poor explanation of the observed correlations and should be revised.

Table 4.4: Cut-off for different goodness-of-fit indices.

Goodness-of-fit indices	Cut-off Criteria
Model Chi-square Statistic (χ^2)	$p > .05$, the higher the p value, the better the model fit (Byrne, 2001)
Comparative Fit Index (CFI)	Values >.94 (Hu & Bentler, 1999)
Adjusted Goodness-of-Fit Index (AGIF)	Values >.9 and approaches unity (Byrne, 2001; McDonald & Ho, 2002)
Root Mean Square Error of Approximation (RMSEA)	Good fit: Values <.05 or the lower bound 90% confidence interval <.05 and the upper bound confidence <.10; Reasonable fit: between 0.5 & .08; Mediocre fit: between .08 & .10; Poor fit: >.10 (Browne & Cudeck as cited in Byrne, 2001; Kline, 2005; MacCallum, Browne, & Sugawara, 1996; see also Hu & Bentler, 1999; McDonald & Ho, 2002)
Expected Cross-Validation Index (ECVI)	No cut-off, smaller values indicate higher likelihood of the model being cross-validated in another sample (Byrne, 2001).
Relative Normed-Fit Index (RNFI)	Values >.94 (Hatcher, 1994).

Finally, having evaluated the global fit of the model, estimates of individual parameters were examined according to two criteria in accord with Byrne (2001), and Schumacker and Lomax (2004). The first criterion evaluates whether the parameter estimates are feasible. That is, whether the sign and magnitude of the parameter estimates are consistent with theory. If that criterion is met, the next step is to test whether or not parameter estimates are statistically different from zero (i.e., t values > |1.96|). Lastly, in keeping with the recommendations of Graham, Guthrie and Thompson (2003), both the

pattern coefficients and structure coefficients are reported and interpreted as correlated factors are assumed.

4.1.5.5 Estimation of the first order correlated factor models

Initial model

The initial model (model 1) derived on the basis of prior analyses (i.e., EFA) was estimated using maximum likelihood estimation. With 13, 6, 5 items per factor, the initial measurement model is over-identified. As shown in table 4.5, a number of fit indices indicated that the initial model had less than ideal fit (χ^2 [df = 347] = 546.09, p <.01). Notably, both the adjusted goodness of fit index (AGFI = .87) and the comparative fit index (CFI = .93) were strong for an unmodified initial CFA model, albeit somewhat below the acceptable threshold values of .90 and .95 respectively. Of further note, the Root Mean Square Error of Approximation was within the acceptable range (RMSEA = .044, CI_{90} = .037-.051). It should be emphasized that these initial results are very encouraging for an unmodified model, suggesting that the proposed 3-factor model is an accurate specification.

4.1.5.6 Model modification

Strictly speaking, a confirmatory approach does not involve re-specification of a model if the hypothesized model has less than ideal fit to data. In practice, however, a strictly confirmatory approach is overly rigid and most research allows for some level of model modification, particularly with scale item analyses (Byrne, 2001, 2005; Kline, 2005). To avoid capitalization on chance, it is prudent, however, that these modifications be grounded in theory as opposed to statistical criteria alone. With this in mind, modification indices were examined to identify possible areas of mis-specification

Table 4.5: Goodness of fit indices for tested models (n = 300)

Model	Change of parameters	χ^2	df	AGFI	CFI	RMSEA	90% CI	ECVI	90% CI	$\Delta\chi^2$	Δdf	RNFI
Null model		2565.08***	253	.26	.00	.175	(.169-.181)	8.733	(8.202-9.289)	-	-	-
Uncorrelated factors model		495.30***	221	.85	.88	.064	(.057-.072)	2.024	(1.821-2.253)	-	-	-
Hypothesized Model		546.09***	347	.87	.93	.044	(.037-.051)	2.221	(2.022-2.447)	-	-	-
Revised Model	items 25, 37, 38, 42, 62 deleted	363.42***	227	.88	.94	.045	(.036-.053)	1.543	(1.382-1.731)	-	-	-
Final 1st order Model (measurement model)	correction for 9 correlated error terms	299.66***	218	.90	.97	.035	(.025-.045)	1.390	(1.252-1.556)	63.76**	9	1.000
Final 2nd order Model	error terms of 1st order factor constrained to be equal	300.46***	220	.90	.97	.035	(.024-.044)	1.379	(1.241-1.545)	.79	2	0.986
Saturated model		0.00	0	-	1.00	-	-	1.846	(1.846-1.846)	-	-	-

Note: GFI = Goodness of Fit Index, AGFI = Adjusted Goodness of Fit index, CFI = Comparative Fit Index, RMSEA = Root Mean Square Error of Approximation, ECVI = Expected Cross-Validation Index, RNFI = Relative Normed Fit Index

** $p < .01$, *** $p < .001$

that could improve model fit. Particular attention was paid to items that cross-loaded across factors and correlated error terms within factors (Byrne, 2005).

Revised model

In light of these findings, post-hoc modifications were made to arrive at a better fitting model. In total, five items were deleted because they failed the following criteria. In a step-wise fashion, items with large modification indices were deleted from the model. For instance, item 37 were deleted because modification indices suggested a number of cross-factors adjustments. Alternatively, if two items were conceptually similar, as in the case between item 21 and item 25, the one with superior parameter estimates was retained. Items 38 and 62 were dropped because the standardized regression estimates or pattern coefficients were below the .3 threshold. Similarly, item 42 was deleted due to low pattern coefficients and low endorsement rate for the upper response alternative (only a combined 5.4% agreed or strongly agreed to the statement).

These adjustments resulted in an overall improvement of model fit, as reflected in the model chi-square value ($\chi^2[df = 227] = 363.42, p < .01$; see model 2 in table 4.9). In addition, the AGFI (.88) and CFI (.94) had both increased, though still below ideal threshold values. This was achieved against a slight decrease of fit with the RMSEA value (RMSEA = .045, CI_{90} = .036-.053).

To further improve model fit, I corrected for correlated error between nine item pairs. All nine errors terms were statistically significant (i.e., t values > 1.96). In a step-wise fashion, correlated errors within factors with the largest modification indices were successively introduced to the model as is required with AMOS (i.e., univariate computation of modification indices). Although correction for correlated error terms is

not without controversy, especially in structural equation modeling, this practice is not uncommon in scale development. In particular, within factor correction as in this case, where items are often conceptually similar; such items are very likely to share error variance. Therefore, it is believed to be empirically viable to correct for correlated error terms between within-factors items.

With these revisions (see Figure 4.4), the revised model (model 3) achieved good to acceptable fit of data ($\chi^2[df = 218] = 299.66, p < .01$. Chi-square difference tests indicate that the model was significantly improved by correcting for correlated error terms overall and in succession, $\Delta\chi^2(df = 9) = 63.76, p < .01$. Both the CFI (.97) and AGFI (.90) are now within the optimal range. The RMSEA also improved with correction (RMSEA = .035, CI_{90} = .025-.045).

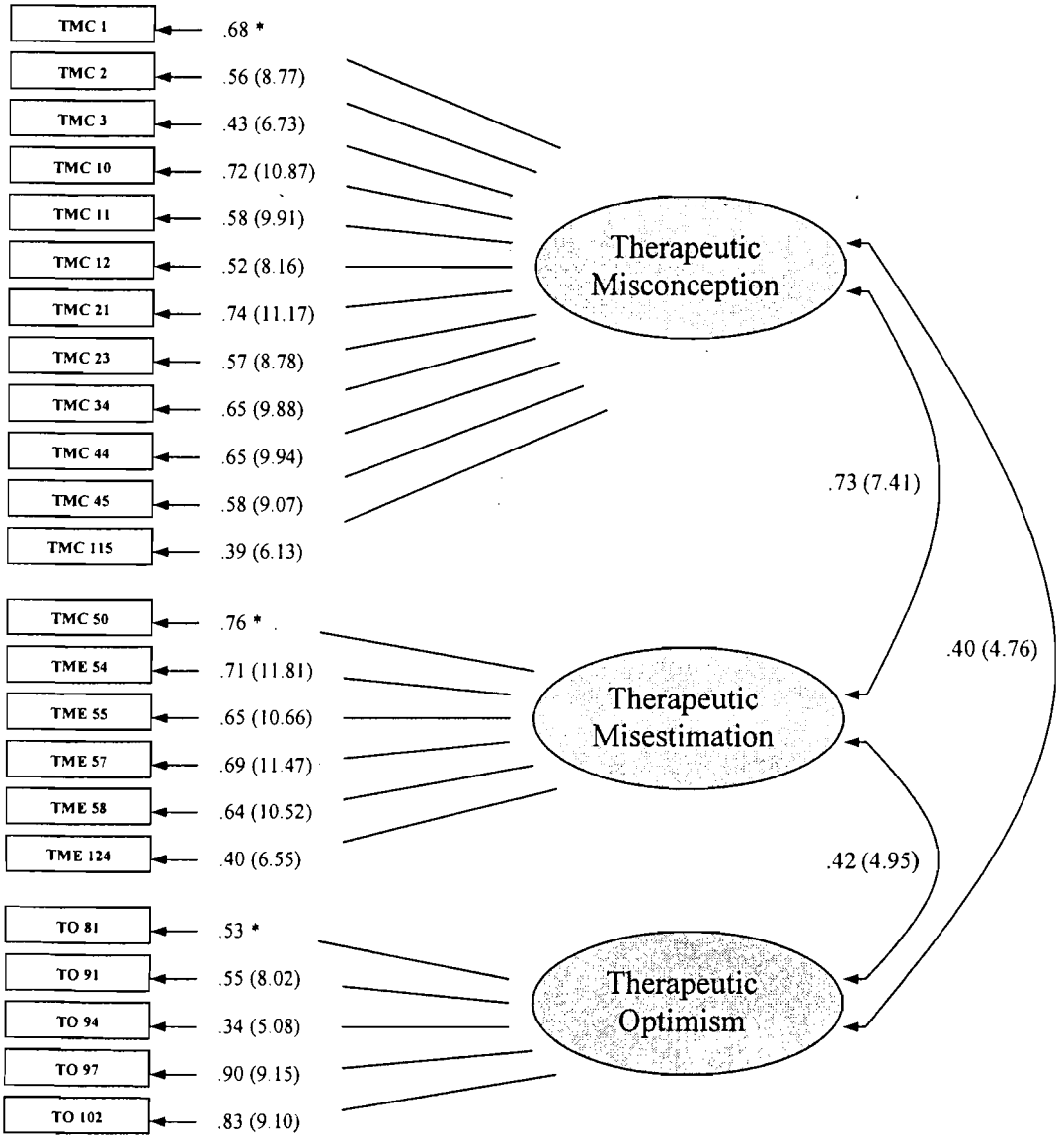
Finally, inspection of the residuals generally supports model fit. For example, both the standardized root mean square residual and root mean square residual are quite small (SRMR = .07, RMR = .05). Although there are no absolute rules for interpreting these indices, SRMR values of .08 or less are considered desirable (Hu & Bentler, 1999). This is consistent with inspection of the residual covariance matrix and the standardized residual covariance matrix. Of note, however, covariance of residuals between the five therapeutic optimism items and a few items from the other two factors are quite large (>.10), indicating that the model has underestimated those correlations in the actual sample. This suggests that this part of the model may have been misspecified because I did not correct for error between these terms.

For the revised model, each individual parameter was significantly different from zero (t values > |1.96|). All 23 pattern coefficients were also greater than the .3 threshold

value. Table 4.6 summarizes the pattern and structure coefficients as well as the square multiple correlation values for each item. As with exploratory factor analysis, the three factors are moderately correlated (see Figure 4.5). Of note, the association between the therapeutic misconception and therapeutic misestimation factors is considerable ($r = .73$). The strong correlation between these factors is also reflected in the structure coefficients for the therapeutic misconception items on Factor 2.

In keeping with previous research (e.g., O'Rourke, 2005; Ullman 2006a), I calculated the zero-order correlation between parameter estimates from model 1 and model 3 to determine the effects of post-hoc modifications on parameter estimates. It was found that the parameter estimates were highly correlated, $r(23) = .99, p < .01$, indicating that correction for correlated error had but a negligible effect on estimation of the individual parameters.

Figure 4.5: Path diagram of final first order three correlated factors model (model 3).



Note: Parameter values expressed as maximum likelihood estimates (standardized solution). Asterisks (*) denote parameters initially fixed to 1.0 for scaling and statistical identification thus significance levels cannot be computed for these three items. Numbers in parentheses indicate significance levels for parameter estimates (statistically significant t values $> |1.96|$).

Table 4.6: Parameter estimates (pattern and structure coefficients) and square multiple correlation of scale items.

	TMISC		TMISE		TO		SMC
	Pattern	r_s	Pattern	r_s	Pattern	r_s	
tmisc001	**.676**	**.676**		**.496**		.272	.456
tmisc002	**.564**	**.564**		**.414**		.227	.318
tmisc003	**.426**	**.426**		**.313**		.172	.182
tmisc010	**.715**	**.715**		**.525**		.288	.512
tmisc011	**.581**	**.581**		**.426**		.234	.337
tmisc012	**.522**	**.522**		**.383**		.210	.273
tmisc021	**.741**	**.741**		**.544**		.299	.549
tmisc023	**.566**	**.566**		**.416**		.228	.321
tmisc034	**.646**	**.646**		**.474**		.260	.417
tmisc044	**.648**	**.648**		**.476**		.261	.420
tmisc045	**.584**	**.584**		**.429**		.235	.341
tmisc115	**.389**	**.389**		.286		.157	.152
tmise050		**.561**	**.764**	**.764**		**.323**	.583
tmise054		**.524**	**.714**	**.714**		**.302**	.510
tmise055		**.475**	**.647**	**.647**		.274	.418
tmise057		**.510**	**.694**	**.694**		.294	.482
tmise058		**.469**	**.639**	**.639**		.271	.408
tmise124		.297	**.404**	**.404**		.171	.164
TO081		.213		.224	**.528**	**.528**	.279
TO091		.223		.234	**.554**	**.554**	.307
TO094		.138		.145	**.342**	**.342**	.117
TO097		**.361**		**.379**	**.895**	**.895**	.801
TO102		**.335**		**.352**	**.832**	**.832**	.692

Note: Pattern = Pattern coefficients, r_s = Structure coefficients, SMR = Square Multiple Correlation

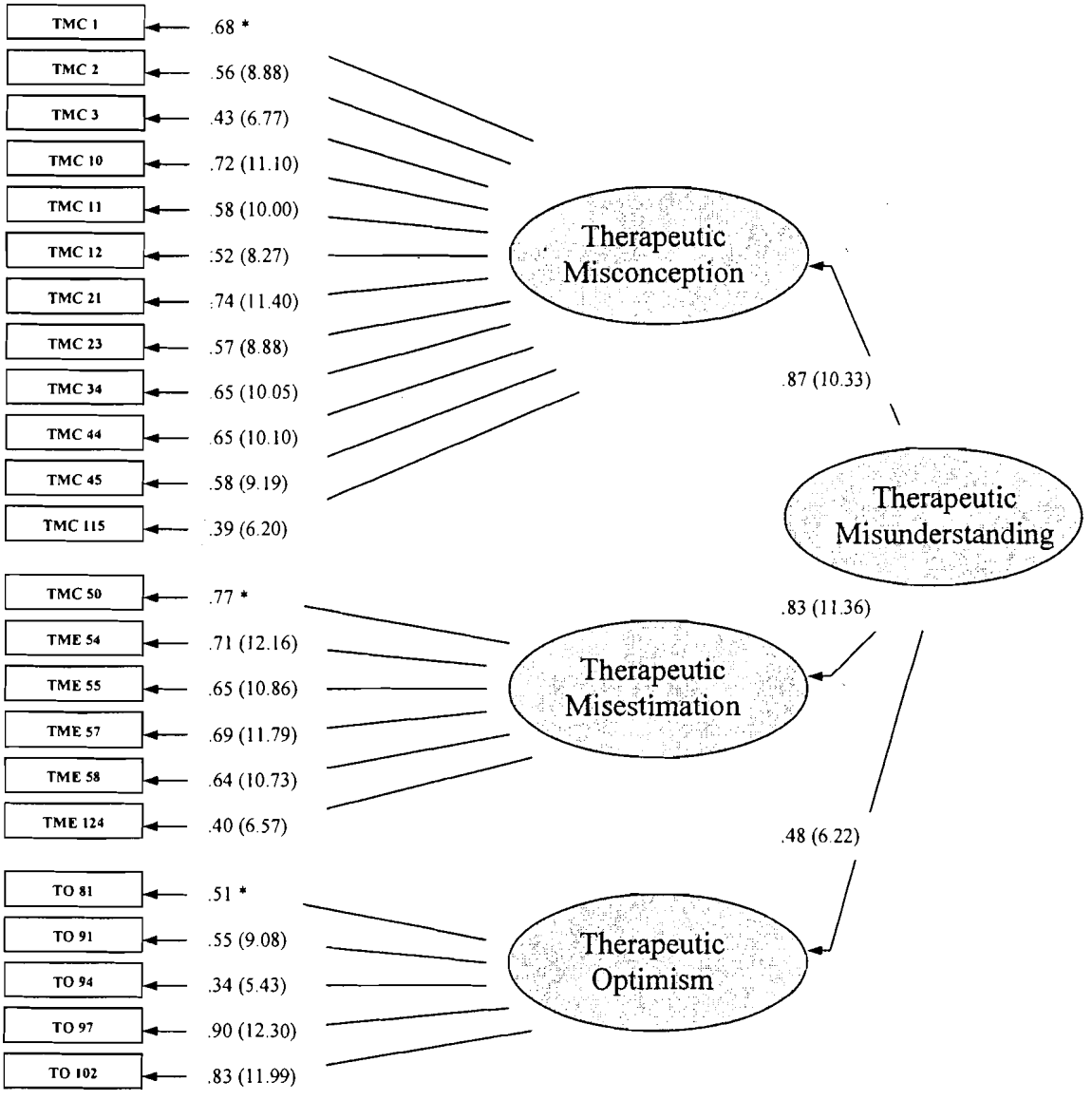
4.1.6 Estimation of a second order factor model

As a final test, I proceeded to identify and estimate a second or higher-order factor model. Of note, the second order factor model is just-identified because there are only three first order factors, and therefore, the degrees of freedom of this portion of the

structural model is zero. In order to fit the model, equality constraints needed to be place between two parameters to free up a degree of freedom for estimation. In accordance with Byrne (2001), I consulted the critical ratio difference score from AMOS to identify candidate parameters for equality constraints. The critical ratio difference statistic tests the hypothesis that the two parameters are equal in the population (Byrne, 2001; Kline, 2005). The critical ratios between the error (residual) variances among the three first order factors of therapeutic misconception and therapeutic misestimation, therapeutic misconception and therapeutic optimism, and therapeutic misestimation and therapeutic optimism, were -.96, -.36, and 1.17 respectively. Given these values were below the critical value of 1.96, the hypothesis that these error variances are equal in the population cannot be rejected. This suggested that it was reasonable to constrain the error variance of the three first order factor to be equal.

The revised second order factor model achieved overall goodness of fit very similar to the first order correlated factors model (see Figure 4.6). For example, the model chi-square value is $\chi^2(df = 220) = 300.46, p < .01$. Similarity, the AGIF (.90) and CFI (.97) for both models are identical whereas the RMSEA (.035, CI_{90} = .024-.044) and ECVI (1.379) values are near identical. Also the chi-square difference test suggests that the second order factor model does not provide significantly worse fit than the first order correlated factors model, $\Delta\chi^2(df = 2) = -.79$, *ns*. The RNFI, which measures fit of only the structural portion of the model, suggests that the revised second order factor model provides slightly poorer fit (RNFI = .986) compared to the revised first order model (RNFI = 1.000). The magnitude of the difference in RNFI values, however, is not sufficiently large to warrant the selection of one model over another.

Figure 4.6: Path diagram of final second order model (model 4).



Note: Parameter values expressed as maximum likelihood estimates (standardized solution). Asterisks (*) denote parameters initially fixed to 1.0 for scaling and statistical identification thus significance levels cannot be computed for these three items. Numbers in parentheses indicate significance levels for parameter estimates (statistically significant t values $> |1.96|$).

Taken together, these suggested that both the first and second order factor models fit the data well as the relative fit between the two models is indistinguishable. In terms of statistical indices, there is insufficient evidence to select one model over another. Conceptually however, the second model may be superior because the existence of an

overarching general factor of makes conceptual sense and is more parsimonious from a methodological perspective.

4.2 The Therapeutic Misunderstanding Scale (TMU)

Based on these results, I herein name my scale the Therapeutic Misunderstanding Scale (TMU; see Table 4.7), to be distinguished from the Therapeutic Misconception Scale (TMS) by Dunn and colleagues (2006). The TMU consists of 23 items, with 12, 6, and 5 items assessing the three facets put forth by Horng and Grady (2003), namely, therapeutic misconception, therapeutic misestimation, and therapeutic optimism respectively. The final 23-item scale has a Flesch-Kincaid Grade Level of 8.5. Given that the current cohort of older adults in Canada has ten years of formal education on average (O'Rourke & Tuokko, 2000), it can be concluded that the scale is at least appropriate for use with 50-60% of the older adults.

Table 4.7: Therapeutic Misunderstanding Scale

Optional Preamble

Imagine you are diagnosed from a new chronic illness or other serious condition. After discussing your condition with your family physician and/or specialist, you have been told that there is a new experimental treatment. It is not known whether or not this new treatment would provide any benefits above and beyond currently available treatments. A physician or clinical nurse has asked you to consider enrolling in this randomized controlled trial. Depending on the group to which you would be assigned, you may receive an inactive treatment (i.e., placebo) or the experimental treatment. The likelihood of being assigned to these two groups is equal (i.e., 50/50). With this in mind, please answer the following questions as if you were faced with this decision.

Based on the previous description, please respond to the following statements. Again, your responses pertain to your decision whether or not to take part in a clinical trial specific to _____ (a hypothetical chronic illness or serious disease). Please don't be concerned if it seems that more than one question is asking for the same information.

	Strongly Disagree – Disagree – Neither Agree/Disagree – Agree – Strongly Agree									
	SD	**D**	**N**	**A**	**SA**					
1.	The main reason that people will be recruited for this study is so that they can benefit from the special treatment in this research project.					SD	D	N	A	SA
2.	The treatment I would receive in this clinical trial would cure my illness.					SD	D	N	A	SA
3.	The treatment/intervention I would receive may be changed in response to the way my medical condition changes.					SD	D	N	A	SA
4.	I am very optimistic about my chances for successful treatment.					SD	D	N	A	SA
5.	The researchers in this study know that one of the treatments or interventions will have better results than others.					SD	D	N	A	SA
6.	My participation in this clinical trial will prolong my life.					SD	D	N	A	SA
7.	The treatment/intervention I would receive in this study will be adapted according to my needs, like the treatment from any other doctor.					SD	D	N	A	SA
8.	There are many ways my participation in this study would help me.					SD	D	N	A	SA
9.	Medical researchers are only allowed to do things that will benefit all patients.					SD	D	N	A	SA

Strongly Disagree – Disagree – Neither Agree/Disagree – Agree – Strongly Agree SD D N A SA									
10. My participation in this study will improve my quality of life.	SD	D	N	A	SA				
11. According to the rules of research studies like these, doctors do not choose the treatment or intervention I receive based on what best suits my needs.	SD	D	N	A	SA				
12. My past medical experiences have prepared me well for participation in this study.	SD	D	N	A	SA				
13. The treatment I would receive is based on my medical needs.	SD	D	N	A	SA				
14. Taking part in this research study would cure my illness.	SD	D	N	A	SA				
15. My physician would tell me which treatment I receive.	SD	D	N	A	SA				
16. I look forward to participating in this study with hope and enthusiasm.	SD	D	N	A	SA				
17. My medication dosage would be adjusted if I do not respond to treatment.	SD	D	N	A	SA				
18. My participation in this clinical trial would boost my immune system.	SD	D	N	A	SA				
19. My doctor would adjust the treatment I receive (e.g., medication dosage) to ensure that I receive the best possible care.	SD	D	N	A	SA				
20. I look forward to being in this study.	SD	D	N	A	SA				
21. My doctor could access the information obtained during the course of this clinical trial.	SD	D	N	A	SA				
22. I'm more likely to benefit than the average person.	SD	D	N	A	SA				
23. This clinical trial is conducted mostly to gather knowledge about my condition.	SD	D	N	A	SA				

4.2.1 Internal consistency of responses to the final scale

Responses to the final 23-item scale were reanalyzed to assess internal consistency (see Table 4.8). Overall, Cronbach's alpha was found to be within optimal parameters (α = .90). Cronbach's alpha of each subscales was also within the good to

acceptable range as α = .87 (Therapeutic Misconception subscale), α = .79 (Therapeutic Misestimation subscale), and α = .75 (Therapeutic Optimism subscale). Overall, responses from this sample appear normally distributed.

Table 4.8: Descriptive features and psychometric properties of final scale and subscales.

	α	IT_{avg}	Mean	SD	Skewness	Kurtosis	Range
Therapeutic Misunderstanding Scale	.90	.28	68.15	11.87	-0.148	0.259	35-104
Therapeutic Misconception Subscale	.87	.36	33.55	8.05	-0.048	-0.066	12-60
Therapeutic Misestimation Subscale	.79	.39	16.21	3.31	-0.213	0.773	6-28
Therapeutic Optimism Subscale	.75	.39	18.39	2.80	-0.580	0.987	8-25

Note: TMU = Therapeutic Misunderstanding Scale; TMCsub = Therapeutic Misconception Subscale; TMEsub = Therapeutic Miestimation Subscale; TOsub = Therapeutic Optimism Subscale; IT_{avg} = Average Inter-Item Correlation.

4.3 Study 2

Study 2, the scale validation study, was conducted to investigate the convergent and discriminant validity of responses of this instrument. Prospective participants (excluded in study 1) responding in the affirmative to either question. "Are you currently enrolled in a clinical drug trial?" [yes/no] or "Have you ever been in a clinical drug trial?" [yes/no] were identified. These participants were separated from Study 1 participants. Their responses were excluded from all Study 1 analyses. A total of 66 self-reported clinical trial participants were re-approached and asked to respond online to the final 23-item therapeutic misunderstanding scale (TMU) and related measures (see Section 3.6). This web-based questionnaire was constructed specifically for Study 2 (see Appendix B).

4.3.1 Data cleaning

A total of 44 respondents participated in Study 2. Of those, 7 were excluded from further analyses because they responded "no" to the re-administered question, "Have you previously participated (now or in the past) in a clinical drug trial?" This resulted in 37 self-identified clinical trial participants. SPSS missing value analysis indicated that 5 questions had more than 5% missing data (question 23 on the therapeutic misunderstanding scale and the four risk perceptions questions). In addition, the relative health stock question had 10.8% missing data. Little's MCAR test was statistically significant ($p < 0.01$), suggesting that the missing data were not missing completely at random. Separate variance t tests on these six variables showed that the questions had different non-random patterns of missing data with a number of variables. For instance, those who did not answer the relative health stock and risk perception questions were more likely to indicate that staff in their clinical trial provided good clinical care, were friendly and pleasant, and showed genuine concern for the participant's well-being. Quantitative scale items with missing data were then imputed using Expectation-Maximization method in SPSS. Repeating the analyses with the original variables did not alter the directionality and only marginally changed the magnitude of the correlation coefficient estimates.

Descriptive statistics show that not all responses to these scales were normally distributed. Most notable, responses to the QuIC-B appear skewed and kurtotic. Given that the scale of this variable is somewhat arbitrary, it was decided to transform QuIBC-B responses using reflect and logarithmic transformation. The applied transformation removed outliers in addition to rendering the response distribution normal. Of note,

results of the correlation analyses using the transformed and original variables did not differ.

Although answers for relative health stock were normally distributed, responses were restricted to the upper end (negatively skewed). Given these results, correlation estimates with these three variables should be interpreted with some caution. Of note, however, inspection of scatter plots did not find evidence of non-linear relationships among study scale measures.

4.4 Participants Clinical Trials Background

Respondent were classified as participants in phases I to IV clinical trials based on their answers to three yes/no questions (see Table 4.9). These questions were, whether or not their treatment was randomly assigned, was a placebo used, and whether or not they were told the treatment condition to which they were assigned. In addition, participants were asked an open ended question regarding their clinical trial (see Appendix B). Participants were classified as phase IV participants if they answered yes to all three questions; phase III if they answered yes to random assignment and use of a placebo; phase II if they answered yes to random assignment, and phase I if they answered no to all three questions. Responses from the open-ended question were then used to corroborate assignments. Classifications were, in general, in accord between these two classification methods.

Among the 37 self-identified current and previous clinical trial participants, 51.4% was determine to be in a phase III clinical trial. This is followed by phase IV open label trial (10.8%), phase I (5.4%), and phase II (5.4%) trials. The large number of

"Don't Know" responses for the three yes/no questions and insufficient information on the open-ended question meant that 27% of participants could not be classified by phase of clinical trial.

Table 4.9: Participants clinical trial background

		Count	Column N %
Phase	Phase I	2	5.4%
	Phase II	2	5.4%
	Phase III	19	51.4%
	Phase IV/Open Label	4	10.8%
	Undetermined	10	27.0%
Random Assignment	Yes	26	70.3%
	No	5	13.5%
	Don't Know	6	16.2%
Placebo	Yes	20	54.1%
	No	7	18.9%
	Don't Know	10	27.0%
Told treatment	Yes	14	38.9%
	No	20	55.6%
	Don't Know	2	5.6%

With respect to participants' experiences in their respective clinical trials, their appraisals were largely positive. Slightly more than 80% of the participants strongly agreed with the statement "clinic staff provided me with good care". A similar percentage (78.4%) strongly agreed with the statement "clinic staff were friendly and pleasant". Seventy-three percent strongly agreed that "clinic staff showed genuine concern for my well-being". Of note, none of the participants disagreed or strongly disagreed with the above statements. When asked to rate their overall experience, all indicated that they were either very satisfied (81.1%) or satisfied (18.9 %). Finally, 75.7% were very

satisfied with the waiting time at the clinic and 67.6% were very satisfied with the information they received from staff.

4.5 Internal Consistency of Responses of Study Scales

Table 4.10 shows the descriptive features and psychometric properties of responses to the scales administered in Study 2. Of note, *t* tests indicated all scale responses were statistically indistinguishable between administrative orders (i.e., no order effects observed for counterbalanced response formats). As previously noted, responses to the QuIC-B was skewed and kurtotic. Responses to all the scales appear to have acceptable to good internal consistency as measured by Cronbach's alpha ($.70 \leq \alpha \leq .94$). Overall, responses to the Therapeutic Misunderstanding Scale achieved strong reliability of responses ($\alpha = .93$), and also for each of the three subscales ($\alpha = .88$, $\alpha = .91$, and $\alpha = .83$ respectively).

Alpha values for responses by this clinical trial participant sample are comparable to those obtain from the non-clinical sample in Study 1. Consistent with the assumption that a more homogenous sample should have higher reliability of responses, the coefficients are of higher magnitude.

Table 4.10: Descriptive features and psychometric properties of Study 2 scales (n = 37).

	α	IT $_{avg}$	Mean	SD	Skewness	Kurtosis	Range
Therapeutic Misunderstanding Scale	.93	.38	61.54	16.08	0.753	1.282	32-112
Misconception Subscale	.88	.39	28.27	9.89	0.811	0.504	14-57
Misestimation Subscale	.91	.62	14.86	4.67	0.677	2.107	6-30
Optimism Subscale	.83	.51	18.41	3.89	-0.749	1.831	6-25
Therapeutic Misconception Scale	.76	.39	0.86	1.34	1.736	2.307	0-5
Life Orientation Test-Revised	.70	.30	22.59	3.53	-0.264	0.209	14-30
Relative Health Stock	-		85.81	8.42	0.164	-0.694	75-100
QUality of Informed Consent-A	-		76.25	9.01	-0.127	-0.453	57.14-93.75
QUality of Informed Consent-B	.94	.31	87.74	17.29	-3.510	15.656	3.57-100
Risk perception 1	-		60.82	17.20	0.019	-0.816	25.5-93.9
Risk perception 2	-		47.26	18.58	0.282	0.432	8.4-95.8
Risk perception 3	-		58.31	14.73	-0.222	-0.025	22.1-87.8
Risk perception 4	-		50.90	22.59	-0.233	-0.405	0.0-95.4

4.6 Convergent and Divergent Validity of Responses

The zero-order correlation coefficients were calculated among study scales to assess the convergent and divergent validity of response of the Therapeutic Misunderstanding Scale relative to these scales (see Table 4.12). Particular attention was on pairs of associations noted in Table 3.3 (partially reproduced here as Table 4.11).

Table 4.11: Expected and actual correlations of interests among study scales.

Measures	Expected Correlation	Actual Correlation	Adjusted Correlation	As Hypothesized?
TMU – TMS	$.36 \leq r \leq .80$	**.50****	.59	Yes
tm – QuIC-Part A & B	$-.36 \geq r \geq -.80$	.05 & -.08	n/a & -.09	No
te – Risk Perception	$-.36 \geq r \geq -.80$	**.36***†	n/a	No
to – LOT-R	$.36 \leq r \leq .80$	.10	.13	No
TMU – Relative Health Stock	+	**.32**	n/a	Yes

† Correlation with risk perception 1 (perceived benefits of experimental treatment)
*$p < .05$, ** $p < .01$

Responses to the Therapeutic Misunderstanding Scale (TMU) were found to be significantly correlated with those of the Therapeutic Misconception Scale (TMS; $r[37] = .50, p < .01$). This moderate correlation between measures provides support for the convergent validity of responses of the TMU. Responses to these two measures of therapeutic misunderstanding were hypothesized to be related and support for this assertion was found, suggesting that the TMU is measuring the same phenomenon as the existing measure of therapeutic misunderstanding. As seen in Table 4.11, only the therapeutic misconception and therapeutic misestimation subscales were positively correlated with the TMS ($r[37] = .60, p < .01$ & $r[37] = .33$ $p < .05$ respectively). Of note, the therapeutic optimism subscale was not statistically associated with TMS ($r[37] = .10$, *ns*). This finding suggests that situational optimism (i.e., therapeutic optimism) is not necessarily related to dispositional optimism, a point that I will elaborate upon in the discussion section.

Table 4.12: Zero-order correlations between study variables (n = 37)

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. TMU	—												
2. TMCsub	.92**	—											
3. TMEsub	.87**	.65**	—										
4. TOsub	.75**	.48**	.75**	—									
5. TMS	.50**	.60**	.33*	.11	—								
6. LOTR	.03	-.02	.07	.10	-.01	—							
7. RHS	.32	.47**	.16	-.06	.20	-.01	—						
8. risk1	.37*	.25	.36*	.47**	.31	.14	-.05	—					
9. risk2	-.14	-.23	-.06	.08	-.14	.02	-.19	.10	—				
10. risk3	.33*	.37*	.18	.20	.44**	.06	.16	.55**	-.02	—			
11. risk4	-.09	-.18	-.02	.12	-.28	-.04	-.13	.10	.76**	-.07	—		
12. QuICA	.21	.05	.32	.36*	.01	-.25	.13	.15	-.13	.08	-.19	—	
13. QUICBLOGR§	-.01	-.08	.13	.00	-.04	.08	.01	.04	-.03	-.14	.07	-.22	—

* $p < .05$, ** $p < .01$

§ The variable QuIC-B was recoded using reflect and log transformation.

Note: TMU = Therapeutic Misunderstanding Scale; TMCsub = Therapeutic Misconception Subscale; TMEsub = Therapeutic Miestimation Subscale; TOsub = Therapeutic Optimism Subscale; TMS = Therapeutic Misconception Scale; LOT-R = Life Orientation Test-Revised; RHS = Relative Health Stock measure; risk 1 = perceived benefits of experimental treatment; risk 2 = perceived risk of experimental treatment; risk 3 = perceived benefits of standard treatment; risk 4 = perceived risks of standard treatment; QuICA = Quality of Informed Consent-Part A; QuICB = Quality of Informed Consent-Part B.

With respect to risk perceptions, the TMU was found to be positively associated with perceived benefits of experimental (r [37] = .37, $p < .05$) and standard treatments (r [37] = .33, $p < .05$). At the subscale level, therapeutic misestimation was moderately correlated with perceived benefits of experimental treatment (r [37] = .36, $p < .05$) but not with other measures of risk reception. Responses to the therapeutic optimism subscale were associated with increased perceived benefits of experimental treatment (r [37] = .47, $p < .01$). Scores for the therapeutic misconception subscale were also positively correlated with perceived benefits of standard treatment (r [37] = .37, $p < .05$). Based on these results, it appears that therapeutic misunderstanding may reflect a distortion of the perceived benefits of the experimental and standard treatments but not the risks involve in these treatment conditions.

Similar patterns were observed between the TMS and risk perceptions. Perceptions of treatment benefits were moderately correlated (r [37] = .55, $p < .01$), but not with perceptions of treatment risk. Risk perception between experimental and standard treatments was found to be strongly correlated in the positive direction (r [37] = .76, $p < .01$). Of note, using the t test for partial correlations from the same sample, none of these comparisons between the correlation coefficients of TMU and TMS with risk perceptions measures were statistically significant. In other words, the magnitude of these associations did not statistically differ.

The other hypothesized associations did not achieve statistical significance but were, in general, in the hypothesized direction. In particular, responses to the therapeutic misconception subscale were uncorrelated with both the objective (r[37] = .05, *ns*) and subjective (r [37] = -.08, *ns*) understanding of informed consent scale (i.e., QuIC-Part A

& B respectively). Nor was the correlation between the TMU and relative health stock statistically significant (r [37] = .32, *ns*) but was moderately correlated in the expected direction. At the subscale level, therapeutic misconception was positively and moderately correlated with the relative health stock (r [37] = .47, p <.01). The association between therapeutic optimism subscale and LOT-R was negligible (r [37] = .10, *ns*). In fact, responses to the LOT-R were not associated with any study measures.

4.7 Test-Retest Reliability

Test-retest reliability for 44 participants over an average of 35 weeks was reported to be r = .54 for the total scale score. Subscale test-retest correlation coefficients were highest for the therapeutic misconception subscale (r = .60), followed by the therapeutic misestimation subscale (r =.51), and the therapeutic optimism subscale (r = .25). Ideally, the test-retest correlation should be at the r = .80 range; however, the average interval between administrations may have a negative impact on this coefficient. If we accept this coefficient, then perhaps the test-retest correlation is too low to consider therapeutic misunderstanding a dispositional trait. In particular, the low correlation for the therapeutic optimism subscale is reflective of the fact that this facet represents a form of situational optimism rather than the more enduring dispositional optimism. If the converse is true and therapeutic misunderstanding is in fact a stable trait, then, the low value is indicative that the TMU is not a reliable measure of a stable construct over time. It is also possible that a relatively low test-retest reliability coefficient resulted due to the extended time interval over which data were collected. An average period of 35 weeks is comparatively long in psychometric research; thus, the reported value likely underestimates true test-retest reliability.

4.8 Summary of Results

Factor and item analyses of responses by 464 community-dwelling older adults (age 49+) recruited via the Internet have led to the development of a 23-item scale. As hypothesized, a three-factor structure was supported by exploratory factor analysis on a random subset of responses (n = 164); confirmatory factor analysis on the remaining sample (n = 300) indicated that both the first order 3-factor model and second order models provide similar fit to data. Internal consistency of responses for the total scale, the therapeutic misconception, therapeutic misestimation, and therapeutic optimism subscales was calculated as α = .90, .87, .79, and .75, respectively.

The internal consistency of responses was largely replicated ($.83 \leq \alpha \leq .93$) on the basis of responses from 37 self-report clinical trial participants. Zero order correlations analyses indicated a moderate correlation between the TMU and TMS (r = .50). In general, the TMU has comparatively higher associations with other related measures than the TMS. Finally, test-retest correlation was found to be r = .54 over an average interval of 35 weeks.

CHAPTER 5 DISCUSSION

This thesis set out to develop a self-report scale to measure therapeutic misunderstanding. This was undertaken in two studies using separate samples of older adult respondents. The objective of Study 1 was to obtain participant responses to an initial pool of items in order to develop and refine the proposed instrument, the Therapeutic Misunderstanding Scale (TMU). The objective of Study 2 was to assess whether responses to the TMU obtained from a sample of clinical trial participants were similar to those from a general community sample of older adults. Together, these two studies address the overarching research question, how we can objectively measure a person level of therapeutic misunderstanding. Results from both studies were encouraging and largely affirm *a prior* hypotheses.

Factor analyses suggested that the structure of responses to this construct is best represented by three factors labelled therapeutic misconception, therapeutic misestimation, and therapeutic optimism. In addition, results from a small validation study suggest that the TMU provides coverage on domains absent in the existing Therapeutic Misconception Scale (Dunn et al., 2006). The comparatively stronger associations between the TMU and similar constructs compared to those found with the TMS lend support to its utility as a comprehensive self-report instrument. In this final chapter, I discuss the major contributions of this thesis in measuring therapeutic misunderstanding, followed by remarks on its limitations and suggestions for future

research. Finally, I conclude with a discussion of study findings in relation to the consent process.

5.1 Internal Structure of Therapeutic Misunderstanding

An important contribution of this thesis was the empirical validation of a 3-facet model of therapeutic misunderstanding. That is, therapeutic misunderstanding may effectively be conceptualized as composed of therapeutic misconception, therapeutic misunderstanding, and therapeutic optimism. Until recently, this construct had been conceptualized and measured as a uni-dimentional construct (Appelbaum et al., 1987; Dunn et al., 2006). Horng and Grady (2003) challenged this view as being too simplistic. Results from this thesis provided the first empirical support for a multi-dimensional conceptualization of therapeutic misunderstanding as asserted by these authors.

Results from exploratory and confirmatory factor analyses generally supported the hypotheses specified for this thesis. The initial hypothesis stated that therapeutic misunderstanding could best be measured as a 3-factor construct. More specifically, that therapeutic misunderstanding could be effectively measured by three factors labelled as therapeutic misconception, therapeutic misestimation, and therapeutic optimism. From the perspective of the scale's internal structure, results from EFA indicate that a 3-factor solution representing the three facets were viable. This 3-facet model was subsequently tested and replicated using CFA (separate sample), providing support for both a first and second order factor solution with three first order factors.

The next two hypotheses pertain to whether or not the factor solution has a simple structure. Findings for these two hypotheses were less conclusive. Hypothesis 1.2

stated that resulting items from an extended item pool would significantly contribute to measurement of their respective factors. The final 23 items in the CFA model all had pattern and structure coefficients above the .3 threshold. This result suggests that items contribute to the measurement of their respective factors; however, the square multiple correlation values (SMC) were less than optimal. Only five items have a SMC value of .5 or above. In other words, 18 items have at least 50% or more of their variances unexplained by the existing three factors. The number of items with low SMC values could be partially attributed to decision to keep items with low communality values in order to achieve better coverage of the domains of therapeutic misunderstanding. It is possible that future revisions could further improve the item content of this scale.

Hypothesis 1.3 state that items would load on only one factor (i.e., no cross loading). Although simple structure was achieved for the final EFA solution, a notable number of items cross-load on more than one factor. In particular for the oblique rotation solution, 10 items have structure coefficients loaded on two or more factors. In retrospect, these results were to be expected. After all, the three facets were hypothesized, and indeed were found, to be moderately correlated with each other. This is in contrast to the orthogonal solution, where only one item cross-load on more than one factor.

With respect to hypothesis 1.4, which stated that factors would be significantly inter-correlated, these findings were unequivocal. It comes as no surprise that participants' appraisal of the risks and benefits of participation and situational outlook (i.e., situational optimism) would be moderately correlated with their conflation (or lack of) between clinical research and treatment. In fact, the magnitudes of the correlation coefficients are exactly as expected. The correlations were sufficiently high to suggest

that the three facets are interrelated but not excessively (i.e., $r \geq .70$) to be considered a single domain. This carries important implications as to how measurement of therapeutic misunderstanding should be approached, which I will discuss more fully in the next section.

The magnitude of correlation between factors was sufficient to warrant examination as to whether or not responses would best be represented as a second order model, with the three factors subsumed under an overarching general therapeutic misunderstanding latent construct. Hypothesis 1.5 stated that these factors would be subsumed by a higher-order, second-level general latent factor labelled therapeutic misunderstanding. This was supported by the near identical model fit indices between the first and second order factor models (see Table 4.5). Indices that access comparative fit, such as the ECVI and RNFI, also suggest that the two are comparable.

Conceptually, it is logical to assume the existence of a general latent factor. Empirically, second order factor solution is more parsimonious (Rindskopf & Rose, 1988 as cited in Chen et al., 2005) and provide addition information on measurement error associated with the three facets measured by first order factors (Chen et al., 2005). Therefore, it appears the internal structure of therapeutic misunderstanding may best be conceptualized as a second order model. At this point, however, further study on the factor structure of therapeutic misunderstanding is needed, before such a recommendation can be made.

5.2 Convergent Validity of Responses

How do responses to the TMU relate to other conceptually similar measures? This question pertains to the convergent validity of responses to my instrument or the degree to which responses to an instrument correlate with scores on others designed to assess related constructs. At the scale level, the TMU was significantly correlated with the existing TMS (r = .50). The moderate magnitude of this coefficient was within the expected range, providing support for the convergent validity of response to the TMU but not overly high to suggest redundancy of measurement.

At the subscale level, TMS was only significantly associated with the TMC subscale (r = .60) and TME subscale (r = .36). The low correlations between TMS and the TME and TO subscales (r = .33 and r = .11 respectively) were expected as these two domains were not part of the operational definition for TMS (see Dunn et al., 2006). These results suggest that the TMU is measuring something above and beyond what is measured by the TMS. These findings also provide support for the construct validity of responses to the TMU.

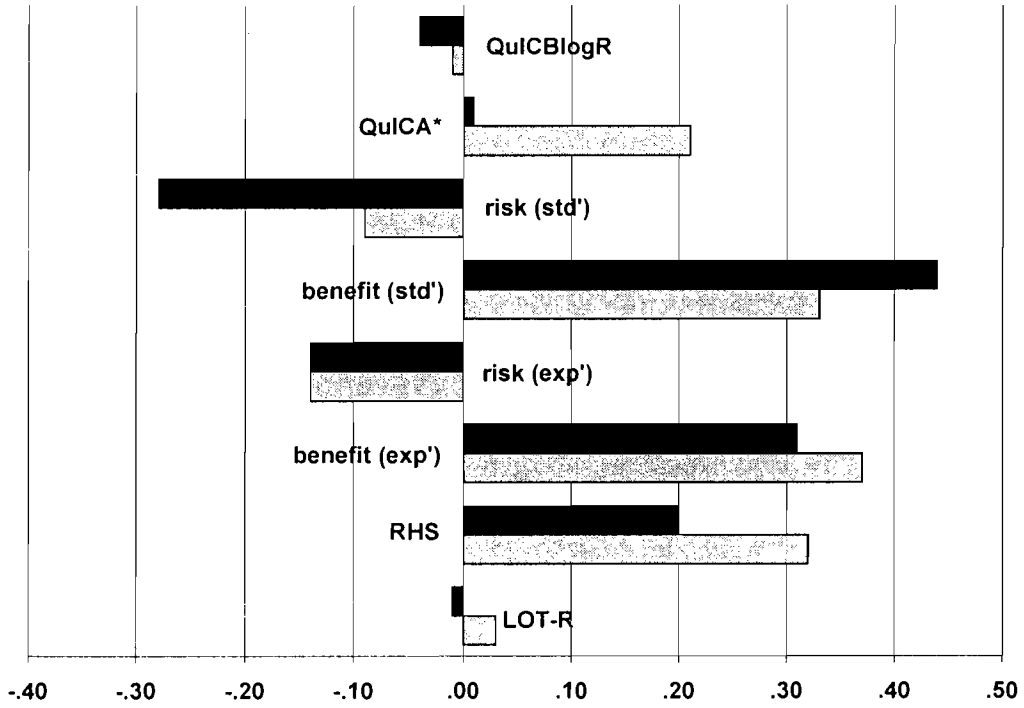
5.3 Concurrent Validity of Responses to the TMU

Importantly, the TMS has low and negligible associations with therapeutic misestimation and therapeutic optimism respectively. Construct validity of responses of TMS suffers because of a lack of sufficient coverage of the construct on these two domains, resulting in poor associations with related constructs (i.e., concurrent validity). For example, the only statistically significant association of the TMS was with perceived benefit from standard treatment (risk perception). Notably, participants' TMS scores were

unrelated with dispositional optimism, their objective and subjective understanding of informed consent, as well as their relative health stock.

In contrast, correlation analyses between the TMU and related constructs suggest the superiority of a 3-facets approach in certain context. In most cases, the TMU scale has comparable or marginally higher associations with other related measures as compared to the TMS (see Table 4.11 & Figure 5.1). Of note, while responses to the TMS were uncorrelated (r = .01) with the QuIC-Part A (an objective measure of understanding), responses to the TMU were somewhat correlated with the QuIC-Part A in the positive direction (r = .21).

Figure 5.1: Comparison of correlation coefficients between the TMU and TMS with other study 2 measures.



Further examination at the sub-scale level suggests that only the therapeutic misestimation and optimism subscales are correlated with QuIC-Part A. Of note, a *t* test for correlations from the same sample found that these two pairs of correlation coefficients are statistically different ($t[34]=2.23, p = .03$). This again suggests that inclusion of these two additional facets provides important information that is lacking in a measure based on a uni-dimensional conceptualization of therapeutic misunderstanding.

Despite these positive results, there were some unexpected findings. First, the overall magnitude of the correlations coefficients was smaller than expected. Inadequate sample size and power could be factors. A small sample size complicated interpretation as the stability of these estimates is questionable. Cohen (1992) noted that for correlation analyses, to detect a medium effect size ($r = .30$) with a power of .80 required a minimum of 85 participants. Nonetheless, if one recalls that these 37 participants were from heterogeneous phases and types of clinical trials (phases I to IV), these correlations may provide conservative estimates of the true associations at the population level.

A few instances of absence of association emerged from these analyses. Therapeutic misunderstanding as measured by both TMU and TMS were found to be unrelated to participants' subjective understanding of informed consent (QuIC-B). The distribution of QuIC-B suggests the presence of ceiling effect. Perhaps this truncated range of response to the QuIC-B limited its association with other measures. It is also possible that therapeutic misunderstanding and subjective understanding are distinct constructs, which has been repeatedly asserted by proponents of this phenomenon (e.g., Lidz & Appelbaum, 2002). If the latter is true, then it adds further credence to the utility of including therapeutic misunderstanding as a separate measure in research and clinical

practice. Participants' responses to the TMU may then be used to supplement results derived from measures of understanding and comprehension. This will provide researchers and clinicians with a better overall understanding as to whether or not the consent process was adequate and truly informed as per Tri-Council Policy guidelines.

Even more surprising was the finding that therapeutic misunderstanding was found to be positively correlated with participant's objective understanding of informed consent. This is in contrast to previous reports and the assumption that those who misperceived aspects of clinical trial participation have reduced objective understanding. In particular, Dunn and colleagues (2006) found that therapeutic misunderstanding, as measured by the TMS, were negatively correlated with the MacCAT-CR understanding subscale (r [87] = -.62, p <. 01) appreciation subscale (r [87] = -.35, p < .01), and reasoning subscale (r [87] = -.34, p <. 01). These divergent results could, in part, be due to the different measures of understanding used for their study. Prior to this study, the psychometric properties of the QuIC had not been reported. In contrast, the utility of the MacCAT-CR is well documented. Future research that adopted the MacCAT-CR or its self report form, the Assessment of Consent Capacity-Randomized Clinical Trials (ACC-RC; Fisher, Cea, Davidson, & Fried, 2006) may explain the discrepant findings.

An alternative explanation worth exploring is whether or not the positive association found between responses to therapeutic misunderstanding and objective understanding may be indicative of adaptive cognitive function (Taylor, 1983; Taylor et al., 2000). In fact, at the subscale level, the relationship was strongest between therapeutic optimism and QuIC-A. Contrary to popular belief, studies in other domains on this topic have demonstrated that optimists are more attentive to risk information

relevant to their health (Aspinwall & Brunhart, 1996). People who exhibit positive illusions such as an optimistic bias appear to pay greater attention to both positive and negative stimuli (Segerstrom, 2001) This, in turn, may have adaptive value as excessive pessimism may lead to the use of maladaptive coping strategies (e.g., avoidance coping; Scheier, Weintraub, Carver, 1986). If future research bares this out, it will add an interesting layer to the ethical dilemma of therapeutic misunderstanding as it may actually have useful positive implications.

Contrary to expectation, measures of therapeutic misunderstanding did not correlate with dispositional optimism as measured by the LOT-R. In fact, dispositional optimism was not significantly associated with any of the study measures. In retrospect, this finding could be due to differences between dispositional and situational optimism. These two types of optimism has been distinguished in health psychology research and were found to be mildly correlated (r = .30; Segerstrom, Taylor, Kemeny, & Fahey, 1998). Of note, these authors found that situational optimism emerged as a stronger predictor of mood and predictor of change in immune functioning. Results reported herein are in accord with this finding given that my measure of situational optimism (TO subscale) emerged as a stronger predictor than the LOT-R relative to all measures except for subjective understanding and appears to predict objective understanding and perceived benefits of experimental treatment. Similarly, Appelbaum and colleagues (2004) found that therapeutic misunderstanding (as measured by their semi-structured interview, the Therapeutic Misconception Index) was positively associated with (situational) optimism specific to one's medical condition in the short term (6 months or less). It would appear that measures of situational optimism are better suited for future

studies in this domain as compared to measurement of optimism as an aspect of disposition or personality (Boland & Cappeliez, 1997; Smith, Pope, Rhodewalt, & Poulton, 1989).

5.4 Consensus Definition Paramount

At present, at least two multi-dimensional models of therapeutic misunderstanding exist in the literature: the three elements definition (Appelbaum et al., 2004); and the three facets definition (Horng & Grady, 2003). This study represents an important first step in validating the three facets approach to therapeutic misunderstanding. Despite advances at the conceptual level, some authors continue to describe therapeutic misunderstanding uni-dimensionally, focusing exclusively on the therapeutic misconception element/facet, and discuss its ethical implications in this light (e.g., Joffe, 2006). Some even go so far as to dismiss therapeutic misunderstanding as misconceived bioethics based on an earlier definition (Belkin, 2006); however, continuing to undertake applied research based on unsubstantiated and incomplete measurement is akin to building a house on a faulty foundation.

Resolving the conflicting and often convoluted debate regarding the appropriate operational definition for therapeutic misunderstanding requires further study. Results from this thesis suggest that a circumscribed definition of therapeutic misunderstanding can be problematic because it could limit its concurrent validity as well as content validity. Perhaps scales such as the TMS that apply a uni-dimensional definition have fallen victim to the *attenuation paradox*. This paradox contends that increasing the internal consistency of responses to a test beyond a certain point will not enhance its construct validity and, in fact, may occur at the expense of validity (Clark & Watson,

1995). Taken together, findings from this study provide empirical support for Horng and Grady's (2004) assertion that therapeutic misunderstanding encompasses more than a misperception of the purpose of clinical trial research (i.e., conflation of treatment and research).

A full discussion of the conceptual definition and ethical implications of therapeutic misunderstanding is beyond the scope of this thesis. It should be emphasized, however, that therapeutic misunderstanding is potentially problematic as it pertains fundamentally to the ethics of RCT research. As Senn (2003) eloquently stated, treatment of patients in clinical research is determined by two competing forces. The first is to do everything one can to maximize benefits for each patient, and the second is to treat them in such a way to maximize derived knowledge to benefit future patients. The two often work in opposition; it may therefore be possible to achieve one only at the expense of the other.

In summary, the state of the current debate can be summarized in terms of tension between the normative and descriptive camps. In their purest form, ethicists from the normative school maintain that participants ought to enrol in clinical trials for exclusively altruistic reasons. Those who espouse this view also tend to advocate for the 'difference' position for resolving the RCT dilemma, which argues that a different ethical framework should govern the conduct of clinical research. Put differently, it should be emphasized that the purpose of clinical trial research is foremost the advancement of knowledge; any personal benefits for current participants is secondary. To them, therapeutic misunderstanding is problematic because it arises from research participants' conflation of two very different goals between research and treatment. Solution of the ethical

implications of therapeutic misunderstanding would then require that the difference between research and treatment be explicitly communicated and fully understood.

Others, from the descriptive school such as Horng and Grady (2003) would argued that therapeutic misunderstanding is not necessarily problematic; indeed, a sense of unbridled optimism can be a good dose of medicine (e.g., Segerstrom et al., 1998; see Jansen, 2006 for an alternative view of how unrealistic optimism may pose problems). Followers of the descriptive school further contend that it might be impossible to fully eliminate therapeutic misunderstanding because clinical trials, as practiced in their modern form, simply share too many elements with day-to-day medical practice (Glannon, 2006). Glannon goes on to comment that it is the irrational therapeutic misconception that needs to be distinguished from the rational therapeutic optimism. Furthermore, even if therapeutic misunderstandings are dispelled, participants might still commit other cognitive and affective mistakes that have the potential to compromise informed consent (Jansen, 2006). Clearly, correcting for the negative implications for therapeutic misunderstanding is no panacea for ensuring ethical research.

Those who espouse this view also tend to be proponents of the 'similarity' position, which hold that treatment and research are already governed by a unified ethical framework to protect the interests of participants. It is this principle of personal care that needs to be protected in clinical research contexts. Therapeutic misunderstanding then can be seen as a natural by-product of this perspective, and a potentially harmful one with which both clinicians and ethicists have to reckon.

A third ethical perspective is worth considering which argues that despite differences between research and treatment, both share convergent goals. The two

dominant camps, the different and similar positions, portray a black and white description and ignore the complexities of both research clinical practice. Both emphasize how research is distinct from treatment but prescribe different solutions to address the potential ethical conflicts. What these two perspectives fail to acknowledge is that from the perspective of individual participants/patients, the distinction is not the issue. Whether research or treatment, individuals want safe treatment and respect for their autonomy. Just because research and treatment have different objectives does not mean that they are irreconcilable (Piantadosi, 2005). In this sense, the bioethics community may have fallen victim to this fallacy by constructing its own ethical crisis.

Ultimately whether therapeutic misunderstanding is problematic, innocuous or adaptive, depends on the ethical perspective to which one adheres. Although empirical study can tell us more about the phenomenon, in the end, one must turn to ethics and values to judge its implication and ascribe meaning.

5.5 Study Limitations

At this point, results of this study need to be interpreted in terms of the limitations of the study design, analytic techniques, as well as sampling and data collection methods. Perhaps the most important limitation of the initial study is the fact that it is an analogue study. From the perspective of internal validity, analogue studies are useful because participants respond based on their perceptions rather than prior experience. Unlike previous studies that did not control for disclosure (e.g., Lidz et al., 2004), analogue scenarios at least standardize the disclosure process; however, analogue scenarios provide an over-simplification of reality. Considerable discussion and information that goes on in real world clinical contexts cannot be simulated. This might explain the substantial

percentage of participants who provided "neither agree nor disagree" resposnes to the working items because of a lack of sufficient information.

Another study design issue that this thesis did not address was the possible role of *socially desirable responding* (SDR). It is prudent in scale construction to provide evidence to support the discriminant validity between responses to a proposed measure of therapeutic misunderstandings and SDR, the most common response bias confounding self-report resposnes (Foster & Cone, 1995; Paulhus, 1991). Paulhus (1991) defined SDR as a systematic tendency to present oneself positively. SDR is a complex phenomenon that involves both deliberate distortion and unintentional selective reporting of behaviours and beliefs (O'Rourke & Cappeliez, 2002). Paulhus's 2-factor conceptualization of biased responding (1984; as cited in O'Rourke & Cappeliez, 2002) reflects this conceptualization. The first involves deliberate distortion or *impression management* (IM) whereas the second entails an honest but overly positive self-presentation or *self deception* (SD).

If affected by impression management, the validity of responses to a measure is suspect (Streiner & Norman, 2003). Therefore, demonstrating the discriminant validity of responses to the proposed measure vis-à-vis impression management is ideal. In future, this could be undertaken by examining correlation coefficients between responses to the TMU and the Paulhus Deception Scales (formerly Balanced Inventory of Desirable Responding (PDS; Paulhus, 1991). Ideally, associations between the three TMU subscales and impression management subscale should not exceed $r = .30$. With the self-deception subscale, however, a moderate association between self-deception and the therapeutic optimism sub-scale is expected. Therapeutic optimism, by definition, involves

a certain degree of positive distortion; indeed, therapeutic optimism could emerge as a distinct response style.

A third design concern pertains to the interpretation and comprehension of scale items. Logistics prevented the use of focus groups or cognitive interviewing to validate the face validity of the TMU. Pilot testing using focus groups can improve the face validity of measures when used appropriately (Vogt, King, & King, 2004). Similarly, cognitive interviewing is a pre-test method used in survey development to identify items not understood by participants as intended (Napoles-Springer, Santoyo-Olsson, O'Brien, & Stewart, 2006). This technique involves the use of probes or recall and qualitative analyses to develop and revise test items specific to the population of interest. Given confusion regarding key terms (Kopelamn, 2002; Resnik, 2005) and issues with probabilistic reasoning (Hertwig et al., 2005; Woloshin et al., 1994), it is possible that participants could have misinterpreted certain items. Future research that uses focus groups or cognitive interviewing to ascertain participants' comprehension of items could clarify the wording of scale items, thus reducing error and enable enhanced measurement.

With respect to analytic techniques, it was noted that maximum likelihood estimation was used for CFA despite indications of multivariate non-normality. As mentioned, software availability prevented use of an alternative estimation method. Therefore, a brief note on how this will impact my findings is needed. In general, the chi-square statistic tends to be overly liberal when data are non-normal, increasing the likelihood of statistical significance (i.e., rejection of the null hypothesis; Fouladi, 2000; R. Fouladi, Personal Communication, Apr 18, 2007). In other words, non-normal data can underestimate model fit. If anything, my data may have fit the CFA model better if an

alternative estimation method had been used. RMSEA values, however, which are relatively robust to violation of the normality assumption, were within acceptable or optimal range throughout; this observation underscores confidence in model fit criteria. With respect to parameter estimates, non-normality can bias estimates of standard error without affecting parameter estimates. This, in turn, can increase the Type I error rates (i.e., t values > $|1.96|$). Therefore, the significance of each pattern coefficient should be interpreted with caution.

Use of internet data collection was successful in recruiting a large number of participants in a short time; however, the derived sample cannot be said to be representative of the current cohort of older adults as participants were a self-selected sample. In addition, computer literacy was an implicit inclusion criterion for participation in this study as well as Internet access. As previously discussed, study participants reported to have an average of 14 years of formal education, about 4 years higher than estimates based on a representative sample of older adults in Canada (O'Rourke & Tuokko, 2000). Thus persons who chose to participate in this type of research are more educated than the norm.

Although the TMU's readability level of grade 8.5 lends confidence that the majority of older adults in this country can comprehend the study questions, I cannot conclude that this applies to all.

Other descriptive statistics also indicated that my sample might not be representative. In particular, the majority of clinical trial participants indicated that they were very satisfied with their experiences. It is likely that Study 2 participants represented a self-selected group whose responses may differ from those who are/were

dissatisfied with, or felt indifferent towards, clinical trial participation. The use of the analogue study format might somewhat mitigate this bias as participants were specifically asked to provide responses to the treatment of a hypothetical condition rather their prior experience. Nonetheless, use of an analogue scenario cannot completely eliminate this potential bias.

5.6 Alternative Approaches

I employed a psychometric approach to tackle the measurement of therapeutic misunderstanding. In particular, a single method approach using self-report measure was adopted (see Lucas & Braid, 2006 for a discussion on this assessment method). At this juncture, it should be noted that alternative approaches exist with their own respective advantages and disadvantages. Table 5.1 summarizes these approaches.

Table 5.1: Alternative approaches to measurement of therapeutic misunderstanding

Alternatives	But ...
Sociology/Communication Theory	Ignore individual processes
Behavioural economics	Require a priori assumptions
Qualitative	Cost-effectiveness & Time

Take behavioural economics as an example. It appears to be possible to define therapeutic misunderstanding strictly as a series of multivariate calculus functions (Byrne & Thompson, 2006). Defining this construct as a state where participant expectations

exceed mathematical expectation, while being very parsimonious, leaving out the mechanisms, and most important, requiring *a priori* assumptions.

Sociological and communication theory approaches, on the other hand, can provide important contextual information on the informed consent process. This can lead to better identification of external antecedents and correlates of therapeutic misunderstanding. It remains doubtful, however, that this approach could replace a psychometric approach to developing an objective measure of therapeutic misunderstanding. Although still equivocal, the literature largely suggests that therapeutic misunderstanding is a phenomenon specific to the individual mediated by both contextual and group factors (see conceptual model Figure 2.1). I believe it is prudent to understand the psychological processes that lead to such beliefs before considering more distal, socio-political and economical factors that possibly affect the prevalence and magnitude of such beliefs.

Qualitative measures such as the Therapeutic Misconception Index (TMI; Appelbaum et al., 2004) have the advantage of being the most comprehensive; indeed, responses to the existing TMI have demonstrated some validity vis-à-vis related constructs such as situational optimism and social-demographic factors (see Appelbaum et al., 2004). The current version of this semi-structure interview,has acceptable inter-rater reliability (Kappa = .40 to .69). However, transcribing interviews and coding them requires substantial amounts of time. The drawback of time-effectiveness may constrain the use of this measure. As with other interview-based instruments, the ability to gather in-depth information on a topic requires additional cognitive resources relative to the use of self-reported instruments. This requirement for additional cognitive capacity may limit

the applicability of this qualitative approach to certain segments of the older adult populations (e.g., mild cognitive impairment).

5.7 Future Research

The development of what appears to be a psychometrically sound instrument opens up many venues for further research. I believe advancement in the field will depend on simultaneous development in a few interlocking area. At this juncture, the most urgent task is to conduct replication studies on the factorial validity of the 3-facets approach using large heterogeneous, and representative samples of clinical trial participants. It should be stress that scale validation is a continue process, and result from this study should be considered preliminary, requiring further studies and replication.

Further studies with groups of clinical trial participants that are more homogenous in terms of phases and types of trial are also required to elucidate the convergent and discriminant of validity of responses to the TMU. Studies that adopted a multi-method approach will help in delineating the convergent and discriminate validity of responses of the TMU (Schmitt, 2006; Diener & Eid, 2006). There is also room for improving the domain coverage of the instrument. Despite the length of the scale, certain areas were not assessed or adequately represented by the 23 items, for example, participants' perception of the dual role of physician/researcher and the importance of trust.

Once the structure of responses has been replicated, applied researchers can begin to document the prevalence and mean level responses of therapeutic misunderstanding using the TMU. It is likely that a differential pattern of responses to the TMU would be observed depending on the phase of the clinical trial. Responses may also differ among

participants in the active medication group, the placebo-responsive group, and the placebo non-response group. Unfortunately, sample size for this study is too small to conduct subgroup analyses to support this assertion. Further studies that compare and contrast mean response levels across the four phases of clinical trial research would enable us to answer this question. It would be interesting to see, for instance, whether or not this phenomenon is more prevalent with certain types and/or phases of clinical trial research (e.g., severity of disease). Large-scale population studies on various age groups would allow norms for scale responses to be identified.

Empirical work that examines the predictors and covariates of therapeutic misunderstanding would be another important area for further research. The literature has hypothesized a good number of factors related to therapeutic misunderstanding (Lidz & Appelbaum, 2002). These have been summarized in my conceptual model (see Figure 2.1). But until recently, there has not been an appropriate measure of this phenomenon to enable testing of these associations. More recent work using the TMI has found therapeutic misunderstanding to be associated with a number of demographics variables (e.g., education) and psychological measures (situational optimism; Appelbaum et al., 2004). The addition of TMU would provide applied researchers a brief instrument that can be easily incorporated into clinical research studies.

Applied and basic research outside of therapeutic misunderstanding will also have barring on our interpretation of therapeutic misunderstanding. In particular, debates on ethics will continue to drive discussion of therapeutic misunderstanding. Depending on the prevailing school of thoughts, therapeutic misunderstanding will be view as problematic on one hand, to harmless, or even adaptive on the other. Continue research

on optimistic bias and positive illusion will help we better understand a plausible pathway and antecedents of therapeutic misunderstanding. Finally, basic research in how people process and understand uncertainty and how they make decision given imperfect knowledge will enable us to better understand the risk/benefit calculus of people, and subsequently allow researcher to pose more specific research questions about therapeutic misestimation.

5.8 Consent Process Revisited

Just as poor recall and retention of the purposes, benefits and risks discussed during the consent process may indicate a lack of comprehension and may raise concern as to whether or not the consent process was truly informed and voluntary, the same applies to situations where participants misconceive the purpose and nature of the clinical trial and misestimate the benefits and risks involved (i.e., therapeutic misunderstanding). When all is said and done, the most important context of concern is the consent process. If deemed to be less than fully informed, therapeutic misunderstanding may raise the spector of ethical violation(s). If deemed problematic, the logical intervention point is the consent process.

We know from the literature that several factors affect whether or not the consent is voluntary and fully informed. These factors can be broadly classified into three groups: the consent forms itself; the consent or disclosure process; and the recall, retention, and comprehension of the consent information. I will briefly revisit these factors and examine the role therapeutic misunderstanding plays in this final section of this thesis.

Practical limitations have constrained this thesis from examining the relationship between specific consent forms and therapeutic misunderstanding. Nonetheless, previous researchers have examined the tone and choice of words that could potentially foster therapeutic misunderstanding among participants. Often it has been discovered that excessively optimistic and therapeutic language was used to describe the potential benefits of clinical trial participation (Horng et al., 2002; Kimmelman & Palmour, 2005; King et al., 2005). Glannon (2006) further noted that when available, population based treatment response rates should be included in consent forms, so that participants can make meaningful comparisons as to the risks and benefits of clinical trial participation.

The inclusion of such information is paramount as the risk perception literature strongly suggests that people have a tendency to overestimate small probabilities and underestimate large probabilities (Slovic, 1987). In fact, clinical trial participants in Study 2 exhibited the same bias for estimating their chances of experiencing side effects due to both the experimental and standard treatments for a hypothetical dementia medication. This peculiar finding is in accord with those previously reported (Chen et al., 2000; Lloyd et al., 2001; Meropol et al., 2003). In these studies, however, consistent with the by-product of risk perceptions hypothesis of therapeutic misestimation, participants also overestimated their benefits. In contrast, estimates of benefits in terms of controlling their symptoms as reported by participants in this study were largely comparable to response rates from dementia related clinical trials (e.g., Lanctôt, Best, Mittmann, Liu, Oh, & Einarson et al., 1998). Once again, however, interpretation is complicated by the different definitions of benefits. If therapeutic effect (drug minus placebo) is used as the reference instead of response rate (i.e., improvement based on the drug alone), participants would

have overestimated their benefits. It is most probable that different classes of drugs produce different response rates and therapeutic effects. These rates are, in turn, dependent on the type of outcome measures used in the studies. More research is needed to examine whether or not therapeutic misestimation operates through distortion of risks only or if the causal pathway involves mis-appraisal of both risks and benefits.

Proper disclosure in the consent process is important for correct understanding of the nature of clinical trial research. In a multi-centres clinical trial for example, Griffin, Struve, Collins, Liu, Nelson, and Bloomfield (2006) found that information recall and retention rates varied between centres. This discrepancy suggests that differences in how research staff discuss the consent process may affect participants' recollection of key information. In addition to inter-centre variation, training research staff to convey consistent information regarding the purpose, nature, benefits, and risks is essential as inconsistent and conflicting messages lead to confusion (i.e., the multiple speaker problem; Weinfurt et al., 2003). Furthermore, imprecise use of words to convey therapeutic intent likely fosters therapeutic misunderstanding among prospective participants (Sankar, 2004). All of this points to the need to have a consistent third party involved in the consent process from beginning to end (Dresser, 2002; Horng & Grady, 2003; Lidz & Appelbaum, 2002; Sales & Lavin, 2000).

Therefore, with respect to the consent process and disclosure, as much as research and treatment share similar elements, I concur with Lidz and Appelbaum (2002) that effort must be made to distinguish their differences if the goal is to reduce therapeutic misunderstanding. I caution whether or not this approach can be universally applied however, given the variability of responses to the TMU reported herein.

At this juncture, it is also unclear whether making explicit the differences will make a different. Early research suggested that therapeutic misunderstanding is a robust phenomenon (Appelbaum et al., 1982, 1987; Mills, Donovan, Smith, Jacoby, Neal, & Hamdy, 2003). Tattersall (2001) also questions whether or not physicians currently have the resources and skills to communicate information impartially. Furthermore, Joffe's (2006) commentary on a recent study by Simon (2006), which examined the role of altruistic considerations in the clinical trial decision-making processes, also noted that emphasizing altruism as the reason for study participation does not appear to reduce the prevalence or magnitude of therapeutic misunderstanding. Care is also needed to avoid being overly zealous; overcorrect; and overemphasizing the differences between research and treatment as this might unduly affect participants' motivations for enrolling in clinical research (Glannon, 2006).

One should also strive to achieve a balance when discussing the risks and benefits of experimental treatments. Despite relatively high subjective and objective understanding of aspects of consent as measured by the QuIC, clinical trial participants on average reported greater therapeutic benefits and risks to both treatment conditions in a hypothetical clinical trial for dementia. Whether or not this reflects undue optimism within this sample is unknown. Regardless, these misestimations may indicate that participants did not fully understand what they are agreeing to undertake.

Finally, participants' recall, retention, and comprehension of information received during the consent process are probably the most important objective indicators for clinicians, policy makers, and ethicists. This is one area this thesis did not sufficiently address. We know from the literature, however, that participants' comprehension of the

randomization process is generally poor (Featherstone & Donovan, 2002; Kodish et al., 2004) and recall of even rudimentary information can be inconsistent (Griffin, Struve, Collins, Liu, Nelson, & Bloomfield, 2006). In a multi-centre study of older veterans, Griffins and colleagues (2006) found that a significant minority of study participants could not recall the study's purpose (35.3%), the medication administered (20.4%), and main side-effect of the medication (68.9%) when asked at their final follow-up visit.

At this juncture, I strongly believe that future research that integrates recall of study information, together with more rigorous control of the disclosure process, will enable us to better examine the antecedents and correlates of therapeutic misunderstanding. This, in turn, will provide applied researchers with knowledge to adjust the consent process accordingly to reduce such misconception if deemed to be problematic. Hopefully the knowledge gained at the basic and applied levels will ultimately translate into a more accurate understanding and appreciation of the nature, intent, benefits and risks of participating in clinical trial research.

APPENDICES

Appendix A

Older Adults' Perceptions of Clinical Trial Research

Department of Gerontology

Are you over 49 years of age and do you have an interest in new treatments for various health conditions? If so, your participation in the following research study would be greatly appreciated!

The goal of this study is to obtain greater understanding of older adults' beliefs regarding various aspects of clinical research. If you agree to participate, you will be asked to complete a set of questionnaires requiring about 30 minutes of your time. The following pages ask questions similar to ones you would encounter if deciding whether or not to enroll in a clinical drug trial. You will also be asked to provide some descriptive information (e.g., age, employment status). Your computer Internet Protocol (IP) address will be logged to allow us to count the number of participants by region. Please be assured that this will not identify you, only the city/town in which you live.

Those who provide an e-mail address (optional) may be asked to complete one final, brief questionnaire three to six weeks from now. (An e-mail notice would be sent to you at that time.) We will not share your e-mail address with other researchers or agencies.

Your contribution to this research will lead to development of new knowledge and tool that could benefit researchers working in this area. There is no known risk or discomfort to you or to society. There is also no known direct benefit to you. Though you may have a better understanding of what a clinical trial is.

You may also request a summary of study findings by contacting Ben at phchou@sfu.ca. Please note that these results may not be available until a year after you filled out the survey.

You are not required to provide your name. No individual responses from this study will be disclosed; only combined data will be reported. Please noted that complete anonymity cannot be guaranteed. Although any information you provided will be kept confidential as permitted by the law. All information will be store in a secured location and will

not be share with any person without your permission. If you have any concerns regarding this study, please contact Dr. Norm O'Rourke at: ORourke@sfu.ca

Participation in this study is strictly voluntary. You are not required to answer questions that make you uncomfortable and you are free to discontinue at any time. Completion of questionnaires will indicate your willingness to participate.

Thank you for taking the time to consider participating in this study.

With Regards,

Ben Chou
MA Candidate
phchou@sfu.ca

Click to proceed

Before proceeding, please read the following paragraph carefully :

Imagine you are suffering from a chronic illness or other serious disease. After discussing your condition with your family physician and/or specialist, you have been told that there is a new experimental treatment for your condition. It is not known whether or not this new treatment would provide any benefits to you above and beyond currently available treatments. A physician or clinical nurse has asked you to consider enrolling in this randomized controlled trial. Depending on the group to which you would be assigned, you may receive an inactive medication (i.e., placebo) or the experimental treatment. The likelihood of being assigned to these two groups is equal (i.e., 50/50). With this in mind, please answer the following questions as if you were faced with this decision.

Click to proceed

Based on the previous description, please respond to the following statements. Again, your responses pertain to your decision whether or not to take part in a clinical trial specific to a hypothetical chronic illness or serious disease. Please don't be concerned if it seems that more than one question is asking for the same information.

SD - Strongly disgree D - Disagree N - Neither agree/disagree A - Agree SA - Strongly agree

There are many ways around my illness.	*SD*	*D*	*N*	*A*	*SA*
I will meet the treatment goals that I set for myself as a result of participating in this study.	*SD*	*D*	*N*	*A*	*SA*
I am confident that I would be among those who benefit from participation.	*SD*	*D*	*N*	*A*	*SA*
My past experiences have prepared me well for participation in this study.	*SD*	*D*	*N*	*A*	*SA*
I believe that controlling my symptoms is possible.	*SD*	*D*	*N*	*A*	*SA*
I would not have been asked to participate if the experimental treatment did not work.	*SD*	*D*	*N*	*A*	*SA*
There was something different about my condition or circumstances as compared to others that led the doctors to ask me to be in this study.	*SD*	*D*	*N*	*A*	*SA*
I will remain hopeful even if there are setbacks in my treatment.	*SD*	*D*	*N*	*A*	*SA*
There is a chance that my condition could worsen during the course of this study.	*SD*	*D*	*N*	*A*	*SA*
I look forward to participating in this study with hope and enthusiasm.	*SD*	*D*	*N*	*A*	*SA*
My participation in this clinical trial may not directly benefit me.	*SD*	*D*	*N*	*A*	*SA*

I am certain that my participation in this clinical trial would directly benefit me.	*SD*	*D*	*N*	*A*	*SA*
My doctor downplays the likelihood that I would benefit from participating in this clinical trial.	*SD*	*D*	*N*	*A*	*SA*
I will know to which treatment group I've been assigned.	*SD*	*D*	*N*	*A*	*SA*
There is no known risk to participants in this study.	*SD*	*D*	*N*	*A*	*SA*
I have great faith in the physicians conducting this clinical trial.	*SD*	*D*	*N*	*A*	*SA*
The experimental treatment could have negative side effect.	*SD*	*D*	*N*	*A*	*SA*
I will lose hope if my recovery does not soon occur.	*SD*	*D*	*N*	*A*	*SA*
I am optimistic about the outcome of my treatment.	*SD*	*D*	*N*	*A*	*SA*
Whether or not I will derive direct benefit from my participation will depend on the design of the study.	*SD*	*D*	*N*	*A*	*SA*
My medication dosage would be adjusted if I do not respond to treatment.	*SD*	*D*	*N*	*A*	*SA*
The goal of research could compromise my treatment needs in this clinical trial.	*SD*	*D*	*N*	*A*	*SA*

I believe my physician has underestimated the risk of participating in this study.	*SD*	*D*	*N*	*A*	*SA*
The experimental treatment is the best therapy available to treat my condition.	*SD*	*D*	*N*	*A*	*SA*
I should give up because there is no treatment that will benefit me.	*SD*	*D*	*N*	*A*	*SA*
My physician would tell me which treatment I receive.	*SD*	*D*	*N*	*A*	*SA*
My doctor has emphasized potential benefits of this study.	*SD*	*D*	*N*	*A*	*SA*
The goal of this clinical trial is to find the best treatment for my condition.	*SD*	*D*	*N*	*A*	*SA*
I don't expect to receive the treatment I need.	*SD*	*D*	*N*	*A*	*SA*
I would enrol in this study to contribute to science.	*SD*	*D*	*N*	*A*	*SA*
I will lose hope if my treatment is not successful.	*SD*	*D*	*N*	*A*	*SA*
I would take part in this research to have someone to talk to about my condition.	*SD*	*D*	*N*	*A*	*SA*
I know that my participation in this trial would help relieve my symptoms.	*SD*	*D*	*N*	*A*	*SA*

I would participate in this clinical trial because it is my last option.	*SD*	*D*	*N*	*A*	*SA*
I believe my doctor has underestimated the likelihood that I would benefit from participating in this study.	*SD*	*D*	*N*	*A*	*SA*
According to the rules of research studies like these, doctors do not choose the treatment or intervention I receive based on what best suits my needs.	*SD*	*D*	*N*	*A*	*SA*
I doubt that the treatment would help relieve my symptoms.	*SD*	*D*	*N*	*A*	*SA*
My participation in this clinical trial will prolong my life.	*SD*	*D*	*N*	*A*	*SA*
The goal of this clinical trial would be to benefit me.	*SD*	*D*	*N*	*A*	*SA*
I am energetically pursuing my goal by participating in this study.	*SD*	*D*	*N*	*A*	*SA*
I believe my physician has overestimated the risks of participating in this study.	*SD*	*D*	*N*	*A*	*SA*
My past medical experiences have prepared me well for participation in this study.	*SD*	*D*	*N*	*A*	*SA*
I doubt that the treatment would help cure my illness.	*SD*	*D*	*N*	*A*	*SA*
Being in this study would lead to improvements in my daily functioning.	*SD*	*D*	*N*	*A*	*SA*

I have plans and goals for my treatment.	*SD*	*D*	*N*	*A*	*SA*
There is little or no hope that I would benefit from participating in this study.	*SD*	*D*	*N*	*A*	*SA*
Assignment to treatment conditions is random to ensure equal number in each treatment condition.	*SD*	*D*	*N*	*A*	*SA*
The odds of receiving standard treatment are the same for all participant.	*SD*	*D*	*N*	*A*	*SA*
Doctors would not do this study if they thought that it might cause some participants to get worse.	*SD*	*D*	*N*	*A*	*SA*
Some participants will receive an inactive substance (i.e., placebo).	*SD*	*D*	*N*	*A*	*SA*
The main purpose of this trial is to obtain knowledge about the usefulness of the experimental treatment.	*SD*	*D*	*N*	*A*	*SA*
Participating in this clinical trial would not help me.	*SD*	*D*	*N*	*A*	*SA*
I believe that recovery is always possible.	*SD*	*D*	*N*	*A*	*SA*
My doctor has downplayed the risks of this study.	*SD*	*D*	*N*	*A*	*SA*
Despite my illness, I see a more positive future for me in the months ahead.	*SD*	*D*	*N*	*A*	*SA*

I doubt that the treatment would benefit me.	*SD*	*D*	*N*	*A*	*SA*
My well-being is of primary importance in this clinical trial.	*SD*	*D*	*N*	*A*	*SA*
It is unlikely that my participation would help me or my condition.	*SD*	*D*	*N*	*A*	*SA*
This clinical trial may not have any effect on my condition at all.	*SD*	*D*	*N*	*A*	*SA*
The purpose of this clinical trial is to determine whether or not the new experimental treatment is effective.	*SD*	*D*	*N*	*A*	*SA*
My doctor would adjust the treatment I receive (e.g., medication dosage) to ensure that I receive the best possible care.	*SD*	*D*	*N*	*A*	*SA*
The experimental treatment is a proven therapy for my condition.	*SD*	*D*	*N*	*A*	*SA*
I worry that my health might worsen despite being in this clinical trial.	*SD*	*D*	*N*	*A*	*SA*
I would enrol in this study to advance the researchers' knowledge of my illness.	*SD*	*D*	*N*	*A*	*SA*
There is little that can be done for people with my condition.	*SD*	*D*	*N*	*A*	*SA*
My participation in this clinical trial would boost my immune system..	*SD*	*D*	*N*	*A*	*SA*

I feel overwhelmed and trapped because of my illness.	*SD*	*D*	*N*	*A*	*SA*
I would choose to take part in this study in order to receive free medical care.	*SD*	*D*	*N*	*A*	*SA*
In this clinical trial, one of the purposes is to test the safety of the experimental treatment.	*SD*	*D*	*N*	*A*	*SA*
I would enrol in this research study to help improve the health of others.	*SD*	*D*	*N*	*A*	*SA*
I am unlikely to obtain any benefit from participating in this study.	*SD*	*D*	*N*	*A*	*SA*
This clinical trial is conducted mostly to gather knowledge about my condition.	*SD*	*D*	*N*	*A*	*SA*
I don't expect the experimental treatment would help me but I remain hopeful that it will.	*SD*	*D*	*N*	*A*	*SA*
The physicians in this study do not know that they are giving everyone the best possible treatment.	*SD*	*D*	*N*	*A*	*SA*
Medical researchers are only allowed to do things that will benefit all patients.	*SD*	*D*	*N*	*A*	*SA*
I believe my doctor has overestimated the likelihood that I would benefit from participating in this study.	*SD*	*D*	*N*	*A*	*SA*
My doctor would discourage my participation in this clinical trial if there would be no direct benefit for me.	*SD*	*D*	*N*	*A*	*SA*

The researchers in this study know that one of the treatments or interventions will have better results than others.	*SD*	*D*	*N*	*A*	*SA*
I might not know the results of this study for months or even years.	*SD*	*D*	*N*	*A*	*SA*
I have plans for the months ahead.	*SD*	*D*	*N*	*A*	*SA*
In this clinical trial, every participant has an equal chance of receiving the experimental treatment.	*SD*	*D*	*N*	*A*	*SA*
The assignment of patients to different treatment conditions does not take into account the fact that some patients' needs are different than others.	*SD*	*D*	*N*	*A*	*SA*
My individual needs will determine the treatment I receive.	*SD*	*D*	*N*	*A*	*SA*
My participation in this clinical trial will provide me with psychological benefits.	*SD*	*D*	*N*	*A*	*SA*
There is nothing that can be done about my condition.	*SD*	*D*	*N*	*A*	*SA*
I will receive the same treatment as everyone else even if my own particular case is somewhat different.	*SD*	*D*	*N*	*A*	*SA*
I feel confident that I would benefit from participating in this study .	*SD*	*D*	*N*	*A*	*SA*
I am less likely to obtain benefit from participating in this study compared to others.	*SD*	*D*	*N*	*A*	*SA*

The main reason that people will be recruited for this study is so that they can benefit from the special treatment in this research project.	*SD*	*D*	*N*	*A*	*SA*
My reason to participate is to improve my condition.	*SD*	*D*	*N*	*A*	*SA*
My participation in this clinical trial may not provide me indirect benefits.	*SD*	*D*	*N*	*A*	*SA*
This study has not been designed primarily to relieve patients and their illness.	*SD*	*D*	*N*	*A*	*SA*
I feel that I would benefit less than others from participation in this study.	*SD*	*D*	*N*	*A*	*SA*
I am very optimistic about my chances for successful treatment.	*SD*	*D*	*N*	*A*	*SA*
Participating in this clinical trial might only benefit others.	*SD*	*D*	*N*	*A*	*SA*
Information obtained during the course of this study would become part of my treatment plan.	*SD*	*D*	*N*	*A*	*SA*
My participation in this study will improve my quality of life.	*SD*	*D*	*N*	*A*	*SA*
I can think of many ways to reach my treatment goals.	*SD*	*D*	*N*	*A*	*SA*
I've been asked to participate because there are no other treatment options available.	*SD*	*D*	*N*	*A*	*SA*

In this clinical trial, the primary purpose is to improve treatment for future patients.	*SD*	*D*	*N*	*A*	*SA*
My physician(s) does not know what therapy I would receive.	*SD*	*D*	*N*	*A*	*SA*
The treatment/intervention I would receive in this study will be adapted according to my needs, like the treatment from any other doctor.	*SD*	*D*	*N*	*A*	*SA*
There are many ways my participation in this study would help me.	*SD*	*D*	*N*	*A*	*SA*
My participation in this clinical trial may not directly benefit me.	*SD*	*D*	*N*	*A*	*SA*
The treatment/intervention I would receive may be changed in response to the way my medical condition changes.	*SD*	*D*	*N*	*A*	*SA*
Every aspect of this clinical trial is to benefit the participants.	*SD*	*D*	*N*	*A*	*SA*
I doubt that the treatment would harm me.	*SD*	*D*	*N*	*A*	*SA*
I'm more likely to benefit than the average person.	*SD*	*D*	*N*	*A*	*SA*
I might be one of the participants who receives the inactive medication (i.e., assigned to the placebo condition).	*SD*	*D*	*N*	*A*	*SA*
I am more prepared to participate in this clinical trial than other participants.	*SD*	*D*	*N*	*A*	*SA*

In this clinical trail, every participant is just as likely to receive standard treatment (or be assigned to the placebo condition).	*SD*	*D*	*N*	*A*	*SA*
I feel like I am aware of all of the important risks in this trial.	*SD*	*D*	*N*	*A*	*SA*
I know that I would be among those who receive the active medication/treatment.	*SD*	*D*	*N*	*A*	*SA*
Treatment is randomly allocated because it is the most exact and fair way to test which works best.	*SD*	*D*	*N*	*A*	*SA*
The treatment I would receive is based on my medical needs.	*SD*	*D*	*N*	*A*	*SA*
I am confident that I would receive the active medication.	*SD*	*D*	*N*	*A*	*SA*
In this clinical trial, one of the goals is to test the toxicity of the experimental treatment.	*SD*	*D*	*N*	*A*	*SA*
I am very optimistic that I would be one of those to benefit from participation in this study.	*SD*	*D*	*N*	*A*	*SA*
I don't expect to receive the care I need.	*SD*	*D*	*N*	*A*	*SA*
I see more negative than positive things to come with regard to my medical condition.	*SD*	*D*	*N*	*A*	*SA*
I look forward to being in this study.	*SD*	*D*	*N*	*A*	*SA*

Taking part in this research study would cure my illness.	*SD*	*D*	*N*	*A*	*SA*
There is a chance that the placebo is just as effective as the experimental treatment.	*SD*	*D*	*N*	*A*	*SA*
The treatment I would receive as a participant in this study will be no different than my previous treatment.	*SD*	*D*	*N*	*A*	*SA*
I'm equally likely to receive the experimental or the standard intervention (or placebo condition).	*SD*	*D*	*N*	*A*	*SA*
The treatment I would receive in this clinical trial would cure my illness.	*SD*	*D*	*N*	*A*	*SA*
My doctor could access the information obtained during the course of this clinical trial.	*SD*	*D*	*N*	*A*	*SA*

Click to proceed

Based on the previous description, please respond to the following statements. Again, your responses pertain to your decision whether or not to take part in a clinical trial specific to a hypothetical chronic illness or serious disease. Please don't be concerned if it seems that more than one question is asking for the same information.

SD - Strongly disgree D - Disagree N - Neither agree/disagree A - Agree SA -

If you do not want to answer the following question(s), simply click the button below to proceed

click to proceed

You have unanswered question(s). Please rate the questions in blue if you intent to answer them. However, you do not have to answer questions that make you uncomfortable.

There are many ways around my illness.	*SD*	*D*	*N*	*A*	*SA*
I will meet the treatment goals that I set for myself as a result of participating in this study.	*SD*	*D*	*N*	*A*	*SA*
I am confident that I would be among those who benefit from participation.	*SD*	*D*	*N*	*A*	*SA*
My past experiences have prepared me well for participation in this study.	*SD*	*D*	*N*	*A*	*SA*
I believe that controlling my symptoms is possible.	*SD*	*D*	*N*	*A*	*SA*
I would not have been asked to participate if the experimental treatment did not work.	*SD*	*D*	*N*	*A*	*SA*
There was something different about my condition or circumstances as compared to others that led the doctors to ask me to be in this study.	*SD*	*D*	*N*	*A*	*SA*

Background Questionnaire

Important! Please do not hit the enter key at any time when filling out the survey as it will inadvertently submit your responses. Only use the submit button provided at the end of the page for submitting your responses.

Your gender (select one)

○ Male ○ Female

Present Age: ┌──

What is your marital status? (select one)

○ Married/Common-law
○ Separated/divorced
○ Widowed
○ Never Married

What is (or do you have) a religious affiliation (e.g., Jewish, Roman Catholic)? ┌──────

How often have you attended religious services over the past 12 months (if at all)? ┌──

How many years of formal education did you complete? ┌──

How would you best describe your ethnicity (select one response)

○ Aboriginal/First Nations/Indigenous/Indian
○ African/African American/Black
○ Asian/Pacific Islander
○ Latina/Latino
○ Middle Eastern/North African
○ White/European
○ Mixed/Multi

What was/is your work or occupation (e.g., housewife, carpenter)? (Describe fully in the space below):

What is your current employment status?

- Full-time
- Part-time
- Retired
- Unemployed

If retired, what year did you leave the paid work force

Is English your first language? (select one)

Yes No

Are you currently enrolled in a clinical drug trial? (select one)

Yes No

Have you ever been in a clinical drug trial? (select one)

Yes No

How would you say your health is these days? (select one)

- Very poor
- Somewhat poor
- Poor
- Satisfactory
- Good
- Very Good
- Excellent

Is your health better now, about the same, or worse than a

year ago? (select one)

Better About the same Worse

Would you say your health is better, about the same, or worse than most people your age? (select one)

Better About the same Worse

How much do health troubles stand in the way of doing the things you want to do (select one response)? (select one)

Not at all A little (some things) A great deal

Regarding your health over the past year, do you have, or have you had any of the following conditions. Please respond either Yes or No as appropriate:

Allergies of any kind	Yes / No
Broken hip	Yes / No
Fractures or broken bones (not hip)	Yes / No
Hip replacement	Yes / No
Breathing problems (e.g., asthma, TB, emphysema, pneunomia, bronchitis)	Yes / No

- Heart or circulation problems (e.g., heart trouble, angina, hardening of the arteries — Yes / No
- Pace maker inserted — Yes / No
- High blood pressure — Yes / No
- Paralysis of any kind — Yes / No
- Kidney condition or disease (including bladder troubles) — Yes / No
- Thyroid disease — Yes / No
- Surgery — Yes / No
- Tumour or cancer — Yes / No
- Diabetes — Yes / No
- Trouble with vision (e.g., cataracts, glaucoma) — Yes

No

- Problems with hearing — Yes / No
- Arthritis or rheumatism — Yes / No
- Troubles with your stomach or digestive problems — Yes / No
- Stroke or effects of a stroke — Yes / No
- Parkinson's disease — Yes / No
- Nervous or been tense — Yes / No
- Trouble getting to, or staying asleep — Yes / No
- Other problem(s) not mentioned — Yes / No

If yes, specify: _____

Would you like to receive a summary of findings following completion of this study? (If yes, please provide your e-mail address below.)

○ Yes ○ No

Would you like to be included in the draw for $500 following completion of this study? If so, please provide contact information below. I may need to contact you so you have to provide an e-mail address in the space below!

○ Yes ○ No

How did you hear about this survey?

Can we contact you in a couple of weeks and ask you to respond to a few additional questions? If yes, please provide your e-mail address below

○ Yes ○ No

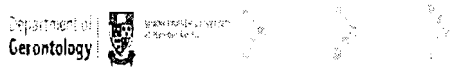
Your email address

Country of residence

Your responses have not been saved yet. Please take a moment to make some comments and suggestions relating to this study before submitting your responses. Thank you!

Click to proceed

Thank you. You have completed the survey!
Your data have been saved.



To visit the Department of Gerontology website click here

To visit the Canadian Association on Aging website click here

To visit the International Association of Gerontology website cli

Psychological Research On the Net

To participate in other psychological research online click here

If you do not want to answer the following question(s), simply click the button below to proceed

click to proceed

You have unanswered question(s). Please rate the questions in blue if you intent to answer them. However, you do not have to answer questions that make you uncomfortable.

Appendix B

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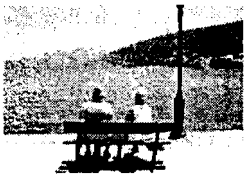
Older Adults' Perceptions of Clinical Trial Research - Part II



Welcome back (DEMO) If you do not see your email address above, please ensure you use the link provided in the email you received.

Thank you for taking the time to participate in the first phase of this study. Your responses have provided valuable information in understanding older adults' beliefs regarding various aspects of clinical research.

As described in the recent e-mail message to you, we now request your participation in the final part of this study.

If you agree to participate, you will be asked to complete nine questionnaires requiring less than 30 minutes of your time. These questions are similar to ones you would encounter if deciding whether or not to enroll in a clinical drug trial.

As a token of our gratitude, participants will receive a $10 Starbucks Gift Card after completion of the survey.

Note, responses provided via this website are electronically encrypted (similar to credit card purchases made on the Internet) for added security.

You are not required to provide your name. No individual responses from this study will be disclosed; only combined data will be reported. All information will be store in a secured location. If you have any concerns regarding this study, please contact Dr. Norm O'Rourke at: ORourke@sfu.ca

Participation in this study is strictly voluntary. You are not required to answer questions that make you uncomfortable and you are free to discontinue at any time. Completion of questionnaires will indicate your willingness to participate.

Thank you for continuing support of this study.

With Regards,

Ben Chou
MA Candidate
phchou@sfu.ca

Click to proceed

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The following questions ask about your past experiences with clinical trial research. Please take a moment to answer these questions as best as you can.

1. Have you previously participated (now or in the past) in a clinical drug trial? (If no, hit the *Proceed Button* at the bottom of this page) ○ Yes ○ No

2. What is/was your diagnosis that led to participation in that study? [ ]

3. If the trial is completed, when did it end? [-Year-] [-Month-] Ago

4. Please breifly summarize the clinical trial in which you were enrolled (e.g., phase III trial, open label)? [ ]

5. Were you randomly assigned to one of various treatment conditions? ○ Yes ○ No ○ Don't Know

5. Did anyone in that clinical trial receive inactive medication (i.e., sugar pill or placebo?) ○ Yes ○ No ○ Don't Know

7. Were you told whether you received the active treamtent or the placebo? ○ Yes ○ No ○ Don't Know

---

8. Please answer the following questions based on the most recent clinical trial in which you participated.

SA - Strongly Agree A - Agree N - Neither Agree or Disagree D - Disagree SD - Strongly Disagree					
A. Clinic staff provided me with good care	○ SA	○ A	○ N	○ D	○ SD
B. Clinic staff were friendly and pleasant	○ SA	○ A	○ N	○ D	○ SD
C. Clinic staff showed genuine concern for my well-being	○ SA	○ A	○ N	○ D	○ SD

VS - Very Satisfied SS - Somewhat Satisfied N - Neutral SD - Somewhat Dissatisfied VD - Very Dissatisfied					
D. Overall experience	○ VS	○ SS	○ N	○ SD	○ VD
E. Waiting time at clinic	○ VS	○ SS	○ N	○ SD	○ VD
F. Information received from clinic staff	○ VS	○ SS	○ N	○ SD	○ VD

Proceed Progress 0%

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Part A

The following questions ask your *perceptions* with various aspects of clinical trial research, not your specific experiences with such studies

Proceed

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Before proceeding, please read the following paragraph carefully:

Dr. John Smith is doing a research study to see how well a new medication, called GP739, treats symptoms of dementia. People in this study will either take the new medication, GP739, or a placebo (A placebo is a sugar pill with no active medication.) In contrast, GP739 is a new, experimental medication that has not yet been approved by the government. Based on other research that has been done so far, the researchers believe that it will help treat symptoms of dementia.

The purpose of the study is to find out whether the new medication, GP739, is effective. The researchers will also look for any side effects.

At the outset, people will be randomly assigned to receive GP739 or the placebo. Participants will have an equal chance (50%) of being assigned to one of these two pills. This means participants will have a 50% chance of getting each type of pill. Participants will not know which they are receiving nor will the study physician know what the people in the study are taking.

1. As part of this study, I will receive the medication that the researcher thinks is most likely to help me	○ Yes	○ No
2. The researcher(s) won't know exactly which medication I am receiving	○ Yes	○ No
3. In this study, I will certainly get a medication that is designed to improve my condition	○ Yes	○ No
4. The researcher(s) will give me the specific dose of medication that s/he thinks is best for me	○ Yes	○ No
5. Once the study has begun, the study physician cannot change the dose of medication depending on my needs and still keep me in the study	○ Yes	○ No
6. The study physician cannot add any other medication while I am in this study, even if s/he thinks it would help me	○ Yes	○ No

Progress 10%

Proceed

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Before proceeding, please read the following paragraph carefully:

Imagine you are diagnosed from a new chronic illness or other serious condition. After discussing your condition with your family physician and/or specialist, you have been told that there is a new experimental treatment. It is not known whether or not this new treatment would provide any benefits above and beyond currently available treatments. A physician or clinical nurse has asked you to consider enrolling in this randomized controlled trial. Depending on the group to which you would be assigned, you may receive an inactive treatment (i.e., placebo) or the experimental treatment. The likelihood of being assigned to these two groups is equal (i.e., 50/50). With this in mind, please answer the following questions as if you were faced with this decision.

Based on the previous description, please respond to the following statements. Again, your responses pertain to your decision whether or not to take part in a clinical trial specific to a hypothetical chronic illness or other serious health condition.

SD - Strongly disgree D - Disagree N - Neither agree/disagree A - Agree SA - Strongly agree

1. The main reason that people will be recruited for this study is so that they can benefit from the special treatment in this research project.	SD	D	N	A	SA
2. The treatment I would receive in this clinical trial would cure my illness.	SD	D	N	A	SA
3. The treatment/intervention I would receive may be changed in response to the way my medical condition changes.	SD	D	N	A	SA
4. I am very optimistic about my chances for successful treatment.	SD	D	N	A	SA
5. The researchers in this study know that one of the treatments or interventions will have better results than others.	SD	D	N	A	SA
6. My participation in this clinical trial will prolong my life.	SD	D	N	A	SA
7. The treatment/intervention I would receive in this study will be adapted according to my needs, like the treatment from any other doctor.	SD	D	N	A	SA
8. There are many ways my participation in this study would help me.	SD	D	N	A	SA
9. Medical researchers are only allowed to do things that will benefit all patients.	SD	D	N	A	SA
10. My participation in this study will improve my quality of life.	SD	D	N	A	SA

11. According to the rules of research studies like these, doctors do not choose the treatment or intervention I would receive based on what best suits my needs.	SD	D	N	A	SA
12. My past medical experiences have prepared me well for participation in this study.	SD	D	N	A	SA
13. The treatment I would receive is based on my medical needs.	SD	D	N	A	SA
14. Taking part in this research study would cure my illness.	SD	D	N	A	SA
15. My physician would tell me which treatment I receive.	SD	D	N	A	SA
16. I look forward to participating in this study with hope and enthusiasm.	SD	D	N	A	SA
17. My medication dosage would be adjusted if I do not respond to treatment.	SD	D	N	A	SA
18. My participation in this clinical trial would boost my immune system.	SD	D	N	A	SA
19. My doctor would adjust the treatment I receive (e.g., medication dosage) to ensure that I receive the best possible care.	SD	D	N	A	SA
20. I look forward to being in this study.	SD	D	N	A	SA
21. My doctor could access the information obtained during the course of this clinical trial.	SD	D	N	A	SA
22. I'm more likely to benefit from participation in this study than the average person.	SD	D	N	A	SA
23. This clinical trial is being conducted mostly to gather knowledge about my condition.	SD	D	N	A	SA

Proceed

Progress 20%

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When some people think about how illness may affect their lives in the future, they describe feeling that their life will lose some of its *fullness*. This change in fullness can affect anything, including the pleasure/enjoyment gotten out of activities, work, time spent with family and friends, how long you think you might live and so forth.

Imagine your life prior to your illness as a whole pie, such as Pie #1. Imagine how much of your life's fullness might have been reduced due to this change in your condition. Please indicate which pie best represents how much of your life's fullness was lost due to this change. For example, if you feel your life's fullness was reduced to half of what it was before, then you would indicate Pie #5.

Pie 1 Pie 2 Pie 3 Pie 4 Pie 5 Pie 6 Pie 7 Pie 8 Pie 9

--Please select a Pie--

Progress 53%

Proceed

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Using the following scale, provide the appropriate response to each statement to indicate how much you agree with the following statements. During the past few weeks, have you felt ...

SD - Strongly disgree D - Disagree N - Neither agree/disagree A - Agree SA - Stronly agree

1. In uncertain times, I usually expect the best	○ SD	○ D	○ N	○ A	○ SA
2. If something can go wrong for me, it will	○ SD	○ D	○ N	○ A	○ SA
3. I'm always optimistic about my future	○ SD	○ D	○ N	○ A	○ SA
4. I hardly ever expect things to go my way	○ SD	○ D	○ N	○ A	○ SA
5. I rarely count on good things happening to me	○ SD	○ D	○ N	○ A	○ SA
6. Overall, I expect more good things to happen to me than bad	○ SD	○ D	○ N	○ A	○ SA

Progress 55%

Proceed

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Part B

The following questions ask your *experiences* with various aspects of clinical trial research. Please base your answers on your current diagonsis and the clinical trial in which you participated (or are how participating).

Proceed

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When you signed the consent form **to participate in your clinical trial, how well did you understand the following aspects of your clinical trial? If you didn't understand the item at all, please select 1. If you understood it very well, please select 5. If you understand it somewhat, please select a number between 1 and 5.**

1 - I didn't understand this at all

-
-
-

5 - I understood this very well

1. The fact that your treatment involved research	1	2	3	4	5
2. What the researchers were trying to find out in the clinical trial	1	2	3	4	5
3. How long you would be in the clinical trial	1	2	3	4	5
4. The treatments and procedures you would undergo	1	2	3	4	5
5. Which of the treatments and procedures were experimental	1	2	3	4	5
6. The possible risks and discomforts of participating in this clinical trial	1	2	3	4	5
7. The possible benefits to*you* of participating in the clinical trial	1	2	3	4	5
8. How your participation in this clinical trial might benefit *future patients*	1	2	3	4	5
9. The alternatives to participation in this clinical trial	1	2	3	4	5
10. The effect of participation on the confidentiality of your medical records	1	2	3	4	5
11. Who would pay for treatment if you are injured or become ill because of participation on this clinical trial	1	2	3	4	5
12. Whom you should contact if you had questions or concerns about the clinical trial	1	2	3	4	5
13. The fact that participation in the clinical trial was voluntary	1	2	3	4	5
14. Overall, how well did you understand your clinical trial when you signed the consent form?	1	2	3	4	5

Progress 60%

Proceed

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Below you will find several statements about clinical trials (otherwise known as clinical research studies). Thinking about your clinical trial, please read each statement carefully, then indicate whether you agree with the statement, you disagree with it, or you are unsure about the statement.

1. When I signed the consent form, I knew that I was agreeing to participate in a clinical trial. ○ Agree ○ Disagree ○ Unsure

2. The main reason clinical trials are done is to improve the treatment of *future* patients. ○ Agree ○ Disagree ○ Unsure

3. I was informed how long my participation in this clinical trial would last. ○ Agree ○ Disagree ○ Unsure

4. All the treatments and procedures in my clinical trial were standard for my type of illness. ○ Agree ○ Disagree ○ Unsure

5. In my clinical trial, one of the researchers' major purposes was to compare the effects (good and bad) of two or more different ways of treating patients with my illness, in order to see which is better/best ○ Agree ○ Disagree ○ Unsure

6. In my clinical trial, one of the researchers' major purposes was to test the safety of a new drug or treatment. ○ Agree ○ Disagree ○ Unsure

7. In my clinical trial, one of the researchers' major purposes was to find the highest dose of a new drug or treatment that can be given without causing severe side effects. ○ Agree ○ Disagree ○ Unsure

8. In my clinical trial, one of the researchers' major purposes was to find out what effects (good and bad) a new treatment has on me and my illness. ○ Agree ○ Disagree ○ Unsure

9. The treatment being researched in my clinical trial has been proven to be the best treatment for my illness. ○ Agree ○ Disagree ○ Unsure

10. In my clinical trial, each group of patients received a higher dose of the treatment than the group before, until some patients have serious side effects. ○ Agree ○ Disagree ○ Unsure

11. After I agreed to participate in my clinical trial, my treatment was chosen randomly (by chance) from two or more possible treatment options. ○ Agree ○ Disagree ○ Unsure

12. Compared with standard treatments for my illness, my clinical trial did not carry any additional risks or discomforts. ○ Agree ○ Disagree ○ Unsure

13. There may not have been direct medical benefit to me from my participation in this clinical trial. ○ Agree ○ Disagree ○ Unsure

14. By participating in this clinical trial, I helped the researchers learn information that may benefit future patients. ○ Agree ○ Disagree ○ Unsure

15. Because I was participating in a clinical trial, it was possible that they study sponsor, various government agencies, or others who were not directly involved in my care could review my medical records. ○ Agree ○ Disagree ○ Unsure

16. My doctors did not offer me alternatives besides treatment in this clinical trial. ○ Agree ○ Disagree ○ Unsure

17. The consent form I signed described who will pay for treatment if I am injured or become ill as a result of participation in this clinical trial. ○ Agree ○ Disagree ○ Unsure

18. The consent form I signed listed the name(s) of person(s) whom I should contact if I had any questions or concerns about the clinical trial. ○ Agree ○ Disagree ○ Unsure

19. If I had not wanted to participate in this clinical trial, I could have declined to sign the consent form. ○ Agree ○ Disagree ○ Unsure

20. I would have had to remain in the clinical trial even if I decided that I wanted to withdraw. ○ Agree ○ Disagree ○ Unsure

Proceed

Progress 72%

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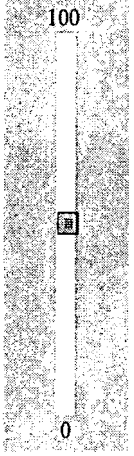
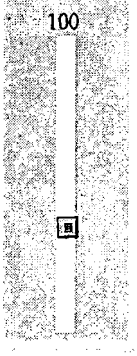
To indicate your answer to the following questions, please "click and drag" the slider on the vertical line at the appropriate value.

Please enter your email address again before continuing: _____

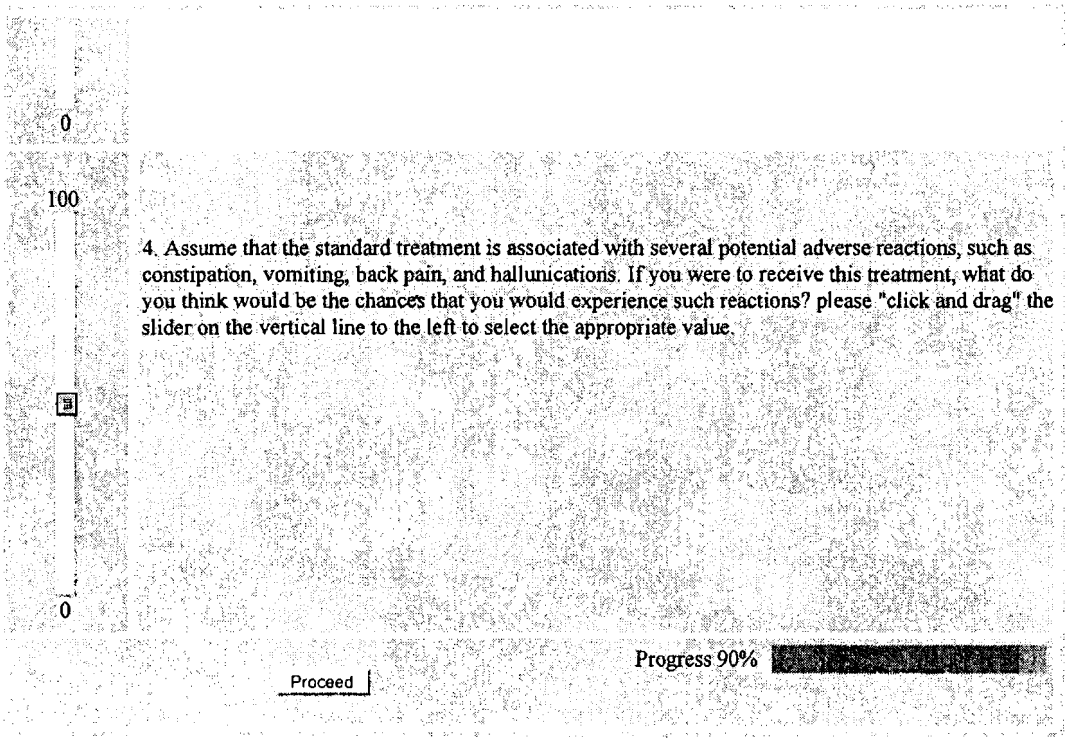
1. Imagine you were asked to participate in a study examining a new experimental treatment for dementia. If you were to receive this treatment, what do you think are the chances it would control your illness? please "click and drag" the slider on the vertical line to the left to select the appropriate value.



2. The experimental treatment you were offered is associated with several potential adverse reactions (e.g., side effects). If you were to receive this treatment, what do you think are the chances that you would experience a severe adverse reaction? please "click and drag" the slider on the vertical line to the left to select the appropriate value.



3. The standard treatment is offered to some patients with dementia. If you were to receive such treatment, what do you think are the chances it would control your illness? Please "click and drag" the slider on the vertical line to the left to select the appropriate value.


0
100
4. Assume that the standard treatment is associated with several potential adverse reactions, such as constipation, vomiting, back pain, and hallunications. If you were to receive this treatment, what do you think would be the chances that you would experience such reactions? please "click and drag" the slider on the vertical line to the left to select the appropriate value.
0
Progress 90%
Proceed

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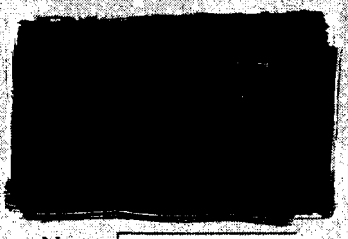
Thank you. You have completed the survey!
Your data have been saved.

Please take a moment to fill out your contact information for us to send you the $10 Starbuck Giftcard.



Name:

Mailing Address:

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Please verify your name and address before submitting

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Thank you again for taking the time to fill out my survey!

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Appendix C

		Study 2	Non CTP	Study 2 NR	Study 1
Age	Mean	62.5	59.9	61.4	59.8
	SD	6.4	6.5	6.4	6.2
Education (Year)	Mean	15.6	15.7	13.2	13.9
	SD	2.7	2.7	5.0	4.0
No. of chronic condition	Mean	4.2	4.4	5.1	3.9
	SD	2.5	2.8	2.6	2.6
Time to complete survey	Mean	00:18:41	00:18:06	00:25:18	00:20:29
	SD	00:08:13	00:05:22	00:25:55	00:29:49

		Study 2	Non CTP	Study 2 NR	Study 1
gender	Male	17	4	11	191
		7.6%	1.8%	4.9%	85.7%
	Female	19	3	12	272
		6.2%	1.0%	3.9%	88.9%
marital status	Married/Common-law	27	6	17	333
		7.0%	1.6%	4.4%	86.9%
	Separated/Divorced	4	1	4	78
		4.6%	1.1%	4.6%	89.7%
	Widowed	3	0	1	33
		8.1%	0.0%	2.7%	89.2%
	Never Married	2	0	1	19
		9.1%	0.0%	4.5%	86.4%
ethnicity	Aboriginal/First Nations/Indigenous/Indian	1	0	0	4
		20.0%	0.0%	0.0%	80.0%
	African/African American/Black	0	0	0	1
		0.0%	0.0%	0.0%	100.0%
	Asian/Pacific Islander	0	0	0	2
		0.0%	0.0%	0.0%	100.0%
	Latina/Latino	0	0	0	1
		0.0%	0.0%	0.0%	100.0%
	Middle Eastern/North African	0	0	0	1
		0.0%	0.0%	0.0%	100.0%
	White/European	34	7	23	431
		6.9%	1.4%	4.6%	87.1%
	Mixed/Multi	1	0	0	16
		5.9%	0.0%	0.0%	94.1%
employ	Full-time	7	2	5	124
		5.1%	1.4%	3.6%	89.9%
	Part-time	3	0	1	59
		4.8%	0.0%	1.6%	93.7%
	Retired	25	5	16	245

		Study 2	Non CTP	Study 2 NR	Study 1
		8.6%	1.7%	5.5%	84.2%
	Unemployed	1	0	0	29
		3.3%	0.0%	0.0%	96.7%
health (overall)	Very poor	0	0	0	6
		0.0%	0.0%	0.0%	100.0%
	Somewhat poor	1	0	5	31
		2.7%	0.0%	13.5%	83.8%
	Poor	1	0	3	35
		2.6%	0.0%	7.7%	89.7%
	Satisfactory	12	4	7	122
		8.3%	2.8%	4.8%	84.1%
	Good	9	3	4	120
		6.6%	2.2%	2.9%	88.2%
	Very good	11	0	3	110
		8.9%	0.0%	2.4%	88.7%
	Excellent	2	0	1	35
		5.3%	0.0%	2.6%	92.1%
health (compared to a year ago)	Better	9	0	5	76
		10.0%	0.0%	5.6%	84.4%
	About the same	24	5	11	305
		7.0%	1.4%	3.2%	88.4%
	Worse	2	2	7	78
		2.2%	2.2%	7.9%	87.6%
health (compared to others)	Better	12	1	6	156
		6.9%	0.6%	3.4%	89.1%
	About the same	18	5	6	203
		7.8%	2.2%	2.6%	87.5%
	Worse	6	1	11	97
		5.2%	0.9%	9.6%	84.3%
health (restrict activity)	Not at all	9	2	5	143
		5.7%	1.3%	3.1%	89.9%
	A little (some things)	25	3	9	242
		9.0%	1.1%	3.2%	86.7%
	A great deal	2	2	9	73
		2.3%	2.3%	10.5%	84.9%

Appendix D

Subscales	*Prospective Items*
Strongly disagree --- Disagree --- Neither Agree/Disagree --- Agree --- Strongly Agree	
1) Therapeutic Misconception [Flesch-Kincaid Grade Level = 8.8]	1. The main reason that people will be recruited for this study is so that they can benefit from the special treatment in this research project (A) 2. The treatment/intervention I receive may be changed in response to the way my medical condition changes (A) 3. The researchers in this study think that one of the treatment or interventions will have better results than others (A) 4. The assignment of patients to different treatment conditions does not take into account the fact that some patients needs are different than others (A) 5. Doctors in this study do not think that they are giving everyone in this study the best possible treatment (A) 6. There was something different about my condition or circumstances as compared to others in the study that influenced the doctors to task me to be in this study (A) 7. Doctors would not do this study if they thought that it might cause some participants to get worse (A) 8. I will receive the same treatment as everyone else even if my own particular case is somewhat different (A) 9. This study has not been designed primarily to relieve patients and their illness (A) 10. The treatment/intervention I receive in this study will be adapted according to my needs, like treatment from any other doctor (A) 11. Medical research studies are only allowed to do things to people that will benefit all patients (A) 12. According to the rules of research studies like these, doctors are not allowed to choose the treatment or intervention I receive based on what best suits my needs (A) 13. In this clinical trial, the primary purpose is to improve treatment for future patients (Q). 14. The purpose of this clinical trial is to determine whether or not this new treatment is effective (Q) 15. In this clinical trial, one of the purposes is to test the safety of the treatment (Q). 16. In this clinical trial, one of the goals is to test the

Subscales	*Prospective Items*
Strongly disagree --- Disagree --- Neither Agree/Disagree --- Agree --- Strongly Agree	
	toxicity of the treatment (Q).
	17. I've been asked to participate because there are no other treatment options available.
	18. Every aspect of this clinical trial is to benefit the participants.
	19. The goal of this clinical trial would be to benefit me.
	20. My well-being is of primary importance in this clinical trial.
	21. The treatment I would receive is based on my medical needs.
	22. My physician(s) does not know what therapy I would receive.
	23. My physician would tell me which treatment I receive.
	24. I will know to which treatment group I've been assigned.
	25. My individual needs will determine the treatment I receive.
	26. My reason to participate is to improve my condition.
	27. I would choose to take part in this study in order to receive free medical care.
	28. I would enrol in this research study to help improve the health of others.
	29. I would enrol in this study to advance knowledge on my illness.
	30. I would enrol in this study to contribute to science.
	31. I would take part in this research to have someone to talk to about my condition.
	32. In this clinical trial, every participant has an equal chance of receiving the experimental treatment.
	33. In this clinical trail, every participant is just as likely to receive standard treatment (or be assigned to the placebo condition).
	34. My medication dosage would be adjusted if I do not respond to treatment.
	35. Some of the participants will receive an inactive substance (i.e., placebo).
	36. I might be one of the participants who receives inactive medication (i.e., assigned to the placebo condition).
	37. My doctor would discourage my participation in this clinical trial if there is no direct benefit for me.

Subscales	*Prospective Items*
Strongly disagree --- Disagree --- Neither Agree/Disagree --- Agree --- Strongly Agree	
	38. Whether or not I will derive direct benefit from my participation will depend on the design of the study.
	39. The experimental treatment is a proven therapy for my condition.
	40. The experimental treatment is the best available to treat my condition.
	41. I'm equally likely to receive the experimental or the standard intervention (or placebo condition).
	42. The treatment I would receive as a participant in this study will be no different than my previous treatment.
	43. Information obtained during the course of this study would become part of my treatment plan.
	44. My doctor would adjust the treatment I receive (e.g., medication dosage) to ensure that I receive the best possible care.
	45. My doctor could access the information obtained during the course of this clinical trial.
	46. I might not know the results of this study for months or even years.
	47. I would not have been asked to participate if the treatment did not work
2) Therapeutic Misestimation	1. My participation in this clinical trial may not directly benefit me (Q).
[Flesch-Kincaid Grade Level = 10.8]	2. Participating in this clinical trial might only benefit others.
	3. The treatment I receive in this clinical trial would cure my illness.
	4. My participation in this clinical trial may not provide me indirect benefits (Q).
	5. My participation in this clinical trial may not directly benefit me.
	6. My participation in this clinical trial will provide me with psychological benefits.
	7. My participation in this clinical trial will prolong my life. (Clinical endpoint)
	8. My participation in this study will improve my quality of life. (Clinical endpoint)
	9. Being in this study would lead to improvements in my daily functioning. (Clinical endpoint)
	10. Taking part in this research study would cure my illness. (Clinical endpoint)
	11. My participation in the clinical trial would boost my

Subscales	*Prospective Items*
Strongly disagree --- Disagree --- Neither Agree/Disagree --- Agree --- Strongly Agree	
	immune system. (Surrogate endpoint)
	12. There is no known risk to participants in this study.
	13. There is a chance that my condition would worsen due to participation in this study.
	14. The experimental treatment could have negative side effect.
	15. I believe my doctor has underestimated the likelihood that I would benefit from participating in this study.
	16. I believe my doctor has overestimated the likelihood that I would benefit from participating in this study.
	17. I believe my physician has overestimated the risks of participating in this study.
	18. I believe my physician has underestimated the risk of participating in this study.
	19. My doctor downplays the likelihood that I would benefit from participating in this clinical trial.
3) Therapeutic Optimism	1. I am certain that my participation in the trial would directly benefit me.
[Flesch-Kincaid Grade Level = 6.7]	2. I know that my participation in the trial would help relieve my symptoms.
	3. I know that I would be the one who receive the active medication.
	4. I am very optimistic that I would be one of those to benefit from participation in this study.
	5. I am confident that I would be among those who benefit from participation.
	6. I am confident that I would receive the active medication.
	7. I don't expect the experimental treatment would help me but remain hopeful that it will.
	8. I feel that I would benefit less than others from participation in this study.
	9. I am unlikely to obtain any benefit from participating in this study (S).
	10. I am less likely to obtain benefit from participating in this study compared to others (S).
	11. I feel confident that I would benefit from participating in this study (S).
	12. It is unlikely that my participation would help me or my conditions (S).
	13. I doubt that the treatment would help relieve my symptom (S).

Subscales	*Prospective Items*
Strongly disagree --- Disagree --- Neither Agree/Disagree --- Agree --- Strongly Agree	
	14. I doubt that the treatment would help cure my illness (S).
	15. I am very optimistic about my chances for successful treatment (S).
	16. I doubt that the treatment would benefit me (S).
	17. I doubt that the treatment would harm me (S).
	18. I'm more prepared to participate in this clinical trial than other participants (S).
	19. There is little or no hope that I would benefit from my participation.
	20. I can think of many ways to reach my treatment goals (H).
	21. Right now, I am optimistic about the outcome of my treatment (H).
	22. There are many ways around my illness (H).
	23. There is nothing that can be done about my condition.
	24. Participating in this clinical trial would not help me.
	25. There are many ways my participation in this study would help me (H).
	26. At present, I am energetically pursuing my goal in participation of this study (H).
	27. I will meet the treatment goals that I set for myself as a result of participating in this study (H).
	28. My past medical experiences have prepared me well for my trial participation in this study (H).
	29. I worry about my health.*
	30. I should give up because there is no treatment that will benefit me.
	31. I look forward to participating in this study with hope and enthusiasm.
	32. I have great faith in the physicians conducting this clinical trial.
	33. I don't expect to receive the treatment I need.
	34. I don't expect to receive the care I need.
	35. My past experiences have prepared me well for participation in this study.
	36. I am looking forward to being in this study.
	37. I have plans and goals for my treatment.
	38. I will remain hopeful even if there are setbacks in my treatment.
	39. I will loss hope if my recovery does not soon occur.

Subscales	*Prospective Items*
Strongly disagree --- Disagree --- Neither Agree/Disagree --- Agree --- Strongly Agree	
	40. I will loss hope if my treatment is not successful.
	41. Despite my illness, I see a more positive future for me in the months ahead.
	42. I have plans for the months ahead.
	43. I believe that recovery is always possible.
	44. I believe that controlling my symptoms is possible.
	45. I see more negative than positive things to come with regard to my medical condition.
	46. I feel overwhelmed and trapped because of my illness.
	47. I would participate in this clinical trial because it is my last option. (b)
	48. There is little that can be done for people with my condition (E)

(A) – items directly from the Participating in Research Questionnaire by Lidz, Appelbaum, & Grisso; (Q) – items adapted from Joffe, S., Cook, E. F., Cleary, P. D., Clark, J. W., & Weeks, J. C. (2001a); (S) –items adapted from Segerstrom et al. (1998); (H) – items adapted from "The Adult Trait Hope Scale by Snyder & Harris et al., (1991); (E) – items adapted from Elsom Therapeutic Optimism Scale (2002).

Appendix E

	extmiss >50% missing				
	< 50 missing	Case 1	Case 2	Case 3	Case 4
	Mean	Mean	Mean	Mean	Mean
Age	60	53	61	67	53
Education	14	18	12	15	14
timescale Time to complete scale	0:20:31	0:05:11	0:55:51	0:03:28	0:00:26
chronic # of Chronic Condition	3.98	5.00	5.00	2.00	6.00

		extmiss >50% missing				
		< 50 missing	Case 1	Case 2	Case 3	Case 4
		Count	Count	Count	Count	Count
gender	Male	222	0	0	0	0
	Female	293	1	1	1	1
marital	Married/Common-law	373	1	0	1	1
	Separated/Divorced	83	0	0	0	0
	Widowed	37	0	0	0	0
	Never Married	22	0	1	0	0
employ	Full-time	134	1	0	0	1
	Part-time	58	0	0	0	0
	Retired	286	0	1	1	0
	Unemployed	30	0	0	0	0
language	Yes	476	1	1	1	1
	No	31	0	0	0	0
trialnow	Yes	9	0	0	0	0
	No	500	1	1	1	1
trialbe	Yes	61	0	0	0	0
	No	442	1	1	1	1
health1	Very poor	6	0	0	0	0
	Somewhat poor	34	0	0	0	0
	Poor	39	1	0	1	1
	Satisfactory	138	0	1	0	0
	Good	133	0	0	0	0
	Very good	123	0	0	0	0
	Excellent	38	0	0	0	0
health2	Better	85	0	1	0	0
	About the same	340	0	0	0	0
	Worse	85	1	0	1	1
health3	Better	171	0	0	0	0
	About the same	229	0	1	0	0
	Worse	108	1	0	1	1
health4	Not at all	157	0	0	0	0
	A little (some things)	272	1	0	0	0
	A great deal	81	0	1	1	1

Appendix F

Items analyses of working items for the therapeutic misconception subscale (In descending order by ITC)

Legends-SD=Strongly Disagree; D=Disagree; N=Neither Disagree or Agree; A=Agree; SA=Strongly Agree; SD=standard deviation; S=skewness; K=kurtosis; ITC=Item-total correlation; SMC= Squared multiple correlation.

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc001 The main reason that people will be recruited for this study is so that they can benefit from the special treatment in this research project.	49	10.6%	190	40.9%	90	19.4%	114	24.6%	21	4.5%	2.72	1.09	0.30	-0.89	0.61	
tmisc002 The treatment/intervention I would receive may be changed in response to the way my medical condition changes.	24	5.2%	94	20.3%	100	21.6%	223	48.1%	23	5.0%	3.27	1.01	-0.58	-0.57	0.40	
tmisc003 The researchers in this study know that one of the treatments or interventions will have better results than others.	36	7.8%	114	24.6%	111	23.9%	165	35.6%	38	8.2%	3.12	1.11	-0.22	-0.87	0.35	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc006 There was something different about my condition or circumstances as compared to others that led the doctors to ask me to be in this study.	41	8.8%	166	35.8%	163	35.1%	84	18.1%	10	2.2%	2.69	0.94	0.17	-0.48	0.36	
tmisc007 Doctors would not do this study if they thought that it might cause some participants to get worse.	30	6.5%	142	30.6%	114	24.6%	141	30.4%	37	8.0%	3.03	1.09	0.01	-0.93	0.38	
tmisc010 The treatment/intervention I would receive in this study will be adapted according to my needs like the treatment from any other doctor.	48	10.3%	170	36.6%	98	21.1%	130	28.0%	18	3.9%	2.78	1.08	0.13	-1.00	0.56	
tmisc011 Medical researchers are only allowed to do things that will benefit all patients.	73	15.7%	223	48.1%	108	23.3%	48	10.3%	12	2.6%	2.36	0.95	0.67	0.16	0.47	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc012 According to the rules of research studies like these doctors do not choose the treatment or intervention I receive based on what best suits my needs.	10	2.2%	48	10.3%	111	23.9%	228	49.1%	67	14.4%	3.63	0.93	-0.65	0.18	-0.32	
tmisc018 Every aspect of this clinical trial is to benefit the participants.	41	8.8%	161	34.7%	118	25.4%	114	24.6%	30	6.5%	2.85	1.09	0.19	-0.83	0.56	
tmisc019 The goal of this clinical trial would be to benefit me.	33	7.1%	115	24.8%	128	27.6%	168	36.2%	20	4.3%	3.06	1.03	-0.27	-0.80	0.50	
tmisc020 My well-being is of primary importance in this clinical trial.	32	6.9%	112	24.1%	97	20.9%	167	36.0%	56	12.1%	3.22	1.15	-0.23	-0.93	0.50	
tmisc021 The treatment I would receive is based on my medical needs.	39	8.4%	149	32.1%	114	24.6%	147	31.7%	15	3.2%	2.89	1.05	-0.06	-0.99	0.53	
tmisc023 My physician would tell me which treatment I receive.	128	27.6%	221	47.6%	63	13.6%	41	8.8%	11	2.4%	2.11	0.98	0.94	0.54	0.37	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc025 My individual needs will determine the treatment I receive.	59	12.7%	186	40.1%	89	19.2%	114	24.6%	16	3.4%	2.66	1.09	0.27	-0.93	0.54	
tmisc026 My reason to participate is to improve my condition.	19	4.1%	55	11.9%	87	18.8%	240	51.7%	63	13.6%	3.59	1.00	-0.81	0.21	0.44	
tmisc028 I would enrol in this research study to help improve the health of others.	4	0.9%	14	3.0%	48	10.3%	286	61.6%	112	24.1%	4.05	0.74	-1.06	2.53	0.33	
tmisc029 I would enrol in this study to advance the researchers' knowledge of my illness.	4	0.9%	14	3.0%	31	6.7%	295	63.6%	120	25.9%	4.11	0.72	-1.22	3.37	0.33	
tmisc031 I would take part in this research to have someone to talk to about my condition.	24	5.2%	96	20.7%	109	23.5%	203	43.8%	32	6.9%	3.27	1.03	-0.45	-0.63	0.39	
tmisc034 My medication dosage would be adjusted if I do not respond to treatment.	36	7.8%	121	26.1%	159	34.3%	135	29.1%	13	2.8%	2.93	0.99	-0.17	-0.69	0.53	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc037 My doctor would discourage my participation in this clinical trial if there would be no direct benefit for me.	28	6.0%	169	36.4%	145	31.3%	105	22.6%	17	3.7%	2.81	0.97	0.22	-0.64	0.36	
tmisc038 Whether or not I will derive direct benefit from my participation will depend on the design of the study.	20	4.3%	95	20.5%	131	28.2%	197	42.5%	21	4.5%	3.22	0.97	-0.45	-0.56	0.35	
tmisc039 The experimental treatment is a proven therapy for my condition.	108	23.3%	192	41.4%	133	28.7%	27	5.8%	4	0.9%	2.20	0.89	0.40	-0.20	0.50	
tmisc040 The experimental treatment is the best therapy available to treat my condition.	27	5.8%	93	20.0%	244	52.6%	86	18.5%	14	3.0%	2.93	0.86	-0.13	0.27	0.49	
tmisc042 The treatment I would receive as a participant in this study will be no different than my previous treatment.	50	10.8%	247	53.2%	142	30.6%	21	4.5%	4	0.9%	2.31	0.76	0.51	0.69	0.33	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc043 Information obtained during the course of this study would become part of my treatment plan.	9	1.9%	53	11.4%	154	33.2%	221	47.6%	27	5.8%	3.44	0.84	-0.58	0.17	0.54	
tmisc044 My doctor would adjust the treatment I receive (e.g. medication dosage) to ensure that I receive the best possible care.	49	10.6%	131	28.2%	116	25.0%	136	29.3%	32	6.9%	2.94	1.13	-0.03	-0.93	0.50	
tmisc045 My doctor could access the information obtained during the course of this clinical trial.	56	12.1%	126	27.2%	107	23.1%	142	30.6%	33	7.1%	2.94	1.16	-0.07	-1.00	0.45	
tmisc047 I would not have been asked to participate if the experimental treatment did not work.	71	15.3%	222	47.8%	104	22.4%	60	12.9%	7	1.5%	2.38	0.94	0.55	-0.20	0.45	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc115 This clinical trial is conducted mostly to gather knowledge about my condition.	30	6.5%	131	28.2%	93	20.0%	171	36.9%	39	8.4%	3.13	1.11	-0.16	-1.00	0.43	
tmisc116 The goal of this clinical trial is to find the best treatment for my condition.	14	3.0%	79	17.0%	61	13.1%	249	53.7%	61	13.1%	3.57	1.02	-0.73	-0.23	0.44	
tmisc030 I would enrol in this study to contribute to science.	5	1.1%	14	3.0%	55	11.9%	284	61.2%	106	22.8%	4.02	0.75	-1.07	2.48	0.27	
tmisc024 I will know to which treatment group I've been assigned.	165	35.6%	207	44.6%	44	9.5%	37	8.0%	11	2.4%	1.97	0.99	1.14	0.94	0.27	
tmisc027 I would choose to take part in this study in order to receive free medical care.	48	10.3%	188	40.5%	112	24.1%	97	20.9%	19	4.1%	2.68	1.04	0.34	-0.69	0.26	
tmisc017 I've been asked to participate because there are no other treatment options available.	33	7.1%	170	36.6%	131	28.2%	109	23.5%	21	4.5%	2.82	1.02	0.23	-0.72	0.26	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc013 In this clinical trial the primary purpose is to improve treatment for future patients.	3	0.6%	7	1.5%	28	6.0%	290	62.5%	136	29.3%	4.18	0.66	-1.07	3.59	0.25	
tmisc015 In this clinical trial one of the purposes is to test the safety of the experimental treatment.	7	1.5%	36	7.8%	66	14.2%	285	61.4%	70	15.1%	3.81	0.84	-1.04	1.35	0.16	
tmisc016 In this clinical trial one of the goals is to test the toxicity of the experimental treatment.	17	3.7%	67	14.4%	147	31.7%	208	44.8%	25	5.4%	3.34	0.92	-0.59	-0.07	0.11	
tmisc118 The main purpose of this trial is to obtain knowledge about the usefulness of the experimental treatment.	1	0.2%	8	1.7%	22	4.7%	275	59.3%	158	34.1%	4.25	0.64	-0.88	2.38	0.11	
tmisc032 In this clinical trial every participant has an equal chance of receiving the experimental treatment.	8	1.7%	10	2.2%	21	4.5%	276	59.5%	149	32.1%	4.18	0.76	-1.57	4.58	0.10	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc126 Treatment is randomly allocated because it is the most exact and fair way to test which works best.	4	0.9%	16	3.4%	49	10.6%	269	58.0%	126	27.2%	4.07	0.77	-1.04	2.08	0.08	
tmisc120 The odds of receiving standard treatment are the same for all participant.	9	1.9%	58	12.5%	58	12.5%	250	53.9%	89	19.2%	3.76	0.97	-0.85	0.25	0.08	
tmisc014 The purpose of this clinical trial is to determine whether or not the new experimental treatment is effective.	0	0.0%	2	0.4%	12	2.6%	299	64.4%	151	32.5%	4.29	0.53	-0.05	0.46	0.07	
tmisc008 I will receive the same treatment as everyone else even if my own particular case is somewhat different.	19	4.1%	57	12.3%	64	13.8%	271	58.4%	53	11.4%	3.61	0.98	-0.99	0.48	0.07	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc117 There is a chance that the placebo is just as effective as the experimental treatment.	34	7.3%	88	19.0%	94	20.3%	219	47.2%	29	6.3%	3.26	1.07	-0.59	-0.59	0.05	
tmisc119 Assignment to treatment conditions is random to ensure equal number in each treatment condition.	0	0.0%	10	2.2%	66	14.2%	294	63.4%	94	20.3%	4.02	0.66	-0.48	0.78	0.05	
tmisc033 In this clinical trail every participant is just as likely to receive standard treatment (or be assigned to the placebo condition).	5	1.1%	25	5.4%	33	7.1%	279	60.1%	122	26.3%	4.05	0.80	-1.22	2.32	-0.02	
tmisc041 I'm equally likely to receive the experimental or the standard intervention (or placebo condition).	2	0.4%	5	1.1%	24	5.2%	286	61.6%	147	31.7%	4.23	0.63	-0.90	3.18	-0.04	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc036 I might be one of the participants who receives the inactive medication (i.e. assigned to the placebo condition).	1	0.2%	7	1.5%	16	3.4%	288	62.1%	152	32.8%	4.26	0.61	-0.84	2.86	-0.04	
tmisc046 I might not know the results of this study for months or even years.	2	0.4%	13	2.8%	30	6.5%	314	67.7%	105	22.6%	4.09	0.66	-1.06	3.32	-0.06	
tmisc009 This study has not been designed primarily to relieve patients and their illness.	26	5.6%	138	29.7%	102	22.0%	160	34.5%	38	8.2%	3.10	1.09	-0.08	-0.99	-0.10	
tmisc004 The assignment of patients to different treatment conditions does not take into account the fact that some patients' needs are different than others.	11	2.4%	101	21.8%	138	29.7%	180	38.8%	34	7.3%	3.27	0.96	-0.22	-0.68	-0.12	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmisc005 The physicians in this study do not know that they are giving everyone the best possible treatment.	15	3.2%	78	16.8%	135	29.1%	193	41.6%	43	9.3%	3.37	0.97	-0.40	-0.39	-0.15	
tmisc035 Some participants will receive an inactive substance (i.e. placebo).	2	0.4%	3	0.6%	15	3.2%	243	52.4%	201	43.3%	4.38	0.62	-1.07	3.36	-0.15	
tmisc022 My physician(s) does not know what therapy I would receive.	12	2.6%	49	10.6%	99	21.3%	225	48.5%	79	17.0%	3.67	0.96	-0.70	0.16	-0.21	
tmisc127 The goal of research could compromise my treatment needs in this clinical trial.	15	3.2%	144	31.0%	152	32.8%	132	28.4%	21	4.5%	3.00	0.95	0.09	-0.75	-0.21	

Items analyses of working items for the therapeutic misestimation subscale (In descending order by ITC)

Legends-SD=Strongly Disagree; D=Disagree; N=Neither Disagree or Agree; A=Agree; SA=Strongly Agree; SD=standard deviation; S=skewness; K=kurtosis; ITC=Item-total correlation; SMC= Squared multiple correlation.

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmise050 The treatment I would receive in this clinical trial would cure my illness.	55	11.9%	139	30.0%	249	53.7%	13	2.8%	8	1.7%	2.53	0.80	-0.11	0.54	0.40	0.45
tmise054 My participation in this clinical trial will prolong my life.	27	5.8%	106	22.8%	287	61.9%	36	7.8%	8	1.7%	2.77	0.74	-0.19	1.12	0.44	0.45
tmise055 My participation in this study will improve my quality of life.	14	3.0%	62	13.4%	286	61.6%	93	20.0%	9	1.9%	3.05	0.73	-0.24	1.07	0.35	0.44
tmise056 Being in this study would lead to improvements in my daily functioning.	9	1.9%	61	13.1%	279	60.1%	98	21.1%	17	3.7%	3.11	0.74	0.06	0.88	0.33	0.44
tmise057 Taking part in this research study would cure my illness.	63	13.6%	157	33.8%	227	48.9%	14	3.0%	3	0.6%	2.43	0.79	-0.23	-0.10	0.35	0.36

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmise058 My participation in this clinical trial would boost my immune system..	40	8.6%	115	24.8%	256	55.2%	45	9.7%	8	1.7%	2.71	0.82	-0.17	0.41	0.37	0.42
tmise062 I believe my doctor has underestimated the likelihood that I would benefit from participating in this study.	23	5.0%	173	37.3%	226	48.7%	38	8.2%	4	0.9%	2.63	0.74	0.12	0.27	0.31	0.34
tmise124 I'm more likely to benefit than the average person.	28	6.0%	149	32.1%	212	45.7%	71	15.3%	4	0.9%	2.73	0.82	-0.02	-0.23	0.30	0.24
tmise064 I believe my physician has overestimated the risks of participating in this study.	20	4.3%	185	39.9%	234	50.4%	23	5.0%	2	0.4%	2.57	0.68	0.01	0.28	0.30	0.31
tmise065 I believe my physician has underestimated the risk of participating in this study.	26	5.6%	182	39.2%	222	47.8%	31	6.7%	3	0.6%	2.58	0.73	0.07	0.24	0.25	0.45

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmise063 I believe my doctor has overestimated the likelihood that I would benefit from participating in this study.	25	5.4%	172	37.1%	227	48.9%	34	7.3%	6	1.3%	2.62	0.75	0.18	0.49	0.21	0.38
tmise066 My doctor downplays the likelihood that I would benefit from participating in this clinical trial.	13	2.8%	125	26.9%	265	57.1%	55	11.9%	6	1.3%	2.82	0.72	0.04	0.55	0.18	0.11
tmise053 My participation in this clinical trial will provide me with psychological benefits.	5	1.1%	38	8.2%	140	30.2%	243	52.4%	38	8.2%	3.58	0.80	-0.60	0.43	0.17	0.25
tmise122 My doctor has downplayed the risks of this study.	19	4.1%	179	38.6%	236	50.9%	28	6.0%	2	0.4%	2.60	0.68	0.02	0.24	0.13	0.31
tmise049 Participating in this clinical trial might only benefit others.	10	2.2%	61	13.1%	54	11.6%	275	59.3%	64	13.8%	3.69	0.94	-0.94	0.44	0.07	0.16

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmise121 My doctor has emphasized potential benefits of this study.	4	0.9%	34	7.3%	184	39.7%	218	47.0%	24	5.2%	3.48	0.74	-0.42	0.34	0.05	0.14
tmise059 There is no known risk to participants in this study.	51	11.0%	187	40.3%	135	29.1%	77	16.6%	14	3.0%	2.60	0.99	0.36	-0.44	0.03	0.18
tmise123 I feel like I am aware of all of the important risks in this trial.	13	2.8%	70	15.1%	100	21.6%	235	50.6%	46	9.9%	3.50	0.96	-0.65	-0.14	0.01	0.20
tmise051 My participation in this clinical trial may not provide me indirect benefits.	3	0.6%	48	10.3%	75	16.2%	288	62.1%	50	10.8%	3.72	0.82	-0.89	0.65	0.00	0.20
tmise061 The experimental treatment could have negative side effect.	5	1.1%	24	5.2%	69	14.9%	310	66.8%	56	12.1%	3.84	0.74	-1.14	2.33	0.00	0.31
tmise052 My participation in this clinical trial may not directly benefit me.	2	0.4%	23	5.0%	40	8.6%	320	69.0%	79	17.0%	3.97	0.70	-1.12	2.61	-0.02	0.33
tmise048 My participation in this clinical trial may not directly benefit me.	1	0.2%	32	6.9%	44	9.5%	314	67.7%	73	15.7%	3.92	0.74	-1.04	1.73	-0.03	0.35

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
tmise125 This clinical trial may not have any effect on my condition at all.	1	0.2%	10	2.2%	36	7.8%	317	68.3%	100	21.6%	4.09	0.63	-0.81	2.69	-0.06	0.31
tmise060 There is a chance that my condition could worsen during the course of this study.	2	0.4%	23	5.0%	59	12.7%	326	70.3%	54	11.6%	3.88	0.68	-1.11	2.44	-0.10	0.32

Items analyses of working items for the therapeutic optimism subscale (In descending order by ITC)

Legends-SD=Strongly Disagree; D=Disagree; N=Neither Disagree or Agree; A=Agree; SA=Strongly Agree; SD=standard deviation; S=skewness; K=kurtosis; ITC=Item-total correlation; SMC= Squared multiple correlation.

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to067 I am certain that my participation in this clinical trial would directly benefit me.	31	6.7%	109	23.5%	192	41.4%	116	25.0%	16	3.4%	2.95	0.94	-0.13	-0.36	0.51	
to068 I know that my participation in this trial would help relieve my symptoms.	42	9.1%	162	34.9%	213	45.9%	42	9.1%	5	1.1%	2.58	0.82	0.03	0.03	0.44	
to069 I know that I would be among those who receive the active medication/treatment.	109	23.5%	189	40.7%	124	26.7%	32	6.9%	10	2.2%	2.23	0.96	0.58	0.07	0.48	
to070 I am very optimistic that I would be one of those to benefit from participation in this study.	9	1.9%	52	11.2%	174	37.5%	196	42.2%	33	7.1%	3.41	0.85	-0.40	0.09	0.41	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to071 I am confident that I would be among those who benefit from participation.	17	3.7%	74	15.9%	209	45.0%	140	30.2%	24	5.2%	3.17	0.89	-0:21	-0.01	0.40	
to072 I am confident that I would receive the active medication.	63	13.6%	144	31.0%	210	45.3%	37	8.0%	10	2.2%	2.54	0.90	0.09	0.01	0.44	
to077 I feel confident that I would benefit from participating in this study .	7	1.5%	42	9.1%	155	33.4%	225	48.5%	35	7.5%	3.52	0.82	-0.54	0.33	0.42	
to081 I am very optimistic about my chances for successful treatment.	3	0.6%	45	9.7%	127	27.4%	252	54.3%	37	8.0%	3.59	0.80	-0.60	0.20	0.35	
to084 I am more prepared to participate in this clinical trial than other participants.	12	2.6%	93	20.0%	260	56.0%	82	17.7%	17	3.7%	3.00	0.79	0.13	0.52	0.31	
to091 There are many ways my participation in this study would help me.	1	0.2%	31	6.7%	145	31.3%	256	55.2%	31	6.7%	3.61	0.72	-0.49	0.22	0.37	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to092 I am energetically pursuing my goal by participating in this study.	5	1.1%	31	6.7%	120	25.9%	267	57.5%	41	8.8%	3.66	0.77	-0.77	0.92	0.36	
to093 I will meet the treatment goals that I set for myself as a result of participating in this study.	17	3.7%	72	15.5%	168	36.2%	180	38.8%	27	5.8%	3.28	0.92	-0.41	-0.17	0.42	
to094 My past medical experiences have prepared me well for participation in this study.	14	3.0%	70	15.1%	161	34.7%	181	39.0%	38	8.2%	3.34	0.93	-0.35	-0.23	0.31	
to097 I look forward to participating in this study with hope and enthusiasm.	0	0.0%	19	4.1%	81	17.5%	284	61.2%	80	17.2%	3.92	0.71	-0.57	0.62	0.33	
to102 I look forward to being in this study.	6	1.3%	14	3.0%	77	16.6%	279	60.1%	88	19.0%	3.92	0.77	-0.97	2.07	0.30	
to110 I believe that controlling my symptoms is possible.	1	0.2%	21	4.5%	96	20.7%	313	67.5%	33	7.1%	3.77	0.65	-0.90	1.51	0.32	
to087 I am optimistic about the outcome of my treatment.	1	0.2%	23	5.0%	134	28.9%	264	56.9%	42	9.1%	3.70	0.71	-0.46	0.39	0.29	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to107 Despite my illness I see a more positive future for me in the months ahead.	0	0.0%	22	4.7%	133	28.7%	277	59.7%	32	6.9%	3.69	0.67	-0.49	0.30	0.29	
to105 I will lose hope if my recovery does not soon occur.	45	9.7%	247	53.2%	118	25.4%	45	9.7%	9	1.9%	2.41	0.86	0.73	0.47	0.26	
to098 I have great faith in the physicians conducting this clinical trial.	5	1.1%	24	5.2%	174	37.5%	220	47.4%	41	8.8%	3.58	0.77	-0.38	0.52	0.25	
to076 I am less likely to obtain benefit from participating in this study compared to others.	40	8.6%	275	59.3%	131	28.2%	12	2.6%	6	1.3%	2.29	0.71	0.82	1.86	0.24	
to085 There is little or no hope that I would benefit from participating in this study.	48	10.3%	264	56.9%	122	26.3%	27	5.8%	3	0.6%	2.30	0.76	0.63	0.71	0.24	
to086 I can think of many ways to reach my treatment goals.	10	2.2%	103	22.2%	197	42.5%	144	31.0%	10	2.2%	3.09	0.84	-0.17	-0.47	0.23	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to104 I will remain hopeful even if there are setbacks in my treatment.	3	0.6%	18	3.9%	53	11.4%	328	70.7%	62	13.4%	3.92	0.68	-1.17	3.15	0.22	
to113 I would participate in this clinical trial because it is my last option.	26	5.6%	142	30.6%	118	25.4%	126	27.2%	52	11.2%	3.08	1.12	0.09	-0.94	0.22	
to074 I feel that I would benefit less than others from participation in this study.	42	9.1%	256	55.2%	149	32.1%	15	3.2%	2	0.4%	2.31	0.70	0.38	0.57	0.21	
to112 I feel overwhelmed and trapped because of my illness.	18	3.9%	129	27.8%	127	27.4%	160	34.5%	30	6.5%	3.12	1.01	-0.09	-0.86	0.20	
to101 My past experiences have prepared me well for participation in this study.	13	2.8%	75	16.2%	168	36.2%	176	37.9%	32	6.9%	3.30	0.92	-0.31	-0.27	0.19	
to103 I have plans and goals for my treatment.	5	1.1%	39	8.4%	163	35.1%	225	48.5%	32	6.9%	3.52	0.79	-0.48	0.30	0.18	
to109 I believe that recovery is always possible.	7	1.5%	32	6.9%	50	10.8%	255	55.0%	120	25.9%	3.97	0.88	-1.07	1.32	0.18	
to106 I will lose hope if my treatment is not successful.	58	12.5%	244	52.6%	109	23.5%	48	10.3%	5	1.1%	2.35	0.87	0.62	0.16	0.14	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to096 I should give up because there is no treatment that will benefit me.	176	37.9%	244	52.6%	34	7.3%	5	1.1%	5	1.1%	1.75	0.73	1.27	3.42	0.14	
to088 There are many ways around my illness.	21	4.5%	93	20.0%	200	43.1%	135	29.1%	15	3.2%	3.06	0.89	-0.24	-0.23	0.11	
to073 I don't expect the experimental treatment would help me but I remain hopeful that it will.	4	0.9%	59	12.7%	105	22.6%	255	55.0%	41	8.8%	3.58	0.85	-0.66	0.01	0.10	
to083 I doubt that the treatment would harm me.	14	3.0%	72	15.5%	195	42.0%	170	36.6%	13	2.8%	3.21	0.84	-0.43	-0.06	0.09	
to089 There is nothing that can be done about my condition.	72	15.5%	230	49.6%	138	29.7%	21	4.5%	3	0.6%	2.25	0.79	0.38	0.23	0.09	
to079 I doubt that the treatment would help relieve my symptoms.	19	4.1%	158	34.1%	252	54.3%	30	6.5%	5	1.1%	2.66	0.71	0.07	0.69	0.06	
to080 I doubt that the treatment would help cure my illness.	16	3.4%	147	31.7%	238	51.3%	55	11.9%	8	1.7%	2.77	0.77	0.19	0.34	0.05	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to075 I am unlikely to obtain any benefit from participating in this study.	27	5.8%	217	46.8%	177	38.1%	32	6.9%	11	2.4%	2.53	0.80	0.64	0.80	0.05	
to114 There is little that can be done for people with my condition.	53	11.4%	203	43.8%	153	33.0%	47	10.1%	8	1.7%	2.47	0.89	0.41	0.01	0.04	
to108 I have plans for the months ahead.	5	1.1%	30	6.5%	89	19.2%	280	60.3%	60	12.9%	3.78	0.79	-0.89	1.22	0.03	
to078 It is unlikely that my participation would help me or my condition.	22	4.7%	186	40.1%	205	44.2%	44	9.5%	7	1.5%	2.63	0.78	0.34	0.30	0.03	
to111 I see more negative than positive things to come with regard to my medical condition.	31	6.7%	208	44.8%	140	30.2%	74	15.9%	11	2.4%	2.63	0.91	0.47	-0.28	0.01	
to090 Participating in this clinical trial would not help me.	27	5.8%	208	44.8%	212	45.7%	16	3.4%	1	0.2%	2.47	0.67	-0.04	0.04	-0.01	
to100 I don't expect to receive the care I need.	42	9.1%	234	50.4%	132	28.4%	45	9.7%	11	2.4%	2.46	0.88	0.69	0.42	-0.02	

	SD		D		N		A		SA		Mean	SD	S	K	ITC	SMC
to095 I worry that my health might worsen despite being in this clinical trial.	13	2.8%	71	15.3%	122	26.3%	224	48.3%	34	7.3%	3.42	0.93	-0.59	-0.17	-0.02	
to099 I don't expect to receive the treatment I need.	19	4.1%	176	37.9%	217	46.8%	49	10.6%	3	0.6%	2.66	0.75	0.15	-0.01	-0.04	
to082 I doubt that the treatment would benefit me.	21	4.5%	197	42.5%	216	46.6%	27	5.8%	3	0.6%	2.56	0.70	0.19	0.35	-0.06	

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