# THE LONG JOURNEY: ANALYZING IMPORTANT FACTORS THAT IMPACT WILLINGNESS TO ENROLL AND TRACKING PATIENTS THROUGHOUT THE ENROLLMENT PROCESS

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## 1. Abstract

Clinical trials are often seen as the gold standard by which the medical community judges the effectiveness of new medications, treatment options, and preventative strategies. When surveyed, around 80% of the general population seems willing to participate in clinical trials if they are offered the opportunity; yet only around 3-5% of adults actually participate, with minority participation often even lower. This gap between initial willingness and actual enrollment has not been well studied, but the barriers to enrollment have been. The most common barriers to enrollment are: a lack of enrollment opportunities, a lack of knowledge about clinical trials, fear of side effects, and a distrust of medical research.

This project attempted to address three of the most common barriers of clinical trial enrollment (lack of knowledge, distrust of clinical trials, lack of enrollment opportunities) as well as better understand the gap between willing to enroll and actual enrollment. Interviews with participants were conducted to see if a video explaining clinical trials could improve knowledge and comfort, and registry patients were tracked throughout the enrollment workflow to see where drop off occurs as well as to see if offering enrollment opportunities to everyone would increase enrollment and decrease racial disparities in enrollment.

Overwhelmingly patients believed that resources like the video increased their knowledge, understanding, and comfort of clinical trials and should be shown to patients considering clinical trials. If a shorter version was developed, it should cover risks, benefits, the ability to withdraw at any time, and what a clinical trial is. Furthermore, the relationship between the caregiver and the patient is of utmost

importance. In tracking patients throughout the enrollment workflow, around 29% did not even engage when given the opportunity and 22% had very little engagement. Furthermore, large drop-offs were seen whenever patients had to enter personal information about themselves. Strong efforts should be made to capture patients attention at the onset in order to motivate individuals to complete the workflow and increase enrollment rates. Furthermore, while only 3% of participants ended up enrolling in our study, when the opportunity to enroll was offered to everyone, African Americans enrolled at the same rates as their White counterparts. Future studies should be sure to offer equitable enrollment in order to ensure adequate enrollment of minority groups that tend to be underrepresented in clinical trials.

## 2. Background and Significance

Clinical trials are one of the most important tools in the advancement of medical care. High–quality clinical trials are often considered the gold standard when assessing and evaluating new treatments or drugs and comparing them against traditional methodologies and practices in a healthcare setting (Avis, 2006)(Bartlett, 2005)(Boland, 2013)(DasMahaparta et al., 2017)(Ford et al., 2011)(McDonald et al., 2006)(Peterson, 2012)(Shaya et al., 2007). In addition, clinical trials are often the only way to test the safety and efficacy of emerging treatments and practices (Chalela et al., 2014)(Hamel et al., 2015)(Hutchison et al., 2015)(Jacobsen et al., 2012). Furthermore, clinical trials are vital in translating medical knowledge into actual benefits for patients (Anwuri et al., 2013)(Baquet et

al., 2008)(Baquet, Mishra, & Weinberg, 2009)(Ford et al., 2011)(Jacobsen et al., 2012)(Penberthy, 2012)(Tan, 2015). Not only do clinical trials benefit future generations, they also have the potential to benefit participants as well (Avis, 2006)(Chalela et al., 2014)(Dang et al., 2014)(DasMahapatra et al., 2017)(Frank et al., 2004)(Huges et al., 2015)(Miller et al., 2013)(Moorcraft et al., 2016)(Petersen, 2012)(Ulrich et al., 2012). Patients in clinical trials have access to new medications not available to the public, often have much more clinical care and oversight, and have access to care that patients otherwise might not receive or be able to afford (Hughes et al., 2015)(Miller et al., 2013)(Petersen, 2012)(Ulrich et al., 2012). The medical community has been quick to understand and embrace the value of clinical trials. In 2012 the number of clinical trials available on www.clinicaltrials.gov - the largest registry and results database on clinical trials in the United States- was 130,000 (Boland, 2013). As of April 24, 2018, there were 271,677 clinical trials registered on the site (www.clinicaltrias.gov). These trials run the gamut from rare diseases such as Abetalipoproteinemia -affecting only 1 out of 1,000,000 individuals in the general population (National Organization for Rare Disorders, 2015)- to cancer, the second leading cause of death in the United States (Centers for Disease Control and Prevention (CDC), 2015). As invaluable as clinical trials are to the medical and scientific community, if clinical trials do not enroll enough participants, they are little more than a waste of valuable resources.

## 2.a. Problem definition

### 2.a.i Low enrollment

Low enrolling clinical trials are far from outliers in the medical community. While every trial faces its own unique limitations and challenges, low enrollment rates in clinical trials are often seen across the board (Dwyer-White et al., 2011)(Ford, 2008)(Galea, 2007)(Harris, 2012)(Kopcke & Prokosch, 2014)(Mudano, 2013) (Penberthy, 2012)(Petersen, 2012) (Sanderson, 2013)(Stewart, 2007)(Strasser, Cola, & Rosenblum, 2013)(Stewart, 2012)(Tan, 2015) (Tang et al., 2017)(Tanner, 2014)(Tanner, 2016)(Treweek, 2010)(Treweek, 2011). Even though some areas of study have seen enrollment rates as high as 63% (Cooley et al., 2003) or 76% (Bedlack et al., 2010), it has been estimated that around 50% of all clinical trials do not reach their original enrollment numbers within their allotted timeframe (McDonald et al., 2006)(Treweek, 2011). Haidich and Ioannidis (2001) suggest that reaching even half of the original target enrollment can be a challenge; stating as much as one in six efficacy trials fail to recruit 50% of their target size. Others have found similarly distressing results. A study of one large medical networks' clinical enrollment rates found that 31% of clinical trials were low enrolling (defined as enrolling one or fewer participants) (Kitterman et al., 2011). Another analysis of enrollment rates in a large United States cancer center found that 77% of trials enrolled less than 5 total patients (Dilts et al., 2010). This same study found 30% of all group trials enrolled a grand total of zero participants after the recruitment period had ended (Dilts et al., 2010). Many studies that fail to reach their target enrollment are simply closed or are prevented from starting. Analyzing the 684 cardiovascular trials on clinicaltrials.gov that were terminated early in

2013, 53% of terminations were due to low recruitment (Bernardez-Pereira et al., 2014). Two separate studies also back up this literature, finding that around 30% of studies reviewed for causes of termination were due to low enrollment (Kitterman et al., 2011)(Dilts et al., 2010). When a survey was sent to the study chairs from five clinical trials cooperative groups, 44% responded that their studies experienced significant enrollment difficulties (Schroen et al., 2011). This is not a United States problem, but a global problem. A review of studies funded by the National Methodology Programme and the Medical Research Council in the United Kingdom by McDonald et al. (2006) reported 68% of studies did not reach their intended enrollment.

Extensions on the original timeframe for recruitment or delays in running clinical trials due to low enrollment are also commonplace (Bernardez-Pereira et al., 2014)(Du et al., 2008)(McDonald et al., 2006)(Tan, 2015)(Thadani, 2009). In analyzing data from the Tufts University Center for Information and Study on Clinical Research Participation, Strasser, Cola, and Rosenblum (2013) reported that 90% of clinical trials in the database were delayed due to low or slow enrollment. Extending the timeframe for a study to meet its original enrollment target, however, does not always guarantee success. In following studies that were granted recruitment extensions, McDonald et al. (2006) reported only small gains in enrollment after the extensions were granted.

These studies show that successfully recruiting and enrolling enough participants to clinical trials is a challenge. All in all, it has been reported that only 3 to 5 percent of all eligible adults in the United States enroll into clinical trials

(Anderson & Olson, 2016), with some estimates reporting less than 2% participation each year (Harris, 2012). While there has been a general decline in volunteerism in the United States (Galea, 2007), there is evidence that people are more likely to enroll into a clinical trial that directly impacts their lives or that involves a particular issue that is salient to them (Galea, 2007). One would think that those suffering from a debilitating disease would be more likely to enroll in a clinical trial, yet trials focused on cancer- one of the leading causes of death worldwide (Centers for Disease Control and Prevention, 2015) – see enrollment rates of only 2.5% to 5% (Ford, 2008)(Murthy, Krumholz, & Gross, 2004)(Penberthy, 2012) (Stewart, 2007)(Stiles et al., 2011)(Tanner, 2016). This number is even lower when discussing surgical trials or trials involving intensive procedures, which often see enrollment fractions of less than 1% (Abraham et al., 2006)(Anderson & Olson, 2016)(Du et al., 2008)(Murthy, Krumholz, & Gross, 2004)(Nasser et al., 2011)(Schroen et al., 2011)(Stiles et al., 2011). These low rates come even after the doubling of the National Cancer Institute's budget in the 1990's and 2000's (Shavers & Brown, 2002). While cancer trials are the most reported, they are not the only types of clinical trials that have low enrollment rates. Other prevalent diseases such as Amyothrophic Lateral Sclerosis (ALS) (Bedlack et al., 2010), Central Nervous System diseases (Gupta, 2017), Alzheimer's Disease (Department of Health and Human Services (DHHS, 2013)(Grill, 2017), and Cerebrovascular Diseases (CVD) (IOM, 2012)(Qureshi et al., 2012) also report low enrollment rates of eligible participants. Clinical trials focused on rare diseases often have difficulty recruiting

an adequate sample as well (Griggs et al., 2009). While clinical trial participation is low overall, minority enrollment into clinical trials is even lower.

### 2.a.ii Low minority enrollment

While low enrollment is a serious problem for clinical trials, a lack of diversity in clinical trial participation is just as important. Enrollment of minorities into clinical trials is significantly lower than the already small fraction of Caucasian enrollment (Anderson & Olson, 2016)(Baquet, Mishra, & Weinberg, 2009)(Branson, 2006)(Bruner et al., 2006)(Byrne et al., 2012)(Chalela et al., 2014)(DasMahaparta et al., 2017)(Foster, 2011)(Murthy, Krumholz, & Gross, 2004)(Petersen, 2013) (Stewart, 2007)(Tanner et al., 2014)(Wendler, 2005)(Williams, 2013). Even after the NIH (1993) mandated inclusion of minorities and other underrepresented groups in the Revitalization Act of 1993, clinical trials still struggle to enroll adequate numbers of ethnic minorities (Anwuri et al., 2013)(Chalela et al. 2014)(Hughes et al., 2015)(Petersen, 2012) (Tan, 2015). According to the NIH, total minority enrollment among all United States clinical studies was only 26% (Williams, 2013). African Americans make up only between 6 and 12% of total clinical trial participants (Tanner et al., 2014). In terms of cancer trials, African Americans made up only 8.2% of National Cancer Institute sponsored clinical trial participants, with Hispanics/Latinos and Asians/Pacific Islanders totaling 4.5% and 1.8% respectively (Anwuri et al., 2013). This trend has held steady, with Bruner et al. (2006) reporting 6% African American and 1% Latino/Asian participation in cancer trials in 2006. Cancer trials are not the only type of clinical trials that see low

minority enrollment however. Panic disorder clinical trials see minority enrollment of around 9% (Williams, 2013), whereas the Coronary Artery Surgery Study saw only 30 minority individuals offered enrollment out of a total of 780; an offering of less than 1% (Wendler, 2005). This is not just a US phenomenon; Bartlett et al. (2005) and Jenkins et al. (2010) report similar findings in the United Kingdom. There are some areas such as Post Traumatic Stress Disorder (Williams, 2013) and smoking cessation (Harris et al., 2003)(UyBico, Pavel, & Gross, 2007), however, where minorities have been offered equitable enrollment into clinical trials. This lack of representative participation in clinical trials and lack of clinical trial participation as a whole can have many negative consequences.

## 2.b Significance

Clinical trials are vital to the advancement of medical research and ensuring the safety and health of a given population. In order for these studies to be effective, they must recruit an adequate number of individuals. In addition, these studies must guarantee that they recruit a diverse pool of participants. The harms of having a small or homogeneous sample of patients in clinical trials are discussed below.

### 2.b.i Power

First and foremost, studies that do not recruit an adequate number of participants cannot answer the fundamental questions that researchers are attempting to address (Kitterman et al., 2011). Small sample sizes directly affect the power of a study (Everitt, 2006). The smaller the sample size, the lower the power

of the study when all else is held constant (Everitt, 2006). Power is extremely important for clinical trials, for without adequate power, one cannot determine the success of an intervention (Gul & Ali, 2010). This can lead to an intervention that is effective being cast aside and not embraced by the medical or public health community (Gul & Ali, 2010)(Harris, 2005)(Nasser et al., 2011)(Treweek, 2011). What could be a life saving procedure or a more cost effective approach could be discarded due to a lack of power.

### 2.b.ii Delays

Not only does a lack of participation have statistical consequences for a study, it also carries logistical and financial ramifications as well. Failures in recruiting an adequate number of participants can lead to delays and an increase in the amount of time a study is left open (Harris, 2005)(Kopcke & Prokosch, 2014)(Tan et al., 2015)(Tanner et al, 2014)(Treweek et al., 2010). One report found that 86% of clinical studies analyzed had delays of 1-6 months due to recruitment failures (Thadani, 2009). Other studies report enrollment delays in up to 90% of clinical trials (Strasser et al., 2013). These delays add to the time and resources that already go into the typical clinical trial from inception to execution (Dilts et al., 2010). Even with extended time for recruitment, it is estimated that around half of clinical trials fail to recruit enough participants to hit their original target sample size (Tan, 2015) (Treweek, 2011).

### 2.b.iii Cost

These terminations and delays deny possible effective treatment to patients and are a drain on institutional resources (Embi et al., 2008)(Gupta, 2015)(Harris, 2005)(Petersen, 2012)(Tanner et al., 2014)(Treweek et al., 2010). Clinical trials themselves are often expensive to maintain and run. Kitterman and colleagues (2011) estimated the average cost to initiate a clinical trial to be $4,800. In an analysis of clinical trials in one United States medical center, Kitterman et al. (2011) calculated the uncompensated cost of studies that enrolled one or zero participants to be $990,000 in the year 2009. There were no estimates for studies that enrolled more than one participant but were classified as under-enrolling, nor were estimates given for the increased financial burden of extending recruitment efforts past the initial enrollment deadline. Rather than benefiting patients with research on new drugs or more effective treatments, the resources that went to these low enrolling and terminated studies were squandered; adding nothing to society as a whole and occupying resources that could have gone to other studies.

### 2.b.iv Ethics

When viewed in this light, studies that under-enroll and are terminated due to low enrollment can also be viewed as unethical (Gul & Ali, 2010). As mentioned previously, studies that do not recruit an adequate number of participants will be underpowered. Since power has a direct impact on the ability of the study to assess the effectiveness of an intervention or drug, by not having enough power one cannot state whether an intervention or drug is successful or beneficial. This can prevent a drug or an intervention that actually is successful or beneficial from advancing into

approval or common practice (Schroen et al., 2011). This can lead to a delay in these drugs and interventions reaching the patients, if not forgotten altogether (Embi et al., 2008)(Ford et al., 2011)(Hamel et al., 2016)(Treweek et al., 2010). At best, underpowered studies can only advocate further exploration into the questions it sets out to solve, demanding more resources be poured into the topic of exploration. In addition, underpowered studies that continue to completion are unethical in that participant time and effort are potentially wasted since no scientific or clinical benefit can be gleaned from these studies (Nasser et al., 2011). This can be especially troubling if the studies put the patient at any sort of risk for complications or add any additional burdens to the participant (Nasser et al., 2011).

### 2.b.v Generalizability/Distributive Justice

While low enrollment is a serious problem for clinical trials, just as important is the lack of diversity in clinical trial participation. Low enrollment of minority participants poses a serious problem in terms of generalizability and distributive justice (Bartlett, 2005)(Hughes et al., 2015)(Petersen, 2012)(Shaya et al., 2007). Oftentimes, these minority groups tend to be the ones that could benefit the most from successful interventions or new therapies (Bartlett, 2005)(IOM, 2003)(Peek et al., 2007)(Robinson et al., 2016)(Shaya et al, 2007). These groups also most often bear the burden of diseases and negative health outcomes (Adams-Campbell et al., 2004)(Branson et al., 2007)(CDC, 2014)(Crowley, 2013)(Ford et al., 2012)(Meng et al., 2016)(Murthy, Krumholz, & Gross, 2004)(Peek et al., 2007)(Powell et al., 2008)(Robinson et al., 2016) (Shaya et al., 2007)(Tanner et al, 2014)(Wendler,

2005). Without adequate representation, these groups may be excluded from care or be given treatment or interventions that are not appropriate (Branson et al., 2007)(Meng et al., 2016)(Powell et al., 2008)(Robinson et al., 2016)(Shaya et al., 2007). Failure to include adequate representation in these groups will lead to further inequalities in healthcare outcomes (Baquet et al., 2006)(Stewart, 2007). Since these groups take on a disproportionate burden of disease and illness relative to their representation in the general population, it is essential that they be adequately represented in trials attempting to reduce these maladies (Dang et al., 2014). In the words of Bruner et al. (2006) "it is patently unfair to deprive those most in need of the benefits of research."

## 3. Literature review

To address the lack of participation in clinical trials, it is important to understand the reasoning behind why people choose to enroll or abstain from enrolling in a clinical trial. The literature reports many, many factors that influence an individual's enrollment into a clinical trial. These factors often fall into one of two spheres of influence: the provider/institution and the patient (Baquet et al., 2008)(Kim et al., 2015)(Manne et al., 2014)(Tanner et al., 2014). When discussing the patient sphere of influence, these factors can further be divided into barriers and benefits. Understanding and addressing these barriers and benefits is key to increasing clinical trial enrollment, especially in underserved populations (Cameron et al., 2013)(Catt et al., 2011)(Gul & Ali, 2010)(Ulrich et al., 2012).

## 3.a Providers

### 3.a.i Informing patients

Outside of internet searches, most people receive health information and enrollment opportunities into clinical trials from their healthcare provider (Comis et al., 2009)(Cohen et al., 2012)(Harris, 2012)(Ramirez, 2012). Physician opinion carries significant weight with patients; with patients relying on the advice and recommendations of their healthcare provider when making clinical trial enrollment decisions (Avis, 2006)(The Center for Information and Study on Clinical Research Participation (CISCRP), 2016)(Tanner, 2016)(Ulrich et al., 2016). Studies have shown patients are more likely to join a clinical trial if their healthcare provider recommends it (Baquet et al., 2006)(Cohen et al., 2012)(Peek et al., 2007)(Ramirez, 2012). It has been estimated that 77% of cancer patients who participate in a clinical trial learn about the trial from a healthcare provider (NIH, 2016a). Overall, evidence exists that the majority of clinical trial participants first learned about and enrolled into clinical trials through their health care professionals (Comis, 2009). In this way physicians are often the most effective means of recruiting patients for clinical trials run through a hospital setting (Cohen et al., 2012)(Rameriez, 2012) and, as such, act as gatekeepers for clinical trial information (Williams, 2004). If they do not pass on enrollment information to their patients, they serve as a barrier to clinical trial recruitment (Baquet, Mishra, & Weinberg, 2009)(Frank, 2004)(Kim et al., 2015)(Owens et al., 2013)(Williams, 2004). Overall, relatively few patients eligible for clinical trial enrollment report being informed of clinical trial opportunities by their physician (Baquet, Mishra, & Weinberg, 2009)(DasMahapatra et al., 2017)(Frank, 2004)(Kim et al., 2015)(Owens et al.,

2013)(Sanderson, 2013). A study by DasMahapatra et al. (2017) found that 61% of eligible patients with chronic conditions had not been informed of clinical trial opportunities by their physician. As dispensaries of information, providers can also contribute to the disparities of recruitment by offering clinical trial information to only certain patients (Branson et al., 2007)(Kim et al., 2015). There is some evidence that providers introduce their own biases when determining who to pass clinical trial information to (Baquet, et al., 2008)(Jenkins et al., 2010)(Kaas et al., 2005). If the provider believes that the potential patient lacks a stable social situation and home life or believes the patient will not follow through to completion, they will be reluctant to offer enrollment information to these individuals (Frank, 2004)(Joseph & Dohan, 2009)(Penberthy, 2012)(Powell et al., 2008). In addition, some studies have eligibility requirements that are subjective and are left up to the provider, which could lead to some patients being unfairly excluded (Petersen, 2012). This, of course, assumes that providers are comfortable discussing clinical trials with their patients in general (Avis, 2006)(Joseph & Dohan, 2009). Ramirez (2012) discovered that around half of physicians surveyed found it difficult to talk to their patients about clinical trials, with Embi and colleagues (2008) reporting only 27% of providers surveyed feeling very comfortable discussing clinical trials with patients.

### 3.a.ii Time burden

Even if physicians are comfortable discussing clinical trials with patients, they often rarely have the time. Adequate resources are not often dedicated to

clinical trial recruitment efforts (Harris, 2005). Clinical trial recruitment is frequently a challenging task in and of itself (Mudano, 2013)(Sanderson, 2013)(Tanner, 2016), but it becomes even more difficult to recruit participants atop the everyday demands of a clinic or hospital setting (Heinemann, 2011)(Madathil, 2013)(Mudano, 2013)(Rameriez, 2012)(Sanderson, 2013)(Thadani, 2009). In recruiting patients, the provider or medical staff must remember which clinical trials are active, remember the eligibility criteria for each trial, explain the trial to eligible participants, and answer any questions that the potential participant may have (Embi et al., 2005)(Jenkins et al., 2010). All of this must be done while also interacting with and attending to the medical needs of their patients. Since medical care of patients comes first, enrollment into clinical trials is not made a priority. This is especially true in busy clinics or where medical staff time is limited (Embi et al., 2005)(Heinemann, 2011) (Mudano, 2013)(Rameriez, 2012)(Sanderson, 2013)(Tanner, 2016). When surveying oncologists on factors that influence provider referrals to clinical trials, Ramirez et al. (2012) found that a one standard deviation increase in agreement that clinical trials were an extra burden was associated with a 65% decrease in the odds of referring patients to clinical trials. This time burden could explain why one study reported that physicians participating in a clinical trial alert system dismissed 90% of the alerts that informed them a patient was eligible to enroll in a study (Embi et al., 2008).

## 3.b Patients

### 3.b.i Willingness to participate

The general populace seems ready and willing to participate in a clinical trial. A study conducted in 2001 found that 75% of people surveyed said they would have been willing to enroll in a clinical trial if they were presented with enrollment opportunities (Harris, 2001). In a recent survey, 85% of North American respondents stated they were at least somewhat willing to participate in a clinical trial, with 60% responding they were very willing to participate in a clinical trial (CISCRP, 2016). After explaining clinical trials to participants, Cameron et al. (2013) found that 57% of patients agreed or strongly agreed that they would join a clinical trial if they had the opportunity. Even in the United Kingdom individuals seem to be willing to participate in medical research, with 70% responding they would be willing to participate in a study comparing different treatments (Jenkins et al., 2010). Even if participation is somewhat invasive or if the trial could have uncomfortable side effects, people still seem at least somewhat willing to participate (Catt et al., 2011)(Moorcraft et al., 2016). While the majority of the populace may be willing to enroll, this willingness matters not as long as individuals are unaware of clinical trial eligibility or how to enroll (Ford, 2008)(Hamel et al., 2016)(Petersen, 2012)(Wendler, 2005).

### 3.b.ii Barriers

#### *3.b.ii.1 Lack of awareness*

Lack of awareness of clinical trial enrollment opportunities among potential participants is perhaps the most significant barrier facing clinical trial enrollment

(Anderson & Olson, 2016)(Baquet et al., 2006)(Byrne et al., 2012)(DasMahapatra et al., 2017)(Du et al., 2008)(Ford, 2008)(Hamel et al., 2016)(Petersen, 2012)(Tanner, 2016). One poll of eligible cancer patients who did not enroll into a clinical trial found that 85% were unaware participation in a clinical trial was an option for them at diagnosis (Harris Interactive, 2001). A study by Weckstein and colleagues (2011) reported 40% of eligible patients who did not participate in a trial were unaware of enrollment opportunities or that they were, in fact, eligible to enroll. When surveying the general population of North America, the Center for Information and Study on Clinical Research Participation (CISCRP) (2016) found that 30% of respondents surveyed did not even know where clinical trials were conducted; saying nothing of those who did not know their eligibility status or how to enroll. There is some hope however; as fortunately it has been stated that lack of awareness is the easiest barrier to clinical trial enrollment to overcome (Ramirez, 2012).

#### *3.b.ii.2 Refusal*

Even when potential enrollees are aware of clinical trial opportunities, many still refuse to participate. Reported refusal rates for those offered clinical trial enrollment opportunities vary. Weckstein et al. (2011) report a refusal rate of 42%, whereas other studies report refusal rates of 49% (Corbie-Smith et al., 2002), 37% (Cooley et al., 2003) and 11% (DasMahapatra et al., 2017). Across clinical trial studies, the most commonly reported reasons for refusing enrollment into clinical trials or barriers to clinical trial enrollment were: lack of knowledge/understanding

of clinical trials; distrust of clinical trials/the medical community; financial costs of participation; increased time and travel; possible side effects/harms of participation; and the trial design itself.

#### 3.b.ii.2.a Lack of knowledge/Understanding

Along with a lack of awareness, many individuals have a lack of knowledge or a lack of understanding surrounding how clinical trials work. It does not help that consent forms for clinical trials have increased in both length and complexity (Gupta, 2015)(Madathil, 2013) and are often written at reading levels that are inappropriately high for the average citizen (Galea, 2007). Several studies cite a lack of information about clinical trials and medical research as a key factor in patient refusal for clinical trial participation (Cameron et al., 2013)(Ejiogu, 2011)(Ford et al., 2011)(Hughes et al., 2015)(Hutchison et al., 2007)(Williams, 2013). It seems the general populace struggles with the ideals of randomization, placebos, and clinical equipoise (Cameron et al., 2013)(Madsen et al., 2007)(Jenkins et al., 2010)(Moorcraft et al., 2016)(Penberthy et al., 2012). When participants were asked questions about randomization, less than half understood the necessity of it (Cameron et al., 2013). In this same study, less than half of patients understood that standard care would still be given if they were not randomized into the treatment group (Cameron et al., 2013). When Jenkins et al. (2010) asked respondents if they were willing to participate in a medical research study comparing different treatments, 70% of respondents answered they were willing to participate; when asked if they would be willing to participate in a study where treatment condition

was randomly assigned, this number fell to 50%. Another study found that patients were very uncomfortable with randomization and did not understand why they were randomly assigned to treatment conditions instead of being assigned to the condition they preferred (Madsen et al., 2007). Some patients interviewed in this study claimed that randomization was unethical, believing the treatment and control conditions were vastly different in terms of effectiveness (Madsen et al., 2007). Studies like these highlight the need to address the lack of knowledge and understanding of clinical trials that is prevalent in the general population.

Studies focusing on improving recruitment to clinical trials have suggested reducing the lack of understanding and increasing knowledge of clinical trials is an important way of improving clinical trial recruitment (Cameron et al., 2013)(Ford et al., 2012)(Hughes et al., 2015)(Tanner, 2016). Misunderstandings can spring up if patients do not have an adequate understanding or knowledge of clinical trials (Ejiogu, 2011). These misunderstandings can lead to negative views and misperceptions of clinical trials – especially surrounding the safety and ethical nature of clinical trials- leading to eligible individuals refusing enrollment into clinical trials (Ejiogu, 2011)(Ford et al., 2012)(Hughes et al., 2015)(Madsen et al., 2007). These misunderstandings can be passed down and spread throughout the community without a chance for correction, affecting not just the individual but potentially biasing whole communities against clinical trials (Hughes et al., 2015). While some studies still question the overall effect that knowledge and understanding has on actual enrollment (Caldwell et al., 2010)(Du et al., 2008)(Hutchison et al., 2007)(Kim et al., 2015)(Miller et al., 2013)(Stiles et al.,

2011), others have found that improved education focused on improving patient knowledge of the research goal and methods was related to higher willingness to participate in clinical trials (Banda et al., 2012)(Comis et al., 2009)(Dang et al., 2014)(Du et al., 2008)(Toms et al., 2016)(Owens et al., 2013). Even more studies encourage further participant education in the clinical trial process and hypothesize that increasing knowledge and understanding will improve enrollment rates (Bedlack et al., 2010)(Byrne et al., 2012)(Caldwell et al., 2010)(Jacobsen et al., 2012)(Manne et al., 2014)(Murthy, Krumholz, & Gross, 2004).

#### 3.b.ii.2.b Distrust of clinical trials/the medical community

Closely related to a lack of knowledge or understanding-and potentially stemming from it- distrust is a common barrier to clinical trial participation. This distrust could stem from past experiences, knowledge of past historical abuses, or knowing others who have had poor experiences in the past (Dang et al., 2014)(Ejiogu, 2011)(Ford et al., 2012)(Hughes et al., 2015)(Williams, 2013). Past abuses of participants by the medical community – especially African American participants - have eroded the public trust in research (Bruner et al., 2007)(Chalela et al., 2014)(Dang et al., 2014)(Davis et al., 2012)(Ejiogu, 2011)(Hutchison et al., 2007)(Hughes et al., 2015)(Tanner, 2016)(Williams, 2013). Studies such as the Tuskegee Syphilis Study and the Willowbrook Study have left the public skeptical and in fear of the medical community (Dang et al., 2014)(Ejiogu, 2011)(Hughes et al., 2015)(Tanner et al., 2014). Fear of becoming a “guinea pig” and discomfort with medical practices have been cited in several studies as reasons for not enrolling into

clinical trials (Chalela et al., 2014)(Ejiogu, 2011)(Hughes et al., 2015)(Tanner, 2016)(Williams, 2004)(Williams, 2013). One study, however, has posited that awareness or knowledge of the Tuskegee Study – the most cited abuse of research participants in American history- did not appear to be a major influencing factor on willingness to participate in medical research, even for African Americans (Davis et al., 2012).

Reducing misperceptions and increasing knowledge of clinical trials among the general population can reduce distrust of the medical community and of clinical trials. Often, misunderstandings and attitudes of the medical profession are passed from generation to generation and throughout the community (Hughes et al., 2015). By attempting to increase the public's knowledge and understanding of clinical trials and breaking the cycle of misperceptions in the community, one takes away a significant barrier that limits enrollment in clinical trials. One intervention saw reductions in anxiety towards the medical community when patients were given informational packets, although this did not necessarily correlate to increased enrollment (Hutchison et al., 2007). Other studies, however, have shown changing misperceptions and improving knowledge of clinical trials improves willingness to enroll in clinical trials (Banda et al., 2012)(Comis et al., 2009)(Dang et al., 2014)(Du et al., 2008)(Toms et al., 2016). Ford et al. (2012) found individuals attending a cancer education program had more favorable attitudes and knowledge after attending the program and also were more willing to enroll in a clinical trial if one was offered.

### 3.b.ii.2.c Cost

The cost of participation in a clinical trial was listed as a main barrier for many potential enrollees (Avis, 2006)(Ejiogu, 2011)(Hamel et al., 2016)(Harris, 2012)(Gul & Ali, 2010)(Mudano, 2013)(Penberthy, 2012)(Sanderson, 2013)(Tanner, 2016)(Ulrich, 2016)(Wendler, 2005)(Williams, 2004). Cost was described in two main forms: the cost in terms of time and travel and the actual financial cost required to participate.

Many studies have cited the time and travel commitment as a large barrier to participation in a clinical trial (Avis, 2006)(Cooley et al., 2003)(Ejiogu, 2011)(Gul & Ali, 2010)(Harris, 2012)(Joseph & Dohan, 2009)(Mudano, 2013)(Penberthy, 2012)(Sanderson, 2013)(Tanner, 2016)(Wendler, 2005). Often, clinical trials in the medical profession require significant commitments by their participants, either by asking participants to dedicate time changing a behavior or by requiring patients to attend check-ups or sessions at locations outside of the patients' homes. This can put a significant burden on patients' daily lives (Avis, 2006)(Cooley et al., 2003)(Mudano, 2013) (Sanderson, 2013)(Ulrich et al., 2012). When comparing clinical trial accepters and decliners in a breast cancer study, Avis et al. (2006) found that decliners were 2.64 times more likely to cite time and travel as factors relating to clinical trial participation. A study of female lung cancer patients revealed not having the time required to commit to the clinical trial was the third most cited reason for declining enrollment (Cooley et al., 2003). Among African American respondents in Baltimore, those that did not have the time required to participate in a clinical trial were .59 times as likely as those who had the time to participate to enroll into a clinical trial (Baquet et al., 2006). In more rural areas, the distance

required to attend a session or clinic vision to comply with a clinical trial can be quite expansive (Joseph & Dohan, 2009)(Mudano, 2013)(Tanner et al., 2014).

Along with time and travel commitments in clinical trial participation, financial concerns involved with participation are also a barrier to potential enrollees. Many studies report on participants or potential participants' concerns that additional financial hardships could be a side effect of clinical trial enrollment (Hamel et al., 2016)(Tan, 2015) (Tanner, 2016)(Ulrich et al., 2012)(Williams, 2004). In fact, some studies cite the extra financial or logistical burden involved with clinical trial participation as the most commonly mentioned reason for declining enrollment (Penberthy, 2012). In one study, of 346 refusals to participate in a clinical trial, 17.6% refusals were due to cost and logistics (Penberthy, 2012). Costs are a special concern for patients enrolling into cancer clinical trials, due to the fact that prescription drug and treatments for cancer can be exorbitantly expensive (Ulrich et al., 2012). Twenty-eight percent of cancer patients surveyed in New England cited added cost of clinical trial participation as reasons for declining participation, with 12% claiming it as the main factor in their decision (Weckstein et al., 2011).

#### 3.b.ii.2.d Perceived harm

Another significant barrier to clinical trial enrollment is the perceived harm that may result from clinical trial participation. The additional risks to health associated with some clinical trials -especially drug and cancer treatment trials- are a major contributor to enrollment decisions (Avis, 2006)(Chalela et al., 2014)

(Hughes et al., 2015) (Madsen et al., 2007) (Moorcraft et al., 2016)(Ulrich et al., 2012). Individuals are more likely to enroll into trials where perceived harms or risks to health are low (Hughes et al., 2015) (Nasser et al., 2011)(Schroen et al., 2011). In a survey of the general population, 18% of respondents believed that clinical trials were not very or not at all safe for people who participate (CISCRP, 2016). In a study of breast cancer patients either accepting or declining enrollment in a clinical trial, perception or fear of negative health outcomes was a significant factor between those who declined participation in a clinical trial and those who agreed to participate (Avis, 2006). Decliners rated potential negative health outcomes as much more important to their decision against participating in a clinical trial than did acceptors (Avis, 2006). A separate study found potential for negative health outcomes to be a major factor in trial decliners' participation decisions, even though these individuals believed the treatment they would receive in the trial was superior to the standard of care they already received (Madsen et al., 2007).

3.b.ii.2.e Trial type/Study design

The design of the trial and what is asked of participants is another key factor in clinical trial enrollment. Included in the design of the trial is the research question the trial is setting out to answer, the different treatment options, the amount of time and effort study participants will be asked to put in, the potential benefits and risks, and the degree to which the study is convenient for patients (Avis, 2006)(Gul & Ali, 2010)(Hughes et al., 2015)(Madsen et al., 2007)(Nasser et al., 2011)(Schoren et al., 2011). Invasive studies or those that require intense medical procedures such as

surgery usually see lower accrual than those that ask less of participants (Abraham et al., 2006)(Anderson & Olson, 2016)(Du et al., 2008)(Gul & Ali, 2010)(Madsen et al., 2007)(Murthy, Krumholz, & Gross, 2004)(Nasser et al., 2011)(Schroen et al., 2011)(Stiles et al., 2011). Many individuals are reluctant to undergo intensive medical procedures if they do not have to (Abraham et al., 2006)(Stewart, 2007). These invasive procedures often put a great burden on the participants and require extensive recovery time. One factor of trial design that is very important to patients is clinical equipoise, or the idea that at the beginning of the study, there is no condition that is inherently superior to another (Freedman, 1987). If potential enrollees deem the treatment condition of the study is superior or the treatment condition is inferior, they may not enroll for fear of being placed in that group (Madsen et al., 2007). Along with equipoise of trial conditions, discomfort with randomization/placebos is related to declining clinical trial enrollment (Abraham et al., 2006)(Cameron et al., 2013)(Penberthy et al., 2012)(Tan et al., 2015). Finally, studies that minimize the burden on patients and mimic everyday life as much as possible are found to be more successful than those that do not (Schroen et al., 2011).

### 3.b.iii Benefits

While there are many barriers and reasons why patients refuse to enroll into clinical trials, there are also enticing reasons and benefits for why individuals should enroll into clinical trials. The most common benefits that patients cite when choosing to

enroll in a clinical trial are the potential for extra/better care, altruism, and/or reduced cost of care; care they may not have otherwise been able to afford.

#### *3.b.iii.1 Extra/better care*

One of the most cited advantages and benefits of participating in clinical trials is access to cutting edge care; care they might otherwise not be able to attain. At worst, participants that are assigned to control arms of a medical study still receive standards of care in addition to a placebo (Catt et al., 2011)(Moorcraft et al., 2016)(Ulrich et al., 2012). Patients in the treatment aim of the study often receive the latest, most advanced forms of treatment or at least what they believe to be the best form of treatment (Byrne et al., 2014)(Chalela et al., 2014)(Hughes et al., 2015)(Madsen et al., 2007) (Ulrich et al., 2012). This is often the primary motivator for patient enrollment in clinical trials (Catt et al., 2011). One study of cancer patients found that 52% of participants were motivated by a belief that the trial contained the best treatment option available to them (Moorcraft et al., 2016). A secondary benefit of participation in a clinical trial is the monitoring of health status (Petersen, 2012)(Ulrich et al., 2012). Often, those who participate in a clinical trial receive more attention and monitoring of an illness or condition than if they did not participate. This holds true across many different areas of research such as smoking (Kralikova et al., 2009)(Oncken et al., 2008)(Yingst et al., 2018), diabetes (Hedderson, Darbinian & Ferrara, 2010)(Heisler et al., 2003)(Powers et al., 2009), and weight loss (Heymsfield et al., 1999)(Jimoh et al., 2018)(Patrick et al., 2009). This can have an impact not only on the patients' physical status, but can often

provide other benefits as well. One participant in a clinical study responded that the peace of mind they received from being closely monitored over years of the study was the reason they participated in a clinical trial (Ulrich et al., 2012).

#### *3.b.iii.2 Reduced cost/Compensation*

Along with receiving the most advanced and innovative care, participation in clinical trials can give patients care they otherwise might not receive due to their financial and socioeconomic situations. This stands in stark opposition to the barrier of increased financial burden for participants (Hamel et al., 2012)(Penberthy, 2012) (Tanner, 2016)(Ulrich, 2016). In a study by Ulrich and colleagues (2012), one of the main benefits of clinical trial participation was having access to medications and treatments that would have been out of reach for patients due to their cost. This is especially true with diseases such as cancer, where the costs for treatment can be exorbitantly high and often not fully covered by insurance (Avis, 2006)(Ulrich et al., 2012). Along with reducing cost of treatment, additional financial incentives for their time and participation can be a benefit to participants (Dang et al., 2014)(Hughes et al., 2015).

#### *3.b.iii.3 Altruism*

Along with the aforementioned benefits, altruism or a desire to help others has consistently been mentioned as a reason for participating in a clinical trial (Avis, 2006)(Dang et al., 2014)(Hughes et al., 2015)(Madsen et al., 2007) (Petersen, 2012)(Ulrich et al., 2012). In one survey, 25% of patients responded their

participation in a clinical trial was due to altruistic reasons (Moorcraft et al., 2016). Indeed, helping others is often the second most mentioned factor behind being involved in the latest or best treatment regimen (Avis, 2006)(Moorcraft et al., 2016). Another study found that altruism was rated significantly higher in clinical trial accepters than clinical trial deniers (Avis, 2006), although this could be the individual rationalizing their decision to participate after enrolling into a study (Madsen et al., 2007). There have been studies on phase I clinical trials, however, that call into question the effect altruism has on participating in clinical trials, or at least early stage cancer trials (Catt et al., 2011).

### 3.c Race

Interestingly enough, belonging to a racial minority has a significant impact on enrolling into a clinical trial. As mentioned previously, unless specifically targeted for a study, there is evidence that racial minorities enroll at a smaller proportion than their white counterparts (Anwuri et al., 2013)(Bruner et al., 2006) (Bartlett et al., 2005)(Jenkins et al., 2010)(Tanner et al., 2014)(Williams, 2013). Many of the barriers faced by potential enrollees are amplified if they are from a minority group (Ejiogu, 2011)(Tanner et al., 2016). There is evidence showing that minorities have less economic resources than their white counterparts on average, which make the barriers for minority participants even harder or impossible to overcome (Ejiogu, 2011)(Sanderson, 2013)(Tanner, 2016)(Ulrich et al., 2012)(Wendler, 2005). In addition to having less financial and temporal resources, there is some evidence that minorities are not offered enrollment opportunities at

the same rate as whites (Adams-Campbell et al., 2004)(Andersen & Olson, 2016)(Baquet et al., 2006)(Baquet et al., 2008)(Branson et al., 2007) (Langford et al., 2010)(Penberthy et al., 2012). Penberthy et al. (2012) found that African American patients were more likely to be deemed ineligible than white patients for clinical trials and were more often given the ineligible tag due to "mental status" and "expected non-compliance;" both subjective terms open to interpretation. In addition to not being offered enrollment into clinical trials at the same rate as whites, African Americans also refuse trial enrollment for which they are eligible at a higher rate than whites (Avis, 2006)(Ford, 2008)(Penberthy et al., 2012).

While the main factors for clinical trial participation refusal seem to be the same across both groups, some differences exist between African Americans and their Caucasian counterparts. White patients cited extra financial or logistical burdens, a preference for specific treatments, and discomfort with randomization more often as reasons for refusal than African American patients. African American patients cited a lack of interest in the clinical trial, family pressures and cultural factors more often as reasons for refusal than their white counterparts (Penberthy, 2012). In addition, African Americans reported refusing participation due to being overwhelmed with the decision making process (Penberthy, 2012). African Americans also tend to hold negative views of the medical community and clinical trials (Bartlett, 2005)(Bruner et al., 2006)(Dang et al., 2014)(Ejiogu, 2011)(Hughes et al., 2015)(Tanner, 2016)(Williams, 2004)(Williams, 2013) and are wary of the medical research community (Chalela et al., 2014)(Dang et al., 2014)(Ford et al., 2011)(Hughes et al., 2015)(Tanner et al., 2014)(Williams, 2004)(Williams, 2013).

This distrust of the medical community is not entirely misplaced; for past abuses by the research community such as the Tuskeegee Syphilis Study have predominantly used this group as test subjects. (Chalela et al., 2014)(Dang et al., 2014)(Ejiogu, 2011) (Ford et al., 2012)(Hughes et al., 2015). This mistrust seems to be passed down from generation to generation and has developed into collective beliefs among the community (Hughes et al., 2015). This may also lead to the low health literacy and lack of knowledge of clinical trials that are found in this population (Ejiogu, 2011)(Ford et al., 2011) (Ford et al., 2012)(Hughes et al., 2015)(Petersen, 2012)(Tanner, 2016).

# 4. Overall Study

## 4.a Goal

The overarching goal of this study is to better understand the clinical trial recruitment process and how informing and offering enrollment to all eligible individuals could improve clinical trial participation.

## 4.b Research Questions

### 4.b.i Research Question 1

*When developing a short 5-minute video to give to patients at the point of care, what are the important topics and information that should be covered in order to improve patient understanding, knowledge, and comfort of clinical trials?*

### 4.b.ii Research Question 2

*At which stages in the enrollment process do patients who are initially willing to participate in a clinical trial drop out?*

### 4.b.ii Research Question 3

*Are there racial disparities in clinical trial enrollment when the opportunity to enroll is offered to all eligible individuals?*

## 4.c Design

The overall design of the project is cross sectional multi-method design that includes quasi-experimental quantitative and qualitative studies involving patients in participating Research Action for Health Network (REACHnet) clinics. Launched in 2015, REACHnet's goal was to build infrastructure for clinical and patient engagement data to supplement collected clinical information from participating health systems in Louisiana, the Gulf Coast, and Texas (Couk, 2016). An electronic application was developed that could be given to patients at the point of care in order to collect patient reported outcomes and enroll them into the Health in Our Hands (HiOH) research registry and/or individual clinical trials such as WeighSmart (Couk, 2016).

## 4.d Theoretical Model

This study is grounded in four theoretical frameworks: the Health Belief Model (Rosenstock et al., 1988), the Theory of Planned Behavior (Ajzen, 1985), the Knowledge, Attitudes, and Behavior model (Manne et al., 2014), and the Precaution Adoption Process Model (Rimer & Glanz, 2005).

### 4.d.i Health Belief Model

The Health Belief Model (HBM) states that behavior change is predicated on six main factors: perceived susceptibility, perceived severity, perceived benefits, perceived barriers, cues to action, and self-efficacy (Rimer & Glanz, 2005). This study focuses on three of these factors: perceived barriers, perceived benefits, and cues to action.

The literature is rife with studies identifying barriers to clinical trial participation. Foremost among them are: a lack of awareness of enrollment opportunities, a lack of knowledge about clinical trials, and the distrust of clinical trials/the medical community. The first Research Question (#1) addresses both the lack of knowledge surrounding clinical trials as well as the distrust of clinical trials. By engaging in qualitative research with patients, this study attempts to influence future developments of educational materials that can be presented to patients during routine care. It is the hope of the researchers that these interviews will identify important topics and themes that need to be included in educational videos that increase patient knowledge, trust, and understanding of clinical trials. While Research Questions #2 and #3 also address the lack of knowledge and distrust of clinical trials by presenting eligible participants with a short explainer of clinical

trials during routine care, the main focus of these research questions is to address and eliminate the lack of awareness of enrollment opportunities. In this study, when a patient initially eligible for a clinical trial (in this case WeighSmart) presented to a participating clinic, they were informed of the clinical trial and were offered a chance at enrollment into the clinical trial at the point of care. This offer not only serves to remove a barrier to clinical trial enrollment, it also serves as a cue to action for the patient.

### 4.d.ii Theory of Planned Behavior

This study also utilizes the Theory of Planned Behavior (TPB) in building its theoretical groundwork. As stated by Rimer and Glanz (2005), the TPB explores the relationship between beliefs, attitudes, and intention. According to this theory, an individuals' likelihood to perform a behavior is based off of their attitude toward the behavior, the perception of societies' approval/disproval of the behavior, and the amount of control they have in performing this behavior (Rimer and Glanz, 2005). The individuals' attitude toward the behavior is influenced by the individuals own behavioral beliefs and personal evaluation of outcomes if they undertook the hypothesized behavior, whereas the perception of societies' approval/disproval is influenced by the perceived approval/disproval of important members of the individuals' life as well as their own personal motivation to comply (Rimer and Glanz, 2005). For this study, the hypothesized behavior in question is enrolling into a clinical trial. This study attempts to affect behavior change by affecting individuals' behavioral beliefs, evaluations of behavioral outcomes, motivations to comply, and

control beliefs. Research Question 1 focuses on uncovering the important themes and topics that would affect these components of behavior change. Conducting interviews with patients from the population of interest will inform us of the most important information and topics that future educational material will need to address to answer patients questions about clinical trials and make them more comfortable with the idea of clinical trial participation. Future educational materials informed by these focus groups will influence patients' attitudes towards clinical trials, which will in turn affect their intention to enroll. By affecting both attitudes and intention, we should see a corresponding increase of clinical trial enrollment. Research Questions 2 & 3 attempt to understand how changing patients' control beliefs and perceived behavioral control could have on clinical trial enrollment. By giving individuals the opportunity to enroll into clinical trials at the point of care, these studies give the individual complete control over the behavior in question. This combined with a short educational video targeted towards influencing an individuals' behavior should show increased enrollment into a clinical trial. Increases in clinical trial enrollment may be even more pronounced in minority groups due to the fact that individuals from these groups have historically believed they have little power in medical care (Dang et al., 2014)(Hughes et al., 2015)(Williams, Beckmann-Mendez, & Turkheimer, 2013).

#### 4.d.iii Knowledge, Attitudes, and Behavior Model

A similar progression is also linked to the Knowledge, Attitude, and Behavior model (KAB) (Manne et al., 2014), which hypothesizes a change in knowledge will

affect attitude, which will eventually be reflected in a behavior change. While all three research questions in this project focus on this progression, this is most evident in Research Question 1. The researchers interviewed patients from the population of interest in order to determine how best to affect knowledge through the use of educational materials at the point of care. By better understanding what type of information the patients need to have and how best to pass on this on, Research Question 1 attempts to inform future development of educational materials in order to positively influence patient attitudes towards clinical trials. Following the causal link of the KAB model, this positive attitudinal change will influence behavior, in this case more clinical trial enrollment.

#### 4.d.iv Precaution Adoption Process Model

The final theoretical model utilized in this project is the Precaution Adoption Process Model (PAPM). Similar to the Stages of Change Model, the PAPM tracks an individual as they move from being unaware of an issue all the way to adopting and maintaining a behavior change (Rimer & Glanz, 2005). This model consists of seven distinct stages that the individual moves through during this journey: being unaware of an issue; being unengaged by an issue; deciding about acting; deciding to act or deciding not to act; acting on an issue; and finally, maintaining their action in addressing an issue (Rimer & Glanz, 2005). The two quantitative Research Questions draw upon this model and focus on different stages of the model. Research Question 2 focuses on the stage where an individual is deciding about acting whereas Research Question 3 focuses on the decision to act or not to act.

Regardless of the method of recruitment, the researcher contacted interested individuals to set up a date and location for the interview at where the individual felt most comfortable and available. Patients were compensated with a $20 gift card for their participation.

## 5. Study 1.

### 5.a Research Question 1:

*When developing a short 5-minute video to give to patients at the point of care, what are the important topics and information that should be covered in order to improve patient understanding, knowledge, and comfort of clinical trials?*

There is a well-documented lack of knowledge and understanding of clinical trials in the general populace. This lack of understanding and knowledge frequently results in misperceptions of clinical trials which can often lead to distrust. Great resources, such as the American Cancer Society's "About Clinical Trials" (2011) video series have been developed to address and dispel this lack of knowledge and understanding. While this resource does a thorough job of covering the intricacies of clinical trials, it is perhaps too thorough; clocking in a run time of over half an hour. A distilled down version of this video series with a runtime of 5 minutes or less could be developed and given to patients during a routine healthcare visit without

interrupting a clinicians' workflow. This could lead to increased discussions on clinical trials between patient and provider and could improve enrollment rates. This research question attempts to uncover the most important concepts and themes of the "About Clinical Trials" video series and highlight what could be cut and what should be included in a 5 minute or less presentation that could be shown during routine patient care.

### 5.b. Recruitment.

All patients presenting to participating clinics over 18 years of age who were able to provide informed consent and had no English language/literacy barriers were also offered enrollment into the HiOH research registry. The goal of the registry was to recruit 10,000 individuals, and as of December 2016, there were 5800 members enrolled into the registry. The workflow for HiOH enrollment mirrored that of WeighSmart. When patients visited a participating clinic, the patient went to their examination room and the nurse or clinical staff pulled up the patients' health record. If the patient was eligible for HiOH enrollment, the nurse/clinical staff member returned with a tablet to the patients' room and gave a brief introduction (less than 30 seconds) to HiOH and asked the patient to watch a short video and answer a few questions (Couk, 2016). Patients then filled in their date of birth on the tablet. If the incorrect date of birth was entered more than twice, a final error message was displayed and the workflow was terminated (Couk, 2016). Once patients entered their correct date of birth, a video giving a brief overview of

the HiOH registry began (Couk, 2016). After the video concluded, an informed consent e-form for enrollment into HiOH was displayed on the tablet authorizing contact with the patient through email or text for the purposes of collecting patient reported outcomes and perspectives of research activities, delivering research findings or health information relevant to the patient, and offering enrollment into eligible clinical trials (Appendix D) (Couk, 2016). If patients chose to consent into the registry, they were asked to provide a first name, a last name, and a preferred method of contact (email, text, or phone number). A message containing a link to the HiOH portal where patients could activate their account was then sent to the email address or phone number that was provided by the consenting patients (Couk, 2016). This link also contained the informed consent e-form for patients to reference at any time.

If patients declined enrollment into HiOH, they were not offered another enrollment invitation for 12 months (Couk, 2016). Patients that did not consent to enroll but did not decline enrollment were given the same workflow during their next visit. Regardless of enrollment into HiOH, all patients were then prompted to answer 5 questions about their health on the tablet. The whole process from the initial introduction by the nurse/staff member to completion of the health questionnaire took approximately 5 minutes. Risk of harm to the patient was minimal.

In-depth interviews with HiOH registry patients were conducted in the Spring of 2018 through the Winter of 2019. All but two of the interviews were conducted in person. The two interviews that were not conducted in person were

conducted over Skype video calls due to logistical difficulties in getting to the interviews in person. To recruit patients for these interviews, an email was sent out to all HiOH members soliciting their participation (recruitment for HiOH has been described previously). This email briefly explained the purpose of the study, the design of the study, and included the researchers' contact information for interested enrollees (Appendix E). Inclusion criteria for this study was the ability to be reached by email or telephone and having an hour of free time to dedicate to the interview. Interested individuals were asked to either call or send an email to the researcher indicating their willingness to participate.

After 10 months of recruitment through the HiOH registry, enrollment numbers were still low. In addition, the researchers noticed that there were few African Americans signing up for the study. To assure that African American voices were heard, the researchers set out to recruit African American participants by partnering with a local African American congregation. The researcher obtained a letter of agreement with the congregation as was allowed to talk about the project at a local congregational meeting. From this, the researcher was able to garner more African American participation.

### 5.b. Methods

Qualitative interviews were conducted with consenting participants. At the beginning of the interview, patients were asked to fill out a modified version of the Public Awareness of Research for Therapeutic Advancements Through Knowledge and Empowerment (PARTAKE) Survey (Burt et al., 2013) with additional questions derived from other previously validated surveys (Joffe et al., 2001; O'Connor 1993;

Sabesan et al., 2011). This baseline questionnaire can be found in Appendix F. The purpose of this survey was to collect information on participants baseline level of knowledge and understanding of clinical trials. After completing this survey, participants were then shown the "About Clinical Trials" video series (ACA, 2011) produced by the American Cancer Society. This video series is comprised of six video segments focused on different aspects of clinical trials that are around 5 minutes in length. After each video segment, participants were asked to give their feedback on that segment. This feedback was open-ended, however participants were encouraged to give their opinion about the segment and what they felt was the important information within the segment. Furthermore, participants were asked to keep in mind that the researchers were focused on a general video about clinical trials, not one focused specifically on cancer unlike this video series. After watching all six video segments, the participant was again given the knowledge and understanding questionnaire from before to determine if the video series had any effect on these areas. These responses were compared to the participants' baseline responses and an improvement score was developed (-1 if the participant answered a question correctly or more positively in the baseline and wrong/less positively after watching the video, 0 if there was no change in baseline and after video answer, and 1 if the participant answered wrong or less positively in the baseline and correctly or more positively after watching the video). In addition to the aforementioned knowledge, understanding, and comfort questions, this survey contained additional questions modified from previously validated studies (Hoffner et al., 2012; Hutchison & Campbell, 2002) which focused solely on satisfaction with

the video series as a whole (Appendix H). After completing this survey, participants were asked a few additional questions about the video series (Appendix I) and a free-listing exercise was conducted with participants. In this free listing exercise, participations were asked to write down on note cards any topics, themes, or ideas that should be included in a video to promote clinical trial knowledge, understanding, and comfort. Participants were told that this video had no length restrictions and could be as long as they wanted it to be. After completing this free-listing exercise, participants were asked to rank their responses from the free-listing exercise. After ranking their responses, participants were asked to imagine that the researchers were going to develop a five minute video to promote clinical trial knowledge, understanding, and comfort. Participants were then asked to take their responses from the free-listing and ranking exercises and divide them into three categories: A) absolutely essential topics, themes, or ideas that should be conveyed to those watching the video, B) topics, themes, or ideas that are important, and should be included if there is time after those in category A are covered; and C) topics, themes, or ideas that could be cut or covered in a different video/format. After completing this pile sort exercise, participants were thanked for their time and the interview was concluded. All interviews were audibly recorded and patient data was de-identified in order to ensure patient anonymity and confidentiality. The interviews were transcribed by the researcher and loaded and coded in ATLAS (Scientific Software Development GmbH, Berlin, Germany).

## 5.c. Measurement instruments

### *5.c.i Qualitative interviews*

In order to better determine what information is important to individuals who might be considering clinical trial enrollment, semi-structured in-depth interviews were conducted with willing participants. During these interviews, patients were asked to fill out a short survey developed from previously published studies (Burt et al., 2013; Hoffner et al., 2012; Hutchison & Campbell, 2002; Joffe et al., 2001; O'Connor, 1993; Phelan et al., 2001) This survey collected demographic information on the participants as well as assessed a baseline level of their knowledge and understanding of clinical trials (Appendix F). After watching the American Cancer Society's (ACA)(2011)"About Clinical Trials" video series, participants were given the same knowledge and understanding survey as before to assess if the video had any impact on these measures (Appendix G). Participants were also given a survey assessing their satisfaction with the video series as a whole (Appendix H).

## 5.d. Results

*Demographics*.

Twenty-four interviews were conducted between the Spring of 2018 and Spring of 2019. Full results of the demographic characteristics of the participants in our study can be found in Table 1.

Table 1. Demographic characteristics of participants.

| Demographic characteristics of participants | |
|---|---|
| **Race** (N=24) | |
| African American | 6(24.00%) |
| Asian | 1(4.00%) |
| Hispanic | 3(12.00%) |
| Native American | 2(8.00%) |
| White | 15(60.00%) |
| **Gender** (n=24) | |

| | |
|---|---|
| Female | 19(76.00%) |
| Male | 6(24.00%) |
| **Age** (N=23) | |
| 18-29 | 4(16.67%) |
| 30-39 | 4(16.67%) |
| 40-49 | 3(12.50%) |
| 50-59 | 2(8.33%) |
| 60-69 | 5(20.83%) |
| 70+ | 6(25.00%) |
| **Education** (N=22) | |
| Less than high school | 1(4.35%) |
| High school degree | 4(17.39%) |
| Some college | 2(8.70%) |
| College degree | 2(8.70%) |
| Trade school/Associates degree | 5(21.74%) |
| Masters degree or equivalent | 5(21.74%) |
| PhD/MD | 4(18.18%) |
| **Had heard of clinical trials** (N=24) | |
| No | 4(16.00%) |
| Yes | 21(84.00%) |
| Not sure | 0(0%) |
| **Had participated in clinical trials** (N=24) | |
| No | 16(64.00%) |
| Yes | 8(32.00%) |
| Not sure | 1(4.00%) |

The majority of those interviewed identified as white (60.0%), followed by African American (24.0%), Hispanic (12.0%), Native American (8.0%) and Asian (4.0%). The participants skewed older, with 46% of our population being 60 years of age or older. Furthermore, our population tended to skew more educated, with 61% of participants having a college degree or higher. Two individuals declined to provide educational information and one individual declined to provide information on their age. The majority (84.0%) had heard about clinical trials, yet only a third had ever participated in a clinical trial (one individual was unsure if they had participated).

*Knowledge and understanding questionnaire.*

Before and after scores on each of the knowledge, understanding and comfort questions were compared to see if the video had any impact on these areas. The results for each question are provided in Table 2.

Table 2. Improvement in knowledge and understanding.

| **Knowledge** (N=25) | |
|---|---|
| *One reason clinical trials are run is to improve the treatment of future patients.* | |
| Regressed | 0(0%) |
| Stayed the same | 23(92.00%) |
| Improved | 2(8.00%) |
| *One of the major purposes of a clinical trial is to compare the effects (good and bad) of two or more different ways of treating patients in order to see which is better.* | |
| Regressed | 1(4.00%) |
| Stayed the same | 21(84.00%) |
| Improved | 3(12.00%) |
| *One of the major purposes of clinical trials is to test the safety of a new drug or treatment.* | |
| Regressed | 3(12.00%) |
| Stayed the same | 21(84.00%) |
| Improved | 1(4.00%) |
| *If I participate in a clinical trial, it is possible that the study sponsor, various government agencies, or others who are not directly involved in my care can review my medical records.* | |
| Regressed | 5(20.00%) |
| Stayed the same | 16(64.00%) |
| Improved | 4(16.00%) |
| *There may not be direct medical benefit to me from my participation in a clinical trial.* | |
| Regressed | 0(0%) |
| Stayed the same | 20(80.00%) |
| Improved | 5(20.00%) |
| *After I agree to participate in a clinical trial, my treatment may be chosen randomly (by chance) from two or more possibilities.* | |
| Regressed | 4(16.00%) |
| Stayed the same | 17(68.00%) |
| Improved | 4(16.00%) |
| *If I had not wanted to participate in a clinical trial, I could have declined to sign the consent form.* | |
| Regressed | 0(0%) |
| Stayed the same | 25(100%) |
| Improved | 0(0%) |
| *I have to remain in the clinical trial even if I decide* | |

| | |
|---|---|
| *someday that I want to withdraw.* | |
| Regressed | 0(0%) |
| Stayed the same | 22(88.00%) |
| Improved | 3(12.00%) |
| **Understanding** (N=25) | |
| *Clinical trials involve research* | |
| Regressed | 0(0%) |
| Stayed the same | 21(84.00%) |
| Improved | 4(16.00%) |
| *What the researchers are trying to find out in a clinical trial* | |
| Regressed | 1(4.00%) |
| Stayed the same | 12(48.00%) |
| Improved | 12(48.00%) |
| *The treatments and procedures you could undergo* | |
| Regressed | 1(4.00%) |
| Stayed the same | 12(48.00%) |
| Improved | 12(48.00%) |
| *The possible risks and discomforts of participating in a clinical trial* | |
| Regressed | 1(4.00%) |
| Stayed the same | 14(56.00%) |
| Improved | 10(40.00%) |
| *The possible benefits to you of participating in a clinical trial* | |
| Regressed | 2(8.00%) |
| Stayed the same | 16(64.00%) |
| Improved | 7(28.00%) |
| *The alternatives to participation in a clinical trial* | |
| Regressed | 3(12.00%) |
| Stayed the same | 11(44.00%) |
| Improved | 11(44.00%) |
| *The effect of the clinical trial on the confidentiality of your medical records* | |
| Regressed | 3(12.00%) |
| Stayed the same | 12(48.00%) |
| Improved | 10(48.00%) |
| *Clinical trial participation is voluntary* | |
| Regressed | 1(4.00%) |
| Stayed the same | 23(92.00%) |
| Improved | 1(4.00%) |
| **Comfort** (N=25) | |
| *I have a good understanding of how clinical trials work* | |
| Regressed | 2(8.00%) |
| Stayed the same | 6(24.00%) |
| Improved | 17(68.00%) |
| *If I had the option, I would definitely consider joining a clinical trial* | |
| Regressed | 0(0%) |
| Stayed the same | 16(64.00%) |
| Improved | 9(36.00%) |

The results from the baseline and after video surveys show relatively minor improvements on actual knowledge improvement. The most improvement was found within the statement "There may not be direct medical benefit to me from my participation in a trial," with 20% of respondents answering correctly after answering incorrectly at baseline. Improvements were also seen in the statements "One of the major purposes of clinical trials is to compare the effects of two or more different was of treating patients" and "I have to remain in a trial even if I decide someday that I want to withdraw. Surprisingly, three questions saw regressions in knowledge in more than two individuals after watching the video, although the results from two of these questions ("If I participate in a clinical trial, it is possible that the study sponsor, various government agencies, or others who are not directly involved in my care can review my medical records"; "After I agree to participate in a clinical trial, my treatment may be chosen randomly (by chance) from two or more possibilities" ) could be explained by the fact that the video series did not touch upon these subjects.

The only response item dealing with clinical trial understanding that did not see improvement by at least two individuals was that clinical trial participation was voluntary, however this could be attributed to the fact that 88% of respondents already understood that trial participation was voluntary. All of the response options outside of one ("Clinical trials involve research") saw a regression of understanding. However, this regression was noted in only one individual per response option outside of the possible benefits to participating in a clinical trial, the

alternatives to participation in a clinical trial, and the effect of the trail on the confidentiality of your medical records. Two individuals (8%) saw regression in understanding of the benefits of participating and the effects of trials on confidentiality, and three individuals (12%) saw regression in the alternatives of participating in trials.

Seventeen individuals (68%) responded more positively after watching the video when answering if they had a good understanding of how clinical trials worked. In addition, 9 (36%) individuals responded that they would definitely consider joining a clinical trial if they had the option after watching the video series. No individuals responded that they would be less likely to consider joining a clinical trial after watching the video.

*Satisfaction.*

The results of the satisfaction survey can be found in Table 3. One participants' responses were thrown out due to the fact that they selected the same answer for every question ("strongly disagree") and completed the survey in a much shorter time than would have been possible had they read and responded to every question individually. The decision to exclude these responses in the final results was deemed appropriate when the researchers compared the answers from this survey with the audio transcripts. The feedback given in the transcripts did not match up with the responses of the survey and thus were removed from analysis.

Table 3. Results from the Satisfaction Questionnaire.

| **Satisfaction** (N=24) | |
|---|---|
| *The video contained too much information.*<br>Strongly disagree | 8(33.33%) |

| | |
|---|---|
| Disagree | 7(33.33%) |
| Neutral | 3(12.50%) |
| Agree | 3(13.50%) |
| Strongly Agree | 3(12.50%) |
| *The video contained too little information.* | |
| Strongly disagree | 9(37.50) |
| Disagree | 12(50.00%) |
| Neutral | 1(4.17%) |
| Agree | 1(4.17%) |
| Strongly Agree | 1(4.17%) |
| *My knowledge of clinical trials has increased after watching this video.* | |
| Strongly disagree | 0(0%) |
| Disagree | 0(0%) |
| Neutral | 2(8.33%) |
| Agree | 8(33.33%) |
| Strongly Agree | 14(58.33%) |
| *Patients should receive information like this before deciding whether or not to join a clinical trial.* | |
| Strongly disagree | 1(4.17%) |
| Disagree | 0(0%) |
| Neutral | 0(0%) |
| Agree | 6(25.00%) |
| Strongly Agree | 17(70.83%) |
| *This material helped me better understand clinical trials.* | |
| Strongly disagree | 0(0%) |
| Disagree | 0(0%) |
| Neutral | 4(16.67%) |
| Agree | 8(33.33%) |
| Strongly Agree | 12(50.0%) |
| *This material would help me in making a decision about joining a clinical trial.* | |
| Strongly disagree | 0(0%) |
| Disagree | 0(0%) |
| Neutral | 1(4.17%) |
| Agree | 8(33.33%) |
| Strongly Agree | 15(62.50%) |
| *I would recommend this material to a friend who needed information about clinical trials.* | |
| Strongly disagree | 1(4.17%) |
| Disagree | 0(0%) |
| Neutral | 1(4.17%) |
| Agree | 5(20.83%) |
| Strongly Agree | 17(70.83%) |
| *The information was easy to understand.* | |
| Strongly disagree | 1(4.17%) |
| Disagree | 0(0%) |
| Neutral | 0(0%) |
| Agree | 11(45.83%) |
| Strongly Agree | 12(50.00%) |
| *I feel more comfortable with clinical trials after watching this video.* | |

| | |
|---|---|
| Strongly disagree | 0(0%) |
| Disagree | 0(0%) |
| Neutral | 2(8.33%) |
| Agree | 9(37.50%) |
| Strongly Agree | 13(54.17%) |
| *I feel better prepared to discuss clinical trials with my physician after watching this material*. | |
| Strongly disagree | 0(0%) |
| Disagree | 0(0%) |
| Neutral | 2(8.33%) |
| Agree | 6(25.00%) |
| Strongly Agree | 16(66.67%) |

Reaction was split in terms of the degree of information presented in the video series. Around 63% of participants disagreed or strongly disagreed that the videos contained too much information. Conversely, 86% of participants also disagreed or strongly disagreed that the video series contained too little information. Outside of these two questions, satisfaction responses to the video series was overwhelmingly positive. Only one participant did not agree that patients should receive information like this before deciding on joining a clinical trial. In addition, 95% of participants agreed with the statement that this material would help them make a decision to join a clinical trial. Furthermore, only two participants did not agree that they would recommend this to a friend who needed information about clinical trials. Again, 91% agreed or strongly agreed that they felt more comfortable with clinical trials after watching the video series and 91% felt better prepared to discuss clinical trials with their doctors. All but four individuals (83%) agreed or strongly agreed that this material helped them better understand clinical trials, and all but one participant stated that the information was easy to understand. While not much change was reported in the knowledge questionnaire,

around 91% of participants agreed or strongly agreed with the statement that their knowledge of clinical trials increased after watching the video series.

*Interview coding.*

Seventy-nine unique codes were identified from the 25 interviews conducted. A list of codes and their descriptions can be found in Appendix J. Overall, 253 instances of positive feedback was given. A word cloud of this positive feedback can be found in Appendix K. Overall, participants looked favorably on the video series, with 114 instances of negative feedback as compared to 253 instances of positive feedback. Each participant gave positive feedback positive feedback, yet 19 (79%) also gave negative feedback with some part of the video series. The most common positive feedback received about the video series and the individual segments was that they were good, helpful (35), informative (30), helped improve understanding (18), and were important (15). As for specific aspects of the video, participants reported positive feedback with the patient prospectives presented in the video (22), the graphics (18), the topic of asking questions to your doctor (13), the doctor perspectives (12), and the topics of safety (12) and safeguards (12). Participants specifically mentioned liking the segments around asking questions (9), hearing from the patients (8), hearing from the doctors (8), the benefits of clinical trials (5), the importance of bringing a caregiver (5), and the topic of altruism (5). In addition, there were seven instances (29%) where patients stated that they learned something specific from the video series, and four patients (17%) stated that after

watching this video, they would be more likely to enroll in a clinical trial and stated they would seek one out.

Of the 114 instances of negative feedback, 22% had to do with the video or topic covered being too long. A word cloud of negative feedback can be found in Appendix L. During the interviews, participants suggested 88 instances where the video could be cut down or topics excluded. All in all, participants felt like each of the video segments could be cut down; video segments five ("Where Can I Turn to for Support"), three ("How Should I Prepare for Discussions With My Doctor"), and two ("How Will I know if a Trial is Right for Me") had the most stated instances of things to cut. While many participants promoted favorable views of the summaries at the end of each video segment, just as many participants stated that these summaries could be cut out to save time. Since the researchers discussed developing a general video rather than one focused on a single malady, the segments covering cancer were the most mentioned topic that could be cut. Other topics suggested that could be cut down or removed entirely included the extra costs associated with clinical trials, the informed consent, and the IRB.

An additional 18% of negative feedback involved the use of jargon in the video series. Some participants expressed concern that the general population may not be as savvy with medical terminology as those who participated in this video, stating that the language "was outrageous to be honest" and that "for your common high school educated Louisiana person who is in your population, it may be a little high." Others expressed the desire to see "someone speaking in plain, ordinary

English and not…not so professional and clinical." Most often participants cited jargon when referring to standard of care, placebos, and double-blind studies.

Another issue that patients had with the video series was the lack of diversity. Participants brought up the fact that there was a lack of people of color and that the large majority of those presented in the video series were " …all white. lots of [those] people who had engaged in clinical trials all white and all look prosperous." Participants were quick to point out that "The video could use diversity in the patients, both in ethnicity and age." and the video should "… have a lot more people of color." An additional suggestion for diversity was to include people from different occupational backgrounds and make it "…a little rougher you know? Go out on the street and talk to truck drivers, getting into their cabs or just a variety of people rather than just this…" One participant was particularly unnerved by the representation of people of color in the video series, stating "I just feel a little offended that the African American woman just has her dog… we have families too, so they need to show the whole family, because she looked like she didn't have any support except for her dog."

Along the same lines as a lack of diversity, an additional issue participants had with the video series was its representativeness. The most commonly expressed issue with representativeness was the doctor/patient relationship presented in the series. It was noted multiple times that the relationship between the doctor and the patient may not be reflect the experience of the average interaction between doctor and patient. Throughout the series, the doctors encourage patients to ask questions about both their diagnosis and clinical trials and seemed to have a very personal

relationship with their patients. Indeed, one participant described these doctors as "…sort of the Uber doctors" stating that "they're the ones that you hope you get, but not all doctors are like that." Several participants expressed concerns that this was not typically how these types of interactions take place. When one of the doctors in the video stated that he liked patients challenging his recommendations, one participant -a doctor no less- stated "most doctors are not comfortable being questioned like that." Rather than discussing the ins and outs of clinical trials and taking the time to explain and answer questions the patient may have, several participants instead felt that doctors were interested in moving through patients as quickly as possible. One participant stated that the typical doctor/patient interaction consisted of " you walk in, they walk in and ask you what's wrong, they take your pulse and then they're gone" and another stated "They want you in and out of there in 10 minutes or less, you're lucky if it's ten minutes." In addition to this lack of representation, participants also called out the scenery and backdrops, stating that "New Orleans doesn't look like that there. No way. Used to a long time ago but not no more." and that our video "could have New Orleans instead of the background of whatever this city is."

During the interviews, participants also gave suggestions on what needed to be kept from the video series. Participants felt that the ability to pull out at any time was very important to keep, stating "I think it would be important to say out loud that you can withdraw from a clinical trial at anytime..." and "there may be consequences and there may side effects we don't even know about with this but if you're not doing well you're not beholden to stay into this test, so I think they need

to be aware of that." Information regarding safeguards and safety was also deemed important. Participants felt that it was "important to stress the safeguards built into the approval process for clinical trials." and that including information on safeguards could take "an individual that may not want to do it and will turn them toward, 'Hey, I'm going to do this' and a person that's already interested in doing it may help them improve their thoughts on, 'Hey, I really want to do this.'" Participants also believed that information regarding informed consent should be kept, saying that this topic "needs to be the take home message: that you will get this stack of papers and the doctor will explain this and this and this and then you will be able to go home and read it and think about it" and that consent "gives you full disclosure of everything and it's also protecting you." Furthermore, participants believed that where to get more information needed to be included as well, stating that "Resources and links are very important." and it was "actually really good to actually put the number [cancer hotline] up on the screen. It's very informational for people who don't know how to go about finding it." Participants also suggested that it was necessary to highlight the importance of communicating with your doctor and also "what we need to ask our physicians and our primary doctors, what we need to know, what we could do for us." Bringing a caregiver was also deemed important, with one participant stating "I feel like everybody should know about that cause you need somebody to support you while you're going through what you're going through."

Participants also suggested areas for the video series to expand upon. The most common suggestions for things to expand upon were the personal benefits

that you could receive by being in a trial, that you can take your time and review all the information about clinical trials and the informed consent, and where to go for reliable and trustworthy information on clinical trials and your diagnosis. Participants thought that personal benefits of clinical trial enrollment "*weren't really highlighted"* and that it was important for future patients to understand the benefits of trial participation. One patient even offered up their own experiences with clinical trials as an example, sharing that "*through my husband's experience he was seeing a physician about once a month where outside of a clinical trial you would only see a physician maybe once or twice a year."* Other participants believed that taking your time and reviewing all the information should have been more of a focus in the series, stating "telling them more about to highlight the paper, write questions on the paper, things like that is really important and could be added." Where to go for reliable and trustworthy information on clinical trials was also an area where participants thought the video series could have elaborated more, with one participant stating "What really stuck out to me with this one was that last bullet point with uh...trusting reliable reputable sources of information. I really wish they would stress more on that."

Participants also suggested to add topics and themes that were not covered in the video series. First and foremost, participants wanted to see someone actually going through the clinical trial process. Participants stated that they would have liked to have seen "what happens in the clinical trial process" and what happens after one has chosen to participate in a clinical trial. Other participants echoed this sentiment, stating that the video "didn't specify the treatment, you know, and what

they do to you through[out] clinical trials." One participant offered that the video should include "a roadmap or a diagram… It could be something fun with like a car on a monopoly board where it goes 'you've chosen to participate in a clinical trial, this is the next step." Participants also suggested developing a handout containing a summary of the material presented and other useful items to go along with the video series, stating "who's going to remember all of the things that they just said? go here, go there, go here, all right, *click* you're done." Participants suggested that if viewers were given a summary handout, they could then take the information home and review it with loved ones and caregivers, stating once again that most people would not remember what was discussed. One participant suggested a "checklist of questions, like things you want to ask if you're interested in a clinical trial" should be included because most people would not know what to ask. Furthermore, one participant did make the point that in the video series, "nobody ever tells people what a clinical trial is" and that this is a fundamental question that should be addressed in a video surrounding clinical trials .

*Free Listing and Pile Sort Exercise.*

After giving feedback on the video series, participants were asked to write down on notecards any topic, theme, or idea that they could think of that should be included in a video designed to improve a persons knowledge, comfort, and understanding of clinical trials. Patients were asked to imagine that there was no time constraint for this video and to write down one topic, theme, or idea per note card. Overall, 23 participants participated in the free-listing exercise; one

participant fell asleep during the exercise and provided no topics or themes. The responses given by participants were grouped into themes and are presented in Table 4 (Reported results include only those that were mentioned by two or more participants. A full list of results of the free-listing exercise can be found in Appendix M).

*Table 4. Standardized Results of Free-Listing Exercise.*

| Theme | Count |
|---|---|
| Benefits | 18 |
| Risks | 16 |
| What is a clinical trial | 11 |
| Additional resources | 10 |
| Length of trial/Time commitment | 10 |
| Safety | 10 |
| Ability to withdraw | 10 |
| Informed consent | 8 |
| Altruism | 7 |
| Standard of care | 7 |
| Confidentiality | 6 |
| Ask questions | 6 |
| Extra costs | 6 |
| What happens in clinical trials | 6 |
| Purpose of clinical trials | 6 |
| Placebos | 5 |
| Safeguards | 4 |
| Consent | 3 |
| Background of clinical trials | 3 |
| Alternatives/Options | 3 |
| Patient prospective | 3 |
| Clinical trial protocols | 3 |
| Renumeration | 3 |
| Who sponsors the clinical trial | 3 |
| Trust | 3 |
| Communication | 2 |
| Cost of participation | 2 |
| Types of clinical trials | 2 |
| Diversity | 2 |
| Eligibility | 2 |
| IRB | 2 |

The most commonly reported topic, theme, or idea that should be included in a video focused on improving the viewers' knowledge, comfort, and understanding of clinical trials was benefits, with 18 of our 24 participants (75%) writing it down in this exercise. Sixteen participants (65%) wrote down risks as important topics to cover, and 10 participants (42%) believed that additional resources and what is a clinical trial needs to be covered as well. Length of trial/Time commitment, safety, and the ability to withdraw at any time were each written down by 10 participants (42%) in this exercise, and 8 participants (33%) felt that informed consent should be included. Seven participants (29%) believed altruism and standard of care should be included, and around 25 % reported that confidentiality, what happens in clinical trials, asking questions, the costs of participation, and placebos should also be discussed.

After participants completed this free listing exercise, they were asked to rank their responses. Twenty-three of the twenty four participants that completed the free-listing exercise ranked their results; one participant stated that they could not rank their results and that they all were inter-dependent on each other and were "Gestalts of the whole." After ranking their free-listing responses, participants were then instructed to imagine they were helping create a video like the one they just watched, but was only five minutes in length or less and was intended to be shown while a patient is in the examination room of their healthcare provider. Participants were asked to divide their free-list responses into three categories: 1) absolutely essential topics, themes, or ideas that should be included in a 5 minute or less video, 2) topics, themes, or ideas that are important and should be included if

there is time, and 3) topics, themes, or ideas that could be cut or saved for a future video. All 24 participants that completed the free listing exercise completed the pile sort exercise. Like the free listing exercise, responses were compiled into topics to standardize responses and are presented in Table 5 (results as they were written appear in Appendix N).

*Table 5. Standardized results of the pile sort exercise.*

| Absolutely should be included | Include if there is time | Could be cut or saved for the future |
|---|---|---|
| Risks- 12<br>Benefits- 11<br>Ability to withdraw- 9<br>What is a clinical trial- 8<br>Safety- 7<br>Additional resources- 6<br>Standard of care- 6<br>Informed consent- 5<br>Altruism- 4<br>Confidentiality- 4<br>Ask questions- 3<br>Procedures- 3<br>Purpose of clinical trials- 3<br>Consent- 2<br>Diversity- 2<br>Length of trial/Time commitment- 2<br>Alternatives/Options- 2<br>Patient prospective- 2<br>Protocol- 2<br>Trust- 2 | Benefits- 5<br>Extra costs- 5<br>Additional resources- 3<br>Length of trial/time commitment- 3<br>Risks- 3<br>What is a clinical trial- 3<br>Altruism- 2<br>Confidentiality- 2<br>Cost- 2<br>Placebo- 2<br>Procedures- 2<br>Safeguards- 2<br>Safety- 2<br>Sponsors- 2 | Length of trial/time commitment- 4<br>Ask questions- 3<br>Informed consent -2<br>Placebos- 2<br>Purpose of clinical trials- 2 |

The most commonly reported topic, theme, or idea that respondents stated should absolutely be included in a five minute or less video focused on improving knowledge, comfort, and understanding of clinical trials was risks and benefits. Twelve participants (50%) reported that risks were absolutely essential to include and 11 participants (46%) thought benefits were absolutely essential. Nine out of the 10 participants that mentioned the ability to withdraw during the free-listing

exercise said that this topic was essential to cover in the video. Eight participants (33%) thought that explaining what a clinical trial is should absolutely be covered, and 7 believed the safety of clinical trials should be presented to the patient. Six participants (26%) thought that additional resources and the standard of care were absolutely essential to cover, and four participants (17%) thought confidentiality and informed consent should definitely included in the video. Altruism, the procedures undergone in a clinical trial, asking questions, and the purpose of clinical trials were topics and themes that were essential to three participants (13%), giving consent, diversity, the trial length/time commitment of the trial, alternatives/options, patient prospectives, protocols, and trust were all mentioned by two participants (9%).

Along with being the second most mentioned topic or theme that should absolutely be included in a video focused on improving clinical trial knowledge, comfort, and understanding, benefits was also the most reported idea in the important and should be included if there's time category. Five participants (22%) believed that discussing extra costs was important and should be included if there is time. Three participants (13%) believed that additional resources, the trial length/time commitment, risks, and what a clinical trial is were important ideas to include if there was time, but not absolutely needed to be covered. Furthermore, altruism, confidentiality, the direct costs of participation, placebos, the procedures of a clinical trial, safeguards, safety, and sponsors were important ideas that should be included if there is time after covering the absolutely essential topics.

Four participants (17%) agreed that the length of the trial/time commitment should not be included in a five minute or less video to improve patient knowledge, comfort, and understanding of clinical trials. Three participants (13%) concluded that asking questions also had no place in our introductory video. Informed consent, placebos, and the purpose of clinical trials were topics and themes that also received at least two mentions (9%) for being cut or saved for a different video.

### 5.e. Discussion

This project set out to determine what topics and information should be covered in a short 5-minute video given at the point of care that would improve patient understanding, knowledge, and comfort of clinical trials. The researchers' underlying hypothesis was that an increase in these three areas would see an increase in willingness to enroll, which should lead to higher levels of enrollment. As found in other studies that offer visual, audial, or text resources to participants (Banda et al., 2012) (Jacobsen et al., 2012)(Manne et al., 2014)(Mason et al., 2003), being presented with educational material such as this increased participants' understanding and knowledge of clinical trials. It also has been hypothesized in the past that a lack of knowledge can lead to feelings of distrust and discomfort with clinical trials and medical community (Dang et al., 2014)(Huges et al., 2015)(Wiliams, 2013) and that by targeting this lack of knowledge through education, researchers can improve trust and comfort with clinical trials among patients, leading to more positive attitudes and more willingness to enroll. This study lends credence to this hypothesis, with all but one individual agreeing or

strongly agreeing that they felt more comfortable with clinical trials after watching this video series.

As mentioned previously, it has been hypothesized by the Knowledge, Attitudes, and Behavior model and the Theory of Planned behavior that increasing an individuals' knowledge, understanding, and comfort with clinical trials should increase their willingness to participate, which theoretically should lead to higher enrollment rates into clinical trials. This project shows that an educational intervention that improves knowledge, comfort, and understanding also improves willingness to enroll into a clinical trial. As compared to baseline measurements, participants stated they were more willing to enroll into a study they were eligible for after watching the video series (Fisher's $p<0.001$). Overall, 37% of participants expressed improved willingness to join a clinical trial after watching the video as compared to baseline, which reflects what has been found in previous studies (Banda et al., 2012)(Du et al., 2008)(Stles et al., 2011). While these results do not show as large an increase in willingness as those found in some of these studies, our hypothesis is that our population was already more willing to join a clinical trial at the baseline measurement. This could be due to the fact that our population tended to be higher educated than the general population, however this should not detract from the fact that improvements were seen even in those who were already willing to join a clinical trial.

Not only does this study show that improving knowledge, understanding, and comfort with clinical trials can increase willingness to enroll, it attempts to uncover the topics and themes that are most important to improve knowledge,

understanding, and comfort. The most important topics and themes that were raised during the free-listing exercise tend to mirror what is found in the literature when describing both the barriers and benefits of joining a clinical. The personal benefits (Bedlack et al., 2010)(Comis et al., 2009)(DasMahapatra et al., 2017)(Haidich & Ioannidis, 2001)(Owens et al., 2013)(Ulrich et al., 2012), risks associated with trials (Comis et al., 2009)(Kim et al,, 2015)(Owens et al., 2013)(Robinson et al., 2016)(Weckstein et al., 2011)(Ulrich et al., 2012), what a clinical trial is (Bauqet et al., 2006)(Owens et al., 2013)(Manne et al., 2014)(Stiles et al., 2011)(Toms et al., 2016), the length/time commitment (Andersen & Olson, 2016)(Baquet et al., 2006)(Owens et al., 2013)(Stiles et al., 2011)(Ulrich et al., 2012), the safety of the trials (Comis et al., 2009)(Corbie-Smith et al., 2002)(Owens et al., 2013)(Tan et al., 2015), altruism (Bedlack et al., 2010)(Strasser, Cola, & Rosenblum, 2013)(Toms et al., 2016)(Ulrich et al., 2012), and confidentiality (Langford et al., 2010)(Wiliams et al., 2013) were all in the top 10 most commonly reported answers in our exercise and have been mentioned in previous literature as being significantly involved in willingness to participate in a clinical trial. Additional resources, highlighting the ability to withdraw, and informed consent were other topics that rounded out the top 10 in our study that have not often been mentioned in previous studies as influencing clinical trial participation willingness. It is worth noting, however, that around $1/6^{th}$ of the video series was dedicated to informed consent and therefore is not surprising that it ended up in the top 10 in this project but not in the relevant literature. Furthermore, the researchers found it interesting that what was reported as important in the free listing exercise did not always

match up with what was stated during the feedback portion of the interview. When giving feedback, the most mentioned topic or theme that was linked with importance and the need to be included/added upon in a video was the ability to withdraw at any time, followed by safeguards, informed consent, additional resources, asking your doctor questions, and bringing a caregiver. Interestingly, while risks and benefits were mentioned as being the top two most important topics and themes to cover in the free listing exercise, they were only linked with being important or needing to include/add upon a total of 6 and 12 times respectively during the interviews. This could show that what participants believe would influence them to join and what they believe would influence the population as a whole are different, an interesting hypothesis that is outside the scope of this project but should be studied in the future.

This project went a step farther than previous studies by asking participants to constrain their topics and themes to only what could be shared within 5 minutes. Recognizing that clinical trial recruitment is often institutionally demanding and intensive (Anderson & Olson, 2016)(DasMahapatra et al., 2017)(Dwyer-White et al., 2011)(Frank, 2004)(Robinson et al., 2016) and that the physician was often the most successful avenue of clinical trial recruitment (Banda et al., 2012)(Ramirez, 2012)(Robinson et al., 2016)(Tanner, 2016), we theorized that a 5 minute or less video that could be shown to patients while they wait to see their doctor had the double advantage of  both make patients more willing to enroll and alleviate the time and resource burden for physicians and healthcare practitioners. With these constraints, participants felt that the most important topics and themes to

communicate were risks, benefits, the ability to withdraw, what a clinical trial is, and additional resources. Surprisingly, when asked to constrain their responses, the length of trial/time commitment became less relevant and the ability to withdraw at any time and the standard of care became more relevant. The authors believe that this was so because participants often suggested this shorter video should be one that is more general, or as one participant put it, "the bait that really hooks people in." The most common negative response to the video series was that it was too long and was and much too long to be shown to patients during routine care, however at the same time participants felt that the majority of topics and themes presented were important and should still be covered. The solution that several participants came up with was similar to the video series. They suggested that there should be more than one video, however the first video was to be the one shown in the clinic. This first video should cover the main topics listed in the pile sort exercises (topics that tended to be more general about clinical trials), and also contain links to the future videos that the individual could watch "once they were hooked." These future videos would discuss clinical trials in more detail and also would give links to where individuals could find trials. The idea of dividing up the video into two or more parts was so prevalent that the third category of the pile sort exercise was changed from "could be cut" to "could be cut or saved for an additional video."

Another important theme that emerged was the doctor/patient relationship and the trust that individuals have in their healthcare provider as essential to clinical trial enrollment. Healthcare providers are oftentimes the avenues through

which individuals learn about clinical trials and enrollment opportunities (Cohen et al., 2012)(NIH, 2016a)(Ramirez, 2012)(Tanner, 2016), oftentimes acting as the gatekeeper and shepherding or preventing patients from joining clinical trials (Abraham et al, 2006)(Avis, 2006)(Comis et al., 2009)(Frank, 2004)(NIH, 2016a). Thus, many individuals' clinical trial enrollment opportunities are reliant on the relationship and trust they have in their healthcare provider (Adams et al. 2015)(Abraham et al, 2006)(Krikby et al., 2012). A juxtaposition emerged from what was presented in the video series and what participants stated was reality. Throughout the series, both patients and providers constantly stressed the importance of having open discourse and even encouraging patients to challenge their physicians recommendations. This implies a strong relationship between patient and provider and permeated throughout the series. Many of our participants felt this relationship did not represent the relationship they had with their provider nor what they believed to be the normal relationships between patient and provider. Participants described interacting with doctors as "*you walk in, they walk in and ask you what's wrong, they take your pulse and then they're gone*" and "*They want you in and out of there in 10 minutes or less, you lucky if it's ten minutes. In fact I said I was going to start timing the next time I go to the doctor [laughter].*" This view was even expressed by the one doctor and one nurse in our study, with them stating "*I just don't find a lot of this [doctor patient interaction] realistic. Especially in the current state of health care where it's, you know, umm... rush in and rush out*" and "*The doctor goes in and says, well, we're going to do this treatment. blah blah. And then he'll say, 'do you have any questions?' And the patient says 'No.' And then the*

*nurse comes in and says, 'do you have any questions about what Dr so and so said?' And out pour the questions because the nurse has been taking care of them."* This lack of interaction between patients and providers is backed up by other studies showing the immense amount of pressure providers are under during patient visits (Anderson & Olson, 2016)(DasMahapatra et al, 2017)(Dwyer-White et al., 2011)(Frank, 2004)(Powell et al, 2008)(Robinson et al., 2016). In some cases, this in-and-out visit is better than the alternative. One participant expressed their experience with a provider as such: *"[I] actually missed a doctor's appointment because I was trying to avoid a fellow. I found him very condescending."* Another participant expressed even less positive interactions: "*The help they are trying to give me, is not helping and it's been more than 4 years getting all this treatment and trying to follow… And if I don't follow, your orders I'm refusing treatment but you don't want to listen what the patient got to say and what's working for them."* Provider interactions erode confidence in the medical community and promote distrust, which is often associated with lower rates of enrollment (Abraham et al., 2006)(Ard et al, 2005)(Banda et al., 2012)(Frank, 2004)(Kim et al., 2015)(Murthy, Krumholz, & Gross, 2004)(Toms et al., 2016). As one can see from patient feedback, the interactions expressed by the participants are a far cry from what was presented in the video. To promote more dialogue and to improve enrollment rates into clinical trials, consideration should also be given to improving relations and the interaction between the provider and the patient.

### 5.f. Limitations

While offering valuable insight into the important topics and themes that should be given to patients when discussing clinical trials, this study does have its limitations. First and foremost, this study suffers from selection bias. Like most qualitative studies, participant recruitment was based on convenience sampling rather than random sampling. Because of this, the opinions and statements expressed throughout the interviews and surveys may be substantially different from those in the population as a whole. Furthermore, the sample for this study tended to be older, more well educated, and consisted largely of White individuals. As such, these results may not be generalizable to the rest of the population. It has been established in the literature that minority and Whites' attitudes and perceptions with clinical trials differ (Baquet et al., 2006)(Frank, 2004)(Foster, 2011)(Katz, 2006)(Kim et al., 2015) (Owens et al, 2013)(Ramirez, 2012) and there is some evidence that willingness to enroll is also affected by age (Peterson et al., 2012)(Owens et al, 2013)(Strasser, Cola, & Rosenblum, 2013). Future studies should solicit feedback from individuals that are younger, less educated, and from other minority backgrounds in order to get a fuller picture of what could influence willingness to enroll; feedback that could very well differ and feedback that this project may have missed.

Furthermore, although self-reported knowledge and understanding of clinical trials seemed to increase, the actual scores on the knowledge and understanding questionnaire did not always reflect this. Three of the 8 questions about knowledge saw at least two participants select the wrong answer after watching the video when they initially answered correctly before, and all but one

question about understanding saw at least one participant respond with less understanding after watching the video series. However, two of the knowledge questions where knowledge regressed after watching the video (*If I participate in a clinical trial, it is possible that the study sponsor, various government agencies, or others who are not directly involved in my care can review my medical records; After I agree to participate in a clinical trial, my treatment many be chosen randomly (by chance) from two or more possibilities*) were not touched upon in the video series so this regression should be taken with caution. In the same vein, the understanding questions that saw the most regression (*The alternatives to participation in a clinical trial; The effect of the clinical trial on the confidentiality of your medical records)* were also not touched upon in the video. This does not explain, however, why 13% of our participants thought that one of the major purposes of clinical trials was not to test the safety of a new drug or treatment after initially reporting this to be true. Other studies have shown a similar lack of connection between self-reported knowledge and actual knowledge change (Davis et al., 2012)(Katz et al, 2008)(Kim et al., 2015), and future studies should examine this connection more in depth. In addition, while 71% saw improved scores in response to the question "I have a good understanding of how clinical trials work," two individuals actually saw their scores decrease after watching the video. The researchers hypothesize that this could be due to the fact that watching the video caused participants to reassess their level of clinical trial understanding, which has been found in other studies (Kim et al., 2015)(Miller et al., 2013)(Stiles et al, 2011). Although outside the scope of this project, how this type of

material could lead to a re-evaluation of previously held beliefs is an area where future studies can and should explore in more detail.

A final limitation involves the actual method of proposed delivery of our project. As mentioned many times previously, our design is to uncover the important topics and themes that should be included in a video to improve patient knowledge, understanding, and comfort with clinical trials that can be shown to patients as they wait to see their healthcare provider. As stated in the discussion, the likelihood that an individual will be exposed to this method of delivery or be open to its messaging is dependent on the relationship that exists between the provider and the patient. This does not take into account those who have limited interaction with the healthcare filed, either due to a lack of resources, knowledge, or trust. In this way, this method of delivery may not reach those who are most in need of this information (Corbie-Smith et al., 2003)(Levkoff & Sanchez, 2003).

## 6. Study 2.

### 6a. Research Question 2

*At which stages in the enrollment process do patients who are initially willing to participate in a clinical trial drop out?*

Prior research has shown many individuals claim they are willing to participate in a clinical trial; yet very few actually enroll. The rate of drop off between each stage of the enrollment workflow is not well studied in the literature. Often, clinical trial studies report only the initial number of participants approached, the number of participants eligible, and the number of participants enrolled. At best,

most studies report the number of patients that dropped out overall during the enrollment period, not reporting at which stage of the enrollment process these individuals dropped out. This research question attempts to better understand where patient drop-off occurs in the recruitment process. Utilizing the WeighSmart database allows researchers to use survival analysis techniques to chart the hazard rate and survival at each step of the enrollment workflow.

### 6.b. Recruitment.

Recruitment for this study comes from the WeighSmart clinical trial. The WeighSmart clinical trial was launched in 2015. Designed as a comparative effectiveness trial, WeighSmart examines whether text message weigh-in reminders encourage weight loss in overweight and obese patients (WeighSmart, 2016a). This trial attempted to recruit 200 patients that met the following criterion: were between 18-66 years of age, had a BMI between 25-35kg/m2, had the ability to receive text messages, had an active email account and internet access to complete monthly surveys, and had a self-reported interest in losing weight. Exclusion criteria for this study included: a history of myocardial infarction, cancer, eating disorder, bariatric surgery, current diagnosed thyroid condition, pregnant or planning to become pregnant in the next 6 months, nursing, currently enrolled in another weight loss study or program, or weighing over 375 pounds (WeighSmart, 2016a). Patients were recruited at the point of care in REACHnet clinics located in New Orleans (Ochsner Health System, Tulane University Hospital System, Daughters of

Charity clinics, and the Lallie Kemp clinic) (Couk, 2016). Upon presenting to the clinic, nurses or clinical staff members pulled up the patients' health record while the patient was brought to the examination room. The staffer/nurse then ran a research query on the patients' health record to determine if the patient was initially eligible for the WeighSmart clinical trial (WeighSmart, 2016b). If the patient met the initial eligibility criteria, the nurse/staffer returned after all regular clinical activities were complete with a tablet loaded with a Patient Trial App Suite; a software system that was designed to engage and recruit patients for clinical trials. Eligible patients were given a brief introduction to the tablet by the nurse/staff and were instructed to fill in their date of birth (Couk, 2016). If the date of birth matched the date of birth in the patients' health record, the tablet played a short video summarizing the WeighSmart trial (if the date of birth did not match the patients' recorded date of birth, the tablet displayed an error message and asked the patient to re-enter their date of birth. If this occurred three times, the tablet displayed a message apologizing about not being able to link to the patients' record and the workflow ended) (WeighSmart, 2016a)(WeighSmart, 2016b). After the conclusion of the short video, patients were asked if they were interested in learning if they were eligible for the WeighSmart clinical trial. If patients responded no, they were thanked for their time and the workflow ended. If patients responded they were interested in learning about their eligibility, they were shown a page on the tablet with further screening questions (Appendix A). If patients met all of the screening criteria, the patient was asked to provide a first name, last name, phone number, and an active email address to continue the enrollment process (WeighSmart,

2016b). An email was then sent to the provided email address containing a link to the WeighSmart portal where patients could create an account and access the informed consent document (WeighSmart, 2016b). Patients then were asked to peruse the document, answer a few questions to determine that they understood the document's content (Appendix B), and consent to enroll into the study (WeighSmart, 2016b). The full recruitment workflow can be found in Appendix C. Once consent was obtained, enrollees were randomly assigned to one of two groups (one group receiving daily reminders to weigh themselves and one group receiving reminders to weigh themselves every two weeks) and patients arranged a time to pick up a digital scale to keep track of their weight change. Patients in both conditions were asked to complete a survey assessing diet, general health, and physical activity changes every four weeks for 6 months. There were three main hypotheses of this trial: patients receiving daily reminders will weigh themselves more often than those receiving reminders every two weeks; those receiving daily reminders will lose significantly more weight over 6 months than those receiving reminders every two weeks; and those receiving daily reminders will report more changes to diet and exercise than those receiving reminders every two weeks (WeighSmart, 2016a).

### 6.c. Methods

Data were drawn from patients who met the criteria for initial approach of offering enrollment (between 18-66 years of age, a BMI between 25-35kg/m2, not weighing over 375 pounds) for the WeighSmart clinical trial. These patients were tracked throughout the entire enrollment workflow process until they either

dropped out, enrolled into the study, or the study began. Those that did not complete the workflow by the time study recruitment ended were considered right censored and were considered to have dropped out of the study at which interval of the workflow they were on. For this study, the enrollment workflow was broken up into 8 stages, highlighted by the green boxes in Appendix C: not interacting at all with the tablet, inputting the correct date of birth and watching some of the video, watched the video and completing at least part of the health assessment, completing the health assessment, still being eligible after completing the health assessment, providing contact information to be sent a link to the portal to access the WeighSmart portal, activating the Weighsmart portal, and finally correctly consenting to the Weighsmart study. For ease of understanding, the steps are summarized in visual form in Table 6.

*Table 6. Stages in WeighSmart enrollment workflow.*

| Created variable | Variable label | Activity |
|---|---|---|
| Surveystep | Start | Were initially eligible for the WeighSmart clinical trial. |
| | 1 | Did not interact with the tablet at all. |
| | 2 | Correctly entered date of birth. Partially interacted with the tablet and watched some of the video |
| | 3 | Correctly entered date of birth. Watched video and did not start/complete health assessment |
| | 4 | Correctly entered date of birth. Watched video. Completed health assessment. Not eligible. |
| | 5 | Correctly entered date of birth. Watched the full video. Filled out health assessment and were still eligible. Did not provide contact information. |
| | 6 | Correctly entered date of birth. Watched the full video. Filled out health assessment. Were still eligible. Provided contact information to access WeighSmart portal. Did not activate WeighSmart portal. |
| | 7 | Correctly entered date of birth. Watched the full video. Filled out health assessment. Were still eligible. Provided |

| | | |
|---|---|---|
| | | contact information to access WeighSmart portal. Activated WeighSmart portal. Did not answer understanding of consent questions/did not answer understanding of consent questions correctly. |
| | 8 | Correctly entered date of birth. Watched the full video. Filled out health assessment. Were still eligible. Provided contact information to access WeighSmart portal. Activated WeighSmart portal. Answered consent questions and consented to the WeighSmart study. |

The variable *Surveystep* was derived from this information and served as the outcome variable for this research question. Participants were assigned a score for *Surveystep* depending on the highest stage of the workflow that they reached. For example, if a participant correctly entered their date of birth, watched the whole video, and did not fill out the health assessment questionnaire, they were assigned a score of 3 for *Surveystep*. Consequently, a participant that made it through the full workflow and consented into the study was assigned a *Surveystep* score of 8. *Racewb*, *Agecat*, and *Pastyear* were variables that were also created for this research question. Due to low numbers of enrollment from other racial groups aside from African American and Caucasians, analysis was limited to these two racial groups. *Agecat* consisted of transforming the variable *Age* (patient age at initial approach) into a categorical variable representing meaningful categories for our analysis. *Pastyear* was created by summing the number of hospital visits within the past year (365 days) and dividing patients into three groups based on the result: low number of visits, medium number of visits, and high number of visits. The derivations of these variables are summarized in Table 7.

Table 7. Derivation of Variables.

| Variable | Derived from | Code | Response categories |
|---|---|---|---|
| *Racewb* | Patient race | White | 0 |
| | | Black | 1 |
| *Agecat* | Patient age | 18-34 | 0 |
| | | 35-44 | 1 |
| | | 45-54 | 2 |
| | | 55-66 | 3 |
| *Pastyear* | Past number of hospital visits | Low number of visits | 0 |
| | | Medium number of visits | 1 |
| | | High number of visits | 2 |
| *Failure* | *Surveystep* | Enrolled | 0 |
| | | Did not enroll | 1 |

### 6.d. Analysis.

Descriptive frequencies were conducted for all variables involved in the analysis. To analyze the rate of drop-off during the enrollment workflow for this study, Kaplan-Meier life tables and graphs were created. For the creation of the life tables, the variable *Surveystep* was considered the unit of time: each step the patient made it through was analogous to one unit of time (analogous to one year or one month of follow-up time in other discrete-interval survival analysis (Singer & Willett, 1993)). For this analysis, count data was transformed to person time using the *stset* command in STATA. Kaplan-Meier life tables were then constructed to analyze the rate of drop-off between each stage and the previous stage. From here, an overall survival curve and survival function was derived and plotted. In addition, individual survival curves with each of the individual predictor variables (*Racewb, Gender, Agecat, Pastyear*) were plotted in order to visually analyze the rate of drop-off. Chi-square tests were then conducted to determine if the rate of drop-off within each level of the predictor differed.

### 6.e. Results

The initial population size for this study was 4,533 participants. Thirty-nine records were excluded due to the fact that they did not have any values for any category nor met the initial inclusion criteria (age under 18, age over 66). Nine more records were excluded due to the fact that the participant entered the incorrect date of birth 3 times and the medical record could not be accurately matched with the patient.

Descriptive statistics for the different variables used in this analysis are provided in Table 8.

Table 8. Descriptive characteristics of sample.

| Descriptive characteristics of sample | |
|---|---|
| **Race** | |
| Native American/Alaskan native | 43 (1%) |
| Asian | 65 (1.5%) |
| African American | 1,900 (46.2%) |
| Native Hawaiian or other PI | 11 (0.3%) |
| White | 2,200 (53.9%) |
| Hispanic | 108 (2.4%) |
| Unknown | 112 (2.5%) |
| **Gender** | |
| Male | 1,895 (42.2%) |
| Female | 2,591 (57.8%) |
| **Age (categorical)** | |
| 18-34 | 766 (17.1%) |
| 35-44 | 853 (19.0%) |
| 45-54 | 1,172 (26.1%) |
| 55-66 | 1,695 (37.8%) |
| **Past year visits** | |
| Low | 1,869 (41.7%) |
| Medium | 1,229 (27.4%) |
| High | 1,388 (30.9%) |

Around 58% of our sample was female. Our sample skewed older, with 64% of the sample being 45 years of age or older. About 42% of the sample were characterized as having a low number of hospital visits within the past year, whereas 27% were characterized as having medium numbers of hospital visits and 31% having high numbers of hospital visits. Just over half (53.9%) of our sample was white, with an additional 46% being Black or African American. Since minority enrollment in WeighSmart outside of African Americans and Whites were extremely low (seven total), analysis was limited to these two racial groups. All in all, 4,486 patient records representing 12,559 total analysis times were analyzed in determining the rate of drop-out in enrollment.

Figure A and Table 9 shows the overall survival curve and life table for this study.

Figure A. Overall Survival Curve.

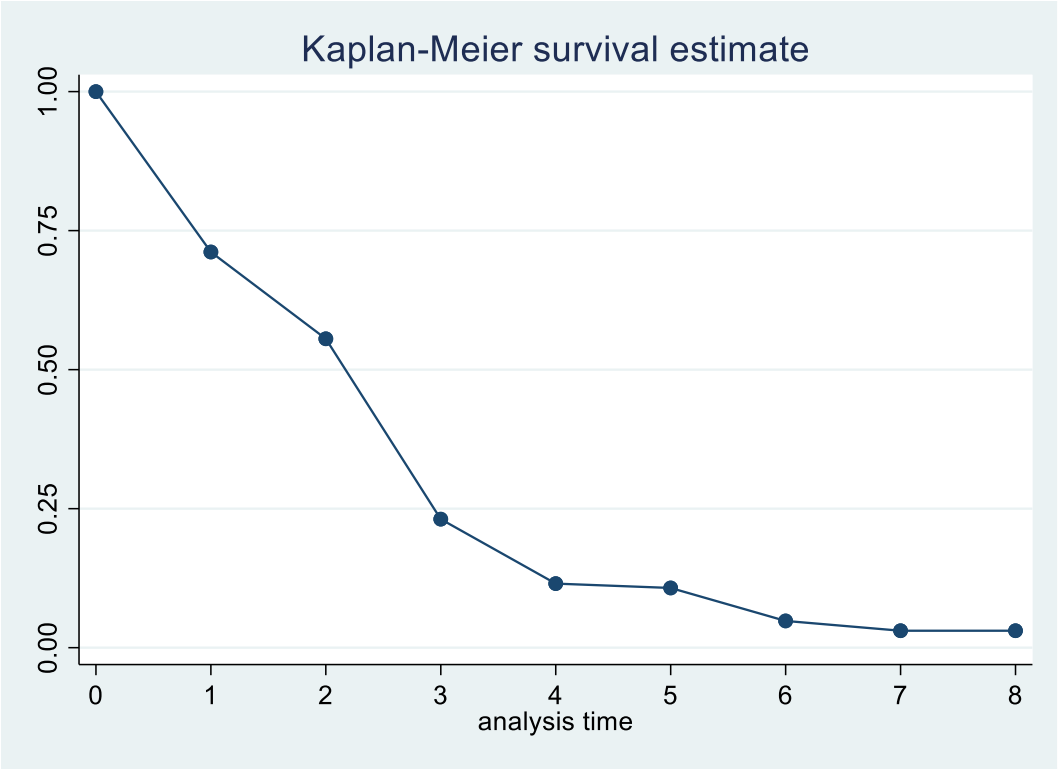


Table 9. Overall life table for Drop-Off.

| Interval | In study at beginning of interval N | Drop out of workflow during interval N | Survived interval N | Survival percentage of interval N | Cumulative survival |
|---|---|---|---|---|---|
| Start | 4486 | --- | --- | --- | --- |
| 0-1 | 4,486 | 1,294 (28.85%) | 3192 | 71.2% | 71.2% |
| 1-2 | 3192 | 700 (21.92%) | 2492 | 78.1% | 55.6% |
| 2-3 | 2492 | 1,455 (58.39%) | 1037 | 41.6% | 23.1% |
| 3-4 | 1037 | 520 (50.14%) | 517 | 49.7% | 11.5% |
| 4-5 | 517 | 35 (6.77%) | 482 | 93.2% | 10.7% |
| 5-6 | 482 | 266 (55.19%) | 216 | 44.8% | 4.81% |
| 6-7 | 216 | 79 (36.57%) | 137 | 63.4% | 3.05% |
| 8 | 137 | --- | --- | --- | --- |

Four thousand four hundred and eighty-six patients were initially included in our sample, and only 137 (3%) survived enrollment into the WeighSmart clinical trial. Almost 29% of patients never interacted with the tablet at all when the nurse or healthcare practitioner gave it to them. Only 12% of the initial individuals eligible for WeighSmart completed the health assessment to determine secondary eligibility for the study. Of those that were eligible, 55% did not provide contact information to access the online portal. Of those that provided their contact information, 63% went online and created an account. Of those that created an account, 63% correctly consented into the study.

Survival curves and life tables for each of the individual predictors were graphed and generated. In addition, Chi-square tests were conducted to determine if there were differences between the groups. The results for each predictor are presented below.

*Race*.

Figure B. Survival curve stratified by race.

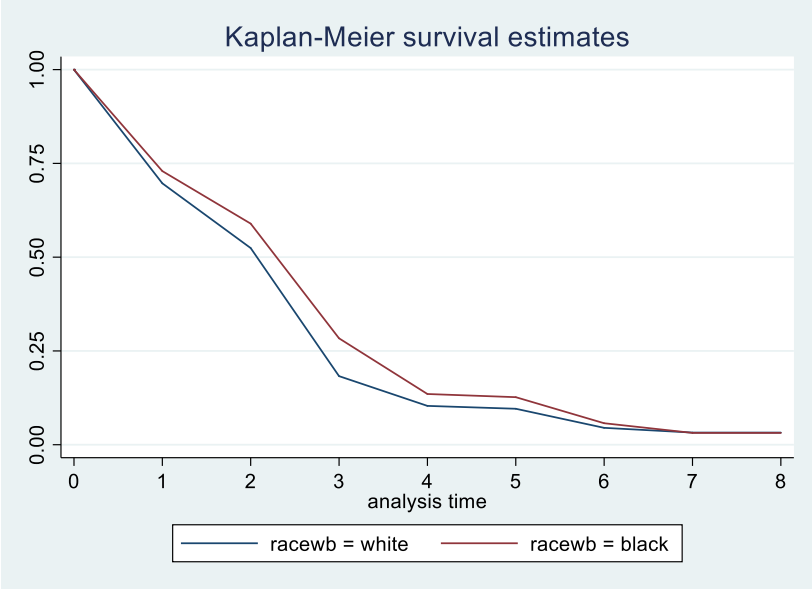


Table 10. Life table stratified by race.

| Stage | Group | In study at beginning of stage N | Drop out of workflow during stage N | Survived stage N | Survival percentage of stage N | Cumulative survival |
|---|---|---|---|---|---|---|
| Start | | | | | | |
| 1 | White | 2220 | 673 (30.3%) | 1547 | 69.7% | 69.7% |
| | African American | 1900 | 514 (27.1%) | 1386 | 72.9% | 73.0% |
| 2 | White | 1547 | 383 (24.8%) | 1164 | 75.2% | 52.4% |
| | African American | 1386 | 266 (19.2%) | 1120 | 80.8% | 59.0% |
| 3 | White | 1164 | 758 (65.1%) | 406 | 34.9% | 18.3% |
| | African American | 1120 | 581 (51.9%) | 539 | 48.1% | 28.4% |
| 4 | White | 406 | 176 (43.3%) | 230 | 56.7% | 10.4% |
| | African American | 539 | 282 (52.3%) | 257 | 47.7% | 13.5% |
| 5 | White | 230 | 17 (7.4%) | 213 | 92.6% | 9.6% |
| | African American | 257 | 16 (6.2%) | 241 | 93.8% | 12.7% |
| 6 | White | 213 | 113 (53.1%) | 100 | 46.9% | 4.5% |
| | African American | 241 | 132 (54.8%) | 109 | 45.2% | 5.7% |
| 7 | White | 100 | 28 (28.0%) | 72 | 72.0% | 3.2% |
| | African American | 109 | 49 | 60 | 55.0% | 3.2% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | (45.0%) | | | |
| 8 | White | 72 | -- | -- | -- | -- |
| | African American | 60 | -- | -- | -- | -- |

**Likelihood-ratio test: p=0.0019

The rate of drop-off in enrollment between African Americans and Whites were compared in this analysis. The overall likelihood-ratio test shows that there is a significant difference in the rate of drop-off between African-American patients and White patients ($p<0.005$). The graph and life table suggest that African-Americans survived longer on the whole throughout the enrollment workflow than their White counterparts, even if similar percentages of African Americans and Whites end up enrolling. This is most highlighted by the fact that 28% of African American participants watched the video as compared to only 18% of White participants. It follows then, that a larger percentage of African Americans drop out after this stage than their White counterparts. This is indeed the case. Of those who completed the health survey, 52% of African Americans were deemed ineligible as compared to 43% of Whites, and 48% of African Americans did not click on the activation link in the workflow as compared to 28% of Whites.

*Gender*.

Figure C. Survival curve stratified by gender.

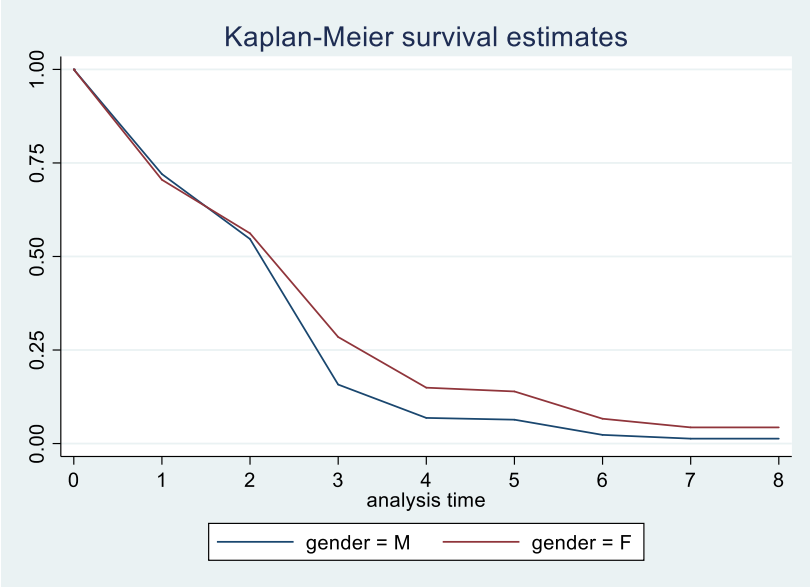


Table 11. Life table stratified by gender.

| Stage | Group | In study at beginning of stage N | Drop out of workflow during stage N | Survived stage N | Survival percentage of stage N | Cumulative survival |
|---|---|---|---|---|---|---|
| Start | | | | | | |
| 1 | Male | 1895 | 530 (28.0%) | 1365 | 72.0% | 72.0% |
| | Female | 2591 | 764 (29.5%) | 1827 | 70.5% | 70.5% |
| 2 | Male | 1365 | 329 (24.1%) | 1036 | 75.9% | 54.7% |
| | Female | 1827 | 371 (20.3% ) | 1456 | 79.7% | 56.2% |
| 3 | Male | 1036 | 737 (71.1%) | 299 | 28.9% | 15.8% |
| | Female | 1456 | 718 (49.3%) | 738 | 50.7% | 28.5% |
| 4 | Male | 299 | 169 (56.5%) | 130 | 43.5% | 6.9% |
| | Female | 738 | 351 (47.6% ) | 387 | 52.4% | 14.9% |
| 5 | Male | 130 | 9 (6.9%) | 121 | 93.1% | 6.4% |
| | Female | 387 | 26 (6.7%) | 361 | 93.3% | 13.9% |
| 6 | Male | 121 | 77 (63.6%) | 44 | 36.4% | 2.3% |
| | Female | 361 | 189 (52.4%) | 172 | 47.6% | 6.6% |
| 7 | Male | 44 | 19 (43.2%) | 25 | 56.8% | 1.3% |
| | Female | 172 | 60 | 112 | 65.1% | 4.3% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | (34.9%) | | | |
| 8 | Male | 25 | -- | -- | -- | -- |
| | Female | 112 | -- | -- | -- | -- |

***Likelihood-ratio test: p<0.001

The difference in drop-off in enrollment between males and females was also compared in this study. Much like the comparison between African Americans and whites, there was also a significant difference between female and male drop-off (p<0.001). Females were significantly more likely to complete the enrollment workflow as compared to their male counterparts. While both groups show similar rates of progress through watching the video, a larger percentage of females completed the health screening assessment than their male counterparts. This trend continued up through actual enrollment into the WeighSmart clinical trial.

*Age*.

Figure D. Survival curve stratified by age(categorical).

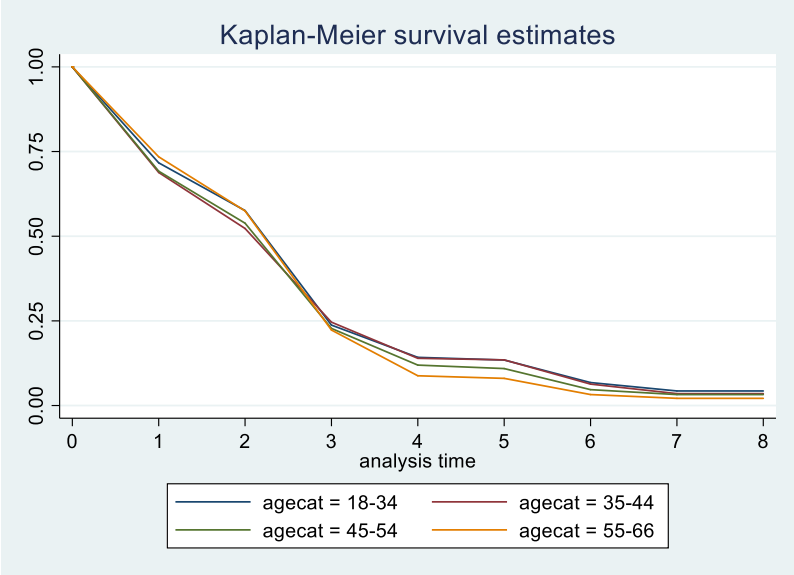

Table 12. Life table stratified by age(categorical).

| Stage | Group | In study at beginning of stage N | Drop out of workflow during stage N | Survived stage N | Survival percentage of stage N | Cumulative survival |
|---|---|---|---|---|---|---|
| Start | | | | | | |
| 1 | 18-34 | 766 | 217 (28.3%) | 549 | 71.7% | 71.7% |
| | 35-44 | 853 | 266 (31.2%) | 587 | 68.8% | 68.8% |
| | 45-54 | 1172 | 361 (30.8%) | 811 | 69.2% | 69.2% |
| | 55-66 | 1695 | 450 (26.5%) | 1245 | 73.5% | 73.5% |
| 2 | 18-34 | 549 | 108 (19.7%) | 441 | 80.3% | 57.6% |
| | 35-44 | 587 | 141 (24.0%) | 446 | 76.0% | 52.3% |
| | 45-54 | 811 | 180 (22.2%) | 631 | 77.8% | 53.8% |
| | 55-66 | 1245 | 271 (21.8%) | 974 | 78.2% | 57.5% |
| 3 | 18-34 | 441 | 259 (58.7%) | 182 | 41.3% | 23.8% |
| | 35-44 | 446 | 236 (52.9%) | 210 | 47.1% | 24.6% |
| | 45-54 | 631 | 364 (57.7%) | 267 | 42.3% | 22.8% |
| | 55-66 | 974 | 596 (61.2%) | 378 | 38.8% | 22.3% |
| 4 | 18-34 | 182 | 73 (40.1%) | 109 | 59.9% | 14.2% |
| | 35-44 | 210 | 91 (43.3%) | 119 | 56.7% | 14.0% |
| | 45-54 | 267 | 127 (47.6%) | 140 | 52.4% | 12.% |
| | 55-66 | 378 | 229 (60.6%) | 149 | 39.4% | 8.8% |
| 5 | 18-34 | 109 | 6 (5.5%) | 103 | 94.5% | 13.5% |
| | 35-44 | 119 | 4 (3.4%) | 115 | 96.6% | 13.5% |
| | 45-54 | 140 | 12 (8.6%) | 128 | 91.4% | 10.9% |
| | 55-66 | 149 | 13 (8.7%) | 136 | 91.3% | 8.0% |
| 6 | 18-34 | 103 | 51 (49.5%) | 52 | 50.5% | 6.8% |
| | 35-44 | 115 | 61 (53.0%) | 54 | 47.0% | 6.3% |
| | 45-54 | 128 | 73 (57.0%) | 55 | 43.0% | 4.7% |
| | 55-66 | 136 | 81 (59.6%) | 55 | 40.4% | 3.2% |
| 7 | 18-34 | 52 | 19 (36.5%) | 33 | 63.5% | 4.3% |
| | 35-44 | 54 | 24 (44.4%) | 30 | 55.6% | 3.5% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 45-54 | 55 | 17 (30.9%) | 38 | 69.1% | 3.2% |
| | 55-66 | 55 | 19 (34.5%) | 36 | 65.5% | 2.1% |
| 8 | 18-34 | 33 | --- | --- | --- | --- |
| | 35-44 | 30 | --- | --- | --- | --- |
| | 45-54 | 38 | --- | --- | --- | --- |
| | 55-66 | 36 | --- | --- | --- | --- |

Likelihood-ratio test: p=0.562

The drop-off in enrollment between the different age groups was also considered for analysis. The likelihood-ratio test concluded that there was no significant differences in drop off between the age categories (p=0.562). Each age group followed a similar rate of drop-off as the other age groups, however more individuals between the ages of 55-66 did not start or complete the health assessment than any other age group.

*Past year visits.*

Figure E. Survival curve stratified by past year visits(tertiled).

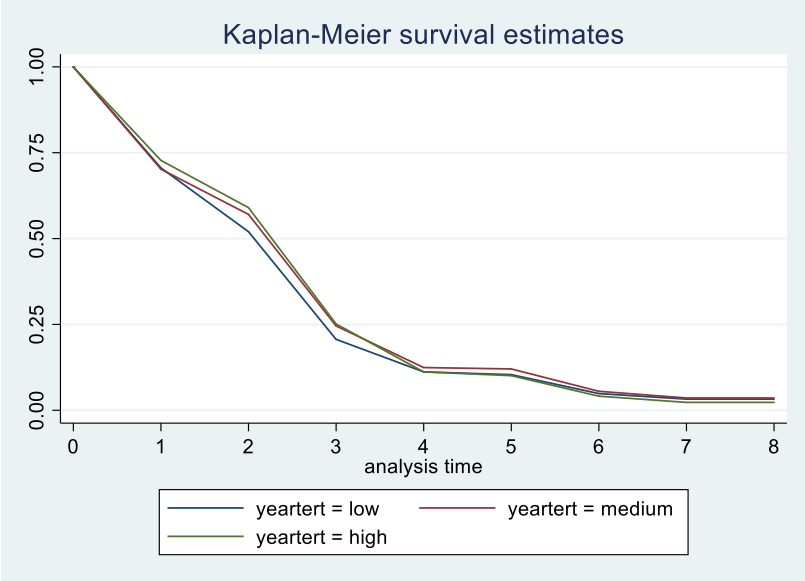

Table 13. Life table stratified by past year visits(tertiled).

| Stage | Group | In study at beginning of stage N | Drop out of workflow during stage N | Survived stage N | Survival percentage of stage N | Cumulative survival |
|---|---|---|---|---|---|---|
| Start | | | | | | |
| 1 | Low | 1869 | 550 (29.4%) | 1319 | 70.6% | 70.6% |
| | Medium | 1229 | 366 (29.8%) | 863 | 70.2% | 70.2% |
| | High | 1388 | 378 (27.2%) | 1010 | 72.8% | 72.3% |
| 2 | Low | 1319 | 347 (26.3%) | 972 | 73.7% | 52.0% |
| | Medium | 863 | 162 (18.8%) | 701 | 81.2% | 57.0% |
| | High | 1010 | 191 (18.9%) | 819 | 81.1% | 59.0% |
| 3 | Low | 972 | 586 (60.3%) | 386 | 39.7% | 20.7% |
| | Medium | 701 | 399 (56.9%) | 302 | 43.1% | 24.6% |
| | High | 819 | 470 (57.4%) | 349 | 42.6% | 25.1% |
| 4 | Low | 386 | 177 (45.9%) | 209 | 54.1% | 11.2% |
| | Medium | 302 | 149 (49.3%) | 153 | 50.7% | 12.5% |
| | High | 349 | 194 (55.6%) | 155 | 44.4% | 11.2% |
| 5 | Low | 209 | 15 (7.2%) | 194 | 92.8% | 10.4% |
| | Medium | 153 | 5 (3.3%) | 148 | 96.7% | 12.0% |
| | High | 155 | 15 (9.6%) | 140 | 90.3% | 10.0% |
| 6 | Low | 194 | 103 (53.1%) | 91 | 46.9% | 4.9% |
| | Medium | 148 | 80 (54.1%) | 68 | 45.9% | 5.5% |
| | High | 140 | 83 (59.3%) | 57 | 40.7% | 4.1% |
| 7 | Low | 91 | 30 (33.0%) | 61 | 67.0% | 3.3% |
| | Medium | 68 | 24 (35.3%) | 44 | 64.7% | 5.6% |
| | High | 57 | 25 (43.9%) | 32 | 56.1% | 2.3% |
| 8 | Low | 61 | --- | --- | --- | --- |
| | Medium | 44 | --- | --- | --- | --- |
| | High | 32 | --- | --- | --- | --- |

Likelihood-ratio test: p=0.361

Finally, the rates of drop-off based on level of previous clinician visits within the last year was analyzed. The likelihood-ratio test determined that there was no significant differences between the different groups (p=0.361). However, much like the overall model, one can see a large drop off in all groups when asked to complete a health screening questionnaire.

### 6.f. Discussion

A large majority of Americans say they are willing to enroll into a clinical trial if one was available (DasMahapatra et al., 2017)(Harris, 2001)(Jenkins et al., 2010)(NIH, 2017a), yet only around 3% of the population enrolls into clinical trials (Anderson & Olson, 2016)(Harris, 2012)(Stiles et al., 2011)(Tanner, 2016). Studies analyzing the reasons as to why individuals are willing to enroll or enroll in clinical trials are prevalent in the literature, however there is a large gap in knowledge when attempting to understand where individuals drop-off between these two stages. “Lasagna’s Law” (Lasagna, 1979) and “Muenchs Third Law” (Bearman et al., 1974) state that researchers should approach many more individuals than what initial estimates initially suggest, offering that this be by a factor of at least three to ten (Cooper et al, 2015)(Nelson, 2017)(Jiang et al., 2016)(Scott et al., 2016). Other studies have confirmed this to be the case and have predicted patient accrual (Carter, 2004) (Gajewski et al., 2015)(Heitjan, Ge, & Ying, 2015)(Zhang & Long, 2010), but these studies focus on recruitment on a macro level, specifically on the beginning and end stages of trial recruitment. This study attempted to better understand where specifically individuals drop out throughout a full enrollment

workflow. It is novel in its approach to this problem by using survival techniques in its analysis, the first study of its kind to the authors knowledge.

The authors found that around 30% of those initially eligible for enrollment had no interaction with the workflow at all, and around 22% of those that did interact had very little interaction. This gives a better understanding on whom could be considered "engaged" and willing to enroll in a clinical trial and shed more light on the gap between willingness to enroll and enrollment. Because so many individuals say they are willing to enroll yet few actually do, the authors suspect the high willingness to enroll can in part be explained by the social desirability bias, or the tendency for individuals to respond in a way that makes them look good or to give a response they believe their audience wants to hear (Paulhus, 1984). Social desirability bias has been found in other studies (Holbrook & Krosnick, 2009)(Krumpal 2013)(Miller et al., 2008) and can lead to inaccurate conclusions (Halpern et al., 2001)(Latkin et al, 2017), especially if the topic revolves around sensitive or personal information. Little research has been conducted on this topic, and the seminal paper (Buchbinder, 2004) on this area only studied hypothetical trial enrolment, not actual trial enrollment (Calamia, Bernstein, & Keller, 2016). It is important for future studies to focus on better understanding the gulf that exists between willingness to enroll and enrollment into actual trials in order to determine if those willing to enroll actually have higher rates of enrollment or that willingness to enroll is simply inflated due to social desirability (Casarett et al., 2004). One suggestion for future studies is to incorporate social desirability measurements in

their baseline assessments and compare these in order to determine how much of an effect this bias has on actual participant willingness to enroll.

Furthermore, this project found the largest drop off between intervals when participants were asked to provide personal information about themselves and also in the follow-up eligibility criterion. This is consistent with other studies that have found participants prefer anonymity (Donovan, Mader, & Shinsky, 2007)(Williams et al., 2013), however this has mostly been analyzed in high risk/stigmatized studies (Boyd et al., 2007)(Gulliver et al., 2010) and other studies have found that anonymity is not as important in some studies (Jones et al., 2009)(Marks & Cavanagh, 2009). Regardless, the increased drop-off when asked to provide personal information could signify a mistrust of the medical system/clinical trials, a barrier to enrollment which has been covered extensively. Unfortunately this study did not measure participants level of comfort or trust with medical institutions and cannot comment on this connection. Future studies should analyze the effect that asking personal information has on drop-off in clinical trial enrollment, specifically trying to uncover what type of personal information interested participants are willing to share and what can be drawn from other sources in order to keep participants in the workflow.

Our results also show differing rates of drop off between men and women as well as African Americans and Whites. Women were significantly more likely than men to complete the enrollment workflow in this study. A higher percentage of women were more likely to be deemed ineligible, however this could be due to the fact that one screening question involved asking if participants were pregnant or

wanting to become pregnant within the next 6 months; a question that males did not qualify for. From this point on, women were more likely to survive the full enrollment workflow than their male counterparts. The researchers hypothesize that since this study was focused on weight loss, the study may have resonated more with women than with men. The literature has found that women tend to be the primary enrollees into non-targeted weight loss studies (Franz et al., 2007; Rounds & Harvey, 2019) and the male to female ratio in this study falls within the bounds of other weight loss studies (Pagoto et al., 2012). Further research should see if this rate of drop-off holds true for clinical trials in other areas outside of weight loss. This research also found no discernable difference between the different age categories and levels of hospital visits within the last year, suggesting that drop-off in enrollment is not affected by these factors. Due to small cell sizes, adjustments for the effect of the other predictors with the predictor of interest was not able to be calculated. Studies in the future should analyze the effects of these predictors in absence of the other predictors to get a more true assessment of their effect.

African Americans were more likely to have engaged with the enrollment workflow than their White counterparts and made it farther on the whole through the workflow, however the final enrollment percentages ended up being roughly equivalent. When prompted to answer some health screening questions, more African Americans declined to answer than their White counterparts, which could reflect African American's distrust of the medical community (Abraham et al., 2006)(Frank, 2004)(Kim et al., 2015)(Langford et al., 2010)(Robinson et al., 216). If

White participants survived to provide contact information and were sent a link to activate an online portal, they were more likely to end up actually activating and engaging the portal. Future studies should attempt to replicate these results and, if replicated, attempt to understand this difference. A better understanding of these differences could lead to more tailored interventions, which could result in higher levels of enrollment and help reduce the racial health disparities that exist today (Owens et al., 2013)(Peek, 2007)(Robinson et al., 2016).

Overall, only 3% of those initially eligible for our trial ended up actually enrolling. While low, this is within the range of the average clinical trial. It is not surprising that our overall enrollment fraction was this low due to the fact that little in-person effort was put forth in recruitment. The only interaction clinician staff had with the patient was the initial presentation of the video. A suggestion for future studies is to focus on the interaction between the patient and the nurse/healthcare worker when initially offering the enrollment opportunity. Higher recruitment has been found when the patient is engaged in the recruitment effort (Estabrooks et al., 2017)(Dononelly et al., 2003)(Gul & Ali, 2009)(Raynor et al, 2009), however there is mixed information regarding the cost effectiveness of active recruitment (Estabrooks et al., 2017)(Foster et al., 2011).

### 6.f. Limitations

While novel and unique, this study has several limitations. First and foremost, this study suffers from selection bias. Participants in our study had to present to our clinic during the recruitment period and be eligible for the

WeighSmart clinical trial to be included in our study. These individuals may differ substantially from the individuals in the general population. Individuals from underserved areas (Baquet et al., 2006)(Bartlett, 2005) (Tanner et al., 2012), those that distrust and/or fear the medical community and shy away from medical care (Hughes et al., 2015), or those that went to clinics other than those participating in our study all could be inherently different from those in our study.

This research is also limited only to analyses between African American and Caucasian individuals. There is evidence that other minority populations, specifically Asian and Latino populations, are even more underrepresented in research than their African American counterparts (Anwuri et al., 2013)(Bruner et al., 2006)(Chalela et al., 2014) (Ford et al., 2008) (Murthy, Krumholz & Gross, 2004) (Stewart et al., 2007). Due to low numbers of other minorities in this hospital system and low numbers of participation in the study, analysis between these groups was not conducted. Future research should examine the effect that offering enrollment to all individuals would have on the enrollment of other racial groups as well. Furthermore, this study was based off of enrollment into a weight loss trial and thus, generalizability both in terms of the population studied and the generalizability of the type of clinical trial analyzed is extremely limited. Future studies should focus on other minority groups as well as other types of trials when examining the rate of drop-off in enrollment.

One drawback of this study is that the reason for why an individual did not continue onto the next workflow stage was not tracked. For example, an individual could have been interrupted by their doctor while filling out the health assessment

and actually had fully intended to complete the assessment rather than losing interest in the workflow process when completing the health assessment. There is no way to delineate these two instances in our analysis. Future studies should take this into consideration when determining where and how enrollment workflow is presented to potential participants. Despite these limitations, this analysis provides valuable insight on the rate of drop-off of a clinical trial enrollment workflow and adds more evidence on how the elimination of the awareness of clinical trials and enrollment opportunity barriers can have an effect on actual enrollment rates.

Furthermore, our study is limited in its generalizability due to the fact that it had many workflow steps that an individual had to go through in order to enroll into the study. An individual had to complete 8 steps from first contact in order to enroll into the WeighSmart clinical trial. Many other studies do not have as many steps in the recruitment workflow, typically only initial approach and explaining the informed consent. There is evidence that the easier the enrollment process, the more likely an individual will enroll (Gul & Ali, 2009)(Thoma, 2010)(Zand et al., 2004). This study cannot determine the effect that the multiple workflow steps had on enrollment, and future studies should focus on the effect that decreasing the number of enrollment workflow steps and subsequently increasing the ease of enrollment has on actual enrollment.

# 7. Study 3.

## 7.a. Research Question 3

*Are there racial disparities in clinical trial enrollment when the opportunity to enroll is offered to all eligible individuals?*

There is evidence of low enrollment across most types of clinical trials. There is also evidence that minorities enroll into clinical trials at a lower proportional rate than their Caucasian counterparts. However, some studies have pointed out that minorities are offered enrollment at a lower rate than Caucasians and that when reasonable attempts are made to enroll minorities, they enroll at a similar rate. This research question attempts to determine if racial disparities in clinical trial enrollment exist when the opportunity to enroll is offered to all eligible individuals.

### 7.b. Recruitment.

Recruitment for this project was the same as the previous study.

### 7.c. Methods

Data were drawn from patients who met the criteria for initial approach of (between 18-66 years of age, a BMI between 25-35kg/m2, not weighing over 375 pounds) the WeighSmart clinical trial. The final outcome variable measured was actual enrollment into the clinical trial. Variables drawn from patient records to use in this analysis included patient race, gender, age, and number of previous visits to a participating clinician within the past year. These variables and their response options are presented below in Table 14.

*Table 14. Variables and Response Categories.*

| Variable | Code | Response categories |
|---|---|---|
| Race | American Indian/Alaska Native | 1 |
| | Asian | 2 |
| | Black or African American | 3 |
| | Native Hawiian or Other PI | 4 |

| | | |
|---|---|---|
| | White | 5 |
| | Hispanic | 6 |
| | Refuse | 7 |
| | No information | 8 |
| | Unknown | 9 |
| | Other | 10 |
| Sex | 0 | Male |
| | 1 | Female |
| Age | 18-99 | 18-99 |
| Clinical visits within the last year | 1-99 | 1-99 |
| Enrolled | No | 0 |
| | Yes | 1 |

Due to low numbers of enrollees outside of African Americans and Caucasians, a new variable for race coded *Racewb* was used in bivariate and multivariable analyses which only included these two groups. Age was collapsed into a categorical variable labeled *Agecat* to better interpret the effect of age on enrollment. In addition, the researchers were also interested in whether the health of the individual would also have an effect on enrollment. Some evidence has shown that healthier individuals tend to be recruited into clinical trials more often due to less co-morbidities (Lind, 2011). The variable *Pastyear* was created which tertiled the number of in network clinician visits within the last year into three categories: low, medium, and high. These changes can be found in Table 15.

*Table 15. Variables and their response categories.*

| Variable | Code | Response categories |
|---|---|---|
| *Racewb* | White | 0 |
| | Black | 1 |

| | | |
|---|---|---|
| *Agecat* | 18-34 | 0 |
| | 35-44 | 1 |
| | 45-54 | 2 |
| | 55-66 | 3 |
| *Pastyear* | Low number of visits | 0 |
| | Medium number of visits | 1 |
| | High number of visits | 2 |

### 7.d. Analysis

Frequencies and percentages were calculated for the predictor and the outcome variable. Bivariate analyses were conducted using Chi-square tests to compare results of the outcome (*Enrolled*) and the predictors (*Racewb, Gender, Agecat, Pastyear*). Logistic regression was used to conduct multivariable analysis on the predictors and the outcome. Due to the low number of enrollees as compared to the overall sample, the Firth method of logistic regression was utilized instead of standard logistic regression to give a better approximate of the effects of the predictors on the outcome (Allison, 2012). The Firth method of logistic regression uses a penalized maximum likelihood estimation rather than the standard maximum likelihood estimation used in standard logistic regression to correct for small sample bias that tends to arise when the proportion of events is small relative to the overall sample size (Allison, 2012). In building the multivariable model, two models were compared: one with only significant predictors and the *Racewb* variable, and one with all four predictors included. *Racewb* was included in both models since we are analyzing whether offering an enrollment opportunity into a clinical trial will have an impact on reducing racial disparities in enrollment. The Akaike information criterion and $R^2$ values for each model were used to assess model fit. Unfortunately,

due to low levels of enrollment, interaction terms between predictors could not be assessed.

### 7.e. Results

*Univariate*

Overall, 4,533 participants were approached to join WeighSmart. Thirty-nine records were excluded due to the fact that they did not have any values for any category or did not meet the initial inclusion criteria (age under 18, age over 66), bringing the overall sample for inclusion in our study to 4,494.

The initial results of the univariate analysis are presented in Table 16. From these initial 4,494 participants, only around 3% (N=136) actually ended up enrolling. Around 42% of the sample identified as Black/African American, and just under half of the sample identified as Caucasian (49.58%). Females comprised 57.79% of our participants, and males comprised the other 42.21%. The age of this sample skewed older: around 17% of participants were between the ages of 18-34, around 19% were between 35-44, around 26% were between 45-54, and 38% were between 55 and 66 years of age. The median number of clinician visits within the last year was 4 and the mean number of visits was 5.8 (SD=5.45), ranging from 0 visits to 63 ($25^{th}$ percentile=2; $75^{th}$ percentile=27). When tertiled, 41.68% were considered to have low visitations, 27.5% had a medium level of visitations, and 31% were considered to have high levels of visitations (the uneven numbers within each category are due to only being able to divide visits by whole integers).

*Table 16. Univariate Results*

| Variable | Total | Did not enroll | Enrolled |
|---|---|---|---|

| | N=4,494 | 4,358 (96.97%) | 136 (3.03%) |
|---|---|---|---|
| **Race** | | | |
| American Indian/Alaska Native | 44 (0.98%) | 43 (97.7%) | 1 (2.27%) |
| Asian | 65 (1.45%) | 64 (98.5%) | 1 (1.54%) |
| Black or African American | 1,906 (42.41%) | 1,849 (97.0%) | 57 (2.99%) |
| Native Hawaiian or Other Pacific Islander | 11 (0.24%) | 11 (100%) | 0 (0%) |
| White | 2,228 (49.58%) | 2,155 (96.7%) | 73 (3.28%) |
| Hispanic | 108 (2.40%) | 106 (98.2%) | 2 (1.85%) |
| Refuse | 13 (0.29%) | 12 (92.3%) | 1 (7.69%) |
| Unknown | 112 (2.49%) | 111 (99.1%) | 1 (0.9%) |
| Other | 7 (0.16%) | 7 (100%) | 0 (0%) |
| **Gender*** ** | | | |
| Male | 1,897 (42.21%) | 1,872 (98.68%) | 25 (1.32%) |
| Female | 2,597 (57.79%) | 2,486 (95.73%) | 111 (4.27%) |
| **Agecat**** | | | |
| 18-34 | 767 (17.07%) | 735(95.83%) | 32 (4.17%) |
| 35-44 | 851 (18.94%) | 820(96.36%) | 31 (3.64%) |
| 45-54 | 1,176 (26.17%) | 1,138 (96.77%) | 38 (3.23%) |
| 55-66 | 1,700 (37.83%) | 1,665 (97.94%) | 35 (2.06%) |
| **Pastyear** | | | |
| Low | 1,873 (41.68%) | 1,814(96.85%) | 59 (3.15%) |
| Medium | 1,236 (27.50%) | 1,192 (96.44%) | 44 (3.56%) |
| High | 1,385 (30.82%) | 1,352 (97.62%) | 33 (2.38%) |

* p<0.01, ** p<0.01, ***p<0.001

*Bivariate*

Bivariate results can be found in Table 17. Chi-square tests show there were significant differences between those who enrolled and those who did not enroll based on gender and age. Women were 3.34 times as likely as men to enroll in the WeighSmart clinical trial. Younger individuals were more likely to enroll into the WeighSmart clinical trial than older individuals. Compared to 55-66 year olds, those who were 45-54 years of age were 1.59 ($p<0.051$) times more likely to enroll. 35-44 year olds were even more likely to enroll (1.80, $p<0.019$) as compared to the 55-66 year olds, and finally 18-34 year olds were 2.04 times ($p<0.003$) as likely to enroll as the oldest age category.

There appeared to be no significant difference in enrollment between African Americans and Caucasians or differences in enrollment by those with low, medium, or high levels of clinician visits within the last year. African Americans were slightly less likely to enroll (.91, p<0.60) than their White counterparts, but this difference was not significant. While those with medium levels of clinician visits within the last year were 1.51 times (p<0.07) as likely as those with the highest level of clinician visits to enroll in the study, this result was not significant. Neither was the lowest level of clinician visits as compared to the highest level of clinician visits (OR= 1.33, p<0.19). Due to low numbers of enrollees, interactive effects between race, gender, age, and clinician visits were not able to be calculated.

*Table 17. Bivariate Results Between Enrollment and Predictor Variables.*

| | Unadjusted | | |
|---|---|---|---|
| Variable | Odds Ratio | Confidence Interval | P-value |
| **Race** | | | |
| White | Ref | --- | --- |
| African American | .91 | .64 – 1.29 | *p*= 0.60 |
| **Gender*** ** | | | |
| Male | Ref | --- | --- |
| Female | 3.34 | 2.16 – 5.18 | *p*<0.001 |
| **Age**** | | | |
| 18-34 | 2.07 | 1.27 - 3.37 | *p*=0.003 |
| 35-44 | 1.80 | 1.10 – 2.94 | *p*=0.019 |
| 45-54 | 1.59 | .997 – 2.53 | *p*=0.051 |
| 55-66 | Ref | --- | --- |
| **Past year visits** | | | |
| Low | 1.33 | .87 – 2.05 | *p*=0.193 |
| Medium | 1.51 | .96 – 2.39 | *p*=0.077 |
| High | Ref | --- | --- |

* p<0.01, ** p<0.01, ***p<0.001

*Multivariable Model.*

The best fitting multivariable model contained all four predictors (race, gender, age, past clinician visits), and the results are shown in Table 18. Although approaching significance, categories of age did not differ significantly after adjusting for other variables in the model. Indeed, when accounting for the effects of the other variables, the only significant predictor of enrollment was gender, with females over three times as likely as their male counterparts to enroll in the WeighSmart clinical trial (OR=3.40, p<0.00). There were no significant age effects nor were there significant effects for number of clinician visits. Since the research question was analyzing racial disparities, we were especially interested in seeing the adjusted effects of race on enrollment. Our multivariable model showed that while African Americans were 19% less likely to enroll in the WeighSmart trial, this result did not approach significance. Once again, interactions between the variables could not be analyzed due to low numbers of enrollees.

Table 18. Multivariable Model Results.

| | Adjusted effects | | |
|---|---|---|---|
| Variable | Odds ratio | Confidence Interval | P-value |
| **Race** | | | |
| White | Ref | --- | --- |
| African American | .81 | .57 – 1.15 | 0.24 |
| **Gender*** ** | | | |
| Male | Ref | --- | --- |
| Female | 3.40 | 2.17 – 5.32 | 0.000 |
| **Age** | | | |
| 18-34 | 1.60 | .97 – 2.64 | 0.067 |
| 35-44 | 1.56 | .94 – 2.59 | 0.085 |
| 45-54 | 1.55 | .97 – 2.48 | 0.064 |
| 55-66 | Ref | --- | --- |
| **Past year visits** | | | |
| Low | 1.37 | .88 – 2.13 | 0.169 |

| | | | |
|---|---|---|---|
| Medium<br>High | 1.47<br>Ref | .92 – 2.36<br>--- | 0.106<br>--- |

Model: Enroll= b1Race + b2Gender + b3Age(categorical) + b4 Clinicanvisits(tertiled)
* p<0.01, ** p<0.01, ***p<0.001

### 7.f. Discussion

Understanding that awareness of and a lack of clinical trial enrollment opportunities is one of the most significant barriers to clinical trial enrollment, this project set out to examine whether racial disparities in clinical trial enrollment existed when the opportunity to enroll was offered equitably to all individuals. Previous literature has found that there tends to be a racial disparity in clinical trial enrollment, with minorities typically being underrepresented unless specifically targeted (Byrne et al., 2012)(Kim et al., 2015)(Langford et al., 2010)(Murhty, Krumholz, & Gross, 2004)(Robinson et al., 2016)(Tan et al., 2015). Reducing racial disparities in clinical trial enrollment and increasing minority enrollment into trials is especially important since minorities tend to bear the burden of disease most heavily (Adams-Campbell et al., 2004)(Anderson & Olson, 2016)(CDC, 2014)(Murthy, Krumholz, & Gross, 2004)(Owens et al., 2013)(Tanner et al., 2014). There is evidence that minorities have less knowledge about enrollment opportunities and are offered less enrollment than Whites (Adams-Campbell et al, 2004)(Baquet et al., 2008)(Brason et al., 2007)(Fisher, 2011)(Wendler, 2005), however recent studies have found that when minorities are offered enrollment and an attempt is made to recruit them, they tend to enroll at similar levels as their White counterparts (Anderson & Olson, 2016)(Kaplan, 2015)(Katz, 2006)(Pinn et al., 2009). The results from this study back up this conclusion. In this study, all

eligible individuals were offered the opportunity to enroll, removing the effect of physician bias in participant selection (Baquet et al., 2008)(Branson et al., 2007)(Penberthy, 2012)(Powell et al., 2008)(Wendler, 2005). Although African Americans were slightly less likely to enroll than their White counterparts, this result did not approach significance in either the bivariate or multivariate models. This suggests that when enrollment barriers relating to access and opportunity to enroll are removed for African Americans, they enroll at a similar rate as their White counterparts. If this is accurate, these results suggest that future trials - especially those struggling to recruit African American participants - should focus on making sure enrollment opportunities are equitably offered to these groups and an honest attempt is made to reach out and recruit these individuals.

While there was no significant difference between African American and White enrollment, there was a significant difference between males and females. Females were over three times more likely to enroll as their male counterparts. As mentioned in the previous study, it is possible that the theme of the study – weight loss - contributed to this disparity. In addition, there were significant differences in enrollment between the different age categories in the bivariate model, with less older individuals enrolling compared to younger individuals. This significance disappeared in the multivariable model, however, signifying that the relationship between age and enrollment seems to be explained at least partially by the other variables in the model. These results should be interpreted with caution due to the width of the confidence intervals, however there is evidence in the literature that older patients tend to be less likely to enroll and less likely to meet inclusion

criterion than younger patients, especially when looking at individuals ages 65 and up (Heiat, Gross, & Krumholz, 2002)(Muthy, Krumholz, & Gross, 2004)(Shenoy & Harugeri, 2015)(Stewart et al., 2007). While outside the scope of our inclusion criteria, future studies should consider increasing the age inclusion criteria to capture patients that fall into this often overlooked age category. Due to low numbers of enrollees in our study, interaction terms were not able to be calculated.

The researchers had hypothesized a priori that by eliminating the most commonly cited barriers to enrollment - the lack awareness and opportunities to enroll - enrollment in the WeighSmart study would be much higher than what was seen in the general population (Hinshaw, Jackson, & Chen, 2007)(Kennedy et al., 2009)(Pina-Robichaux & Watson, 2010)(Rubin et al., 2002). This combined with the fact that the WeighSmart study was designed to be as unobtrusive as possible for the patient, had researchers estimating a higher enrollment fraction than what is seen across most clinical trials (CISCRP, 2016)(Harris, 2012)(Getz, 2007). Surprisingly, this was not the case and elimination of this barrier saw no increased enrollment rate above the industry standard and other diabetic and weight-loss trials (Ames et al., 2005)(Basnet et al., 2017)(Crowley, 2013) (Getz, 2007) (Harris, 2012)(Hazama et al., 1994). It is important to note, however, that the workflow process for this study contained many steps to actual enrollment and saw drop-offs at each stage. It would not be prudent to compare these results with other studies which typically have lower steps to enrollment. The researchers hypothesize that while the opportunity to enroll was offered to all individuals, no real effort was made by the clinician staff to enroll patients. The nurse or healthcare provider

simply asked the individual to watch a short video about clinical trials and, if the patient finished the video, filled out a health questionnaire, and provided contact information, they were then sent the enrollment information. It is the researchers hypothesis that if more of an effort was made by the healthcare staff to encourage these individuals to participate or cover the benefits of enrollment, this study would have seen higher enrollment. Other studies in this area with higher recruitment rates tend to involve in depth recruitment of patients (Friebel et al., 2004)(Lam, Partridge, & Allman-Farinelli, 2006)(Sarkin et al., 1998), but this is not seen across the board (Donnely et al., 2003)(Lam, Partridge, & Allman-Farinelli, 2006). While this study was mainly conducted to see what happens to racial disparities in enrollment when the opportunity to enroll is offered to everyone, future research should take this a step further and analyze if racial disparities in enrollment exists when an honest attempt to recruit all individuals into a clinical trial, not just offering the opportunity to enroll.

### 7.g. Limitations

Drawing from the same population as the previous study, this study suffers from the same limitations. This study suffers from selection bias and a lack of generalizability. Much like the previous study, no other minority group outside of African Americans were compared to the majority in this analysis and generalizability of this study is extremely limited. In addition, a further limitation of our study is that income and educational status were not collected from our patients. These two variables are known influence enrollment (Baquet et al.,

2006)(Chalela et al. 2014)(Katz et al., 2006)(Langford, Resnicow, & An, 2010)(Strasser, Cola, & Rosenblum, 2013) and could possibly attenuate the effect of race on enrollment. Since our data came from electronic medical records, there was no precise way to construct an income variable, and future studies should strive to include these variables in their analysis. Finally, due to low numbers of final enrollment, interactive terms could not be generated for this analysis, possibly obscuring important connections between the variables.

## 8. Innovation

This project is innovative in that it offers enrollment to all initially eligible individuals. One study conducted by the Center for Information and Study on Clinical Research Participation (CISCRP, 2013) found 87% of North American respondents surveyed were at least somewhat willing to participate in a clinical trial if one was offered to them (CISCRP, 2013), yet it has been stated across different studies that relatively few are asked to participate or aware of clinical trials (Bedlack et al., 2010)(Comis et al., 2009)(DasMahapatra et al., 20017)(Owens et al., 2013)(Weckstein et al., 2011). By offering enrollment to all eligible individuals that present to a healthcare visit, this study eliminates one of the most important barriers to enrollment: lack of awareness of enrollment opportunities (Ford, 2008) (Hamel et al., 2016) (Powell et al., 2008) (Williams, 2004) (Wendler, 2005). As shown in previous studies (Bartlett, 2005)(Embi et al., 2005)(Heinemann, 2011)(Jenkins et al., 2010)(Joseph & Dohan, 2009)(Kopcke & Prokosch, 2014)(Penberthy, 2012) (Ramirez, 2012)(Schoren et al., 2011)(Tanner,

2016)(Williams, 2004) the physician can also act as a barrier in recruitment, especially when recruiting minority populations. By offering enrollment to all individuals based on eligibility criteria only, this study removes any conscious or unconscious biases that may result from physician selection while still utilizing one of the most effective communication channels to reach individuals (Ramirez, 2012)(Tanner, 2016)(Ulrich 2016).

This study is also innovative in that it tracks the survival of patients from initial contact all the way through enrollment. A rule of thumb for patient recruitment is "Lasagna's Law" (Lasagna, 1979) which states that only around 10% of the total number of participants available for a study will actually pass through to enrollment. While this has been an oft-cited statistic (Frank, 2004)(Tan et al., 2015)(Treweek, 2011), there has been little analysis of the rate of patient drop-off in the recruitment process. At best, the large majority of clinical trial studies report simply the number of those approached for inclusion, the number that are eligible, the number that drop out, and the final sample. This leaves a dearth of information about which steps in the enrollment process can be improved upon in order to increase clinical trial participation. This study is unique in that it employs survival analysis to determine the rate of patient drop-off in the enrollment process. To the authors knowledge, it is the first study to utilize these techniques in this way to visually track and represent the drop-off in the workflow process.

In addition, this study addresses two other major barriers to clinical trial participation previously identified in the literature. It has been well documented that a lack of knowledge of clinical trials affects a patients enrollment decision

(Abraham et al., 2006)(Anderson & Olson, 2011)(Banda et al., 2012)(Byrne et al., 2012)(Du et al., 2008)(Hughes et al., 2015) (Kaplan, 2015)(Langford et al., 2010) (Miller et al., 2013)(Owens et al., 2013)(Robinson et al., 2016)(Stiles et al., 2011) (Strasser, Cola, & Rosenblum, 2013)(Tanner et al., 2016) and that this lack of knowledge can lead to distrust/misperceptions of clinical trials (Ejiogu, 2011)(Ford et al., 2011)(Owens et al., 2013). It has been estimated that up to 40% of enrolling patients do not have enough information or knowledge to make a truly informed enrollment decision (Stiles et al., 2011). An increase in clinical trial knowledge has shown to have an impact on decisional conflict during enrollment (Manne et al., 2014), attitudes towards clinical trials (Banda et al., 2012)(Du et al., 2008)(Owens et al., 2013), and has been theorized to improve clinical trial participation (Abraham et al., 2006) (Banda et al., 2012)(Baquet et al., 2006)(Baquet, Mishra, & Weinberg, 2009)(Miller et al., 2013)(Owens et al., 2013) (Robinson et al., 2016). However, the actual impact of improving knowledge on increasing enrollment is in dispute (Caldwell et al., 2010)(Stiles et al., 2011) and largely unstudied.

While there are educational materials describing clinical trials published by the American Cancer Society (ACA) (ACA, 2011) and the National Institutes of Health (NIH, 2007), these materials are hard to incorporate during a routine healthcare visit. In 2011, the ACA published “About Clinical Trials;” a comprehensive 30 minute video series that educates patients about the importance and inner workings of clinical trials. Around half of physicians spend less than 17 minutes per patient interaction (Peckham, 2016), leaving little room for clinical trial discussion. For an educational video to be successfully shown at the point of care, it must address the

most important aspects of clinical trials as well as be short enough to deliver to patients during a routine visit. This study is innovative in that it attempts to understand and tease out the most important topics presented in this video with the intent to distill this information into a future video (5 minutes or less) that can be presented to patients while they wait to see their healthcare professional. In this way, this study addresses the additional time burden put on clinicians that explaining clinical trials to patients entails in an attempt to increase the amount of physicians discussing clinical trials with patients.

## 9. Overall Conclusions and Recommendations.

This study shows that addressing low enrollment rates into clinical trials is a complicated issue. By attempting to address the barriers associated with low enrollment from the beginning, during enrollment, and assessing the results of enrollment, this project has come to some key conclusions and recommendations.

The first recommendation is that a video resource such as the About Clinical Trials video series could be very beneficial in raising knowledge, understanding, and comfort with clinical trials in the population as a whole; however this resource is too lengthy on its own for many individuals and is not feasible to be shown in a healthcare setting while waiting to be seen by a healthcare professional. Developing a short 5 minute or less video that could be shown to patients as they wait for their healthcare provider could improve knowledge, understanding, and comfort with clinical trials and could influence patients willingness to enroll in clinical trials. Not only could this video have an impact on patients willingness to enroll, it would also

free up the provider as well by already covering the basics of clinical trials. Furthermore, a resource such as this has the potential to open up lines of dialogue between the patient and physician, which often leads to increased enrollment.

This dialogue can only happen, however, if there is already a solid relationship between the provider and patient. Past literature has shown that trust in the provider is essential to not only clinical trial recruitment, but to improved health outcomes as a whole. Our qualitative study backs up this claim, yet also shows that the patient/provider relationship may not be today where it needs to be. Although well outside the scope of this project, an increased focus on developing deeper, more personalized connections between doctor and patient could improve clinical trial enrollment and health outcomes for the population as a whole. The authors suggest additional training with physicians and staff on how to recruit and discuss clinical trial opportunities with patients and an increased focus on dialogue between patients and physicians. However this recommendation comes with a caveat in that improved relations can only happen when there is a relationship to build upon in the first place. Often, those with the worst health outcomes tend to have the least resources and tend not have many touchpoints with the medical sector. These sorts of improvements may not reach these individuals that clinical trials may most benefit, and thus alternate methods of delivery of this video may be considered for future research.

Through qualitative interviews, our research has also lent evidence to the important topics and themes that should go into the development of this educational video resource. According to these interviews, risks, benefits, the ability

to withdraw at any time without penalty, what a clinical trial is, links to additional information about clinical trials and health resources, and safety and standard of care are topics and themes that are absolutely essential to cover in the video. Furthermore, this video should be a general video about clinical trials and should not go into too much depth on the mechanizations behind them, instead leaving that to additional resources that are more in depth that the individual can watch at their own leisure. In addition, this initial video needs to contain links to enrollment opportunities for interested individuals to easily enroll into trials that they are eligible for.

While the development of this video has the potential to increase willingness to enroll, there is no guarantee that this willingness to enroll will translate into actual enrollment. As stated many times previously, the large majority of Americans state that they are willing to enroll into a clinical trial, yet very few actually do. Our second study found that even when presented with the possibility to enroll, around 44% of participants had little or no interaction with the enrollment workflow, with the majority of these individuals having no interaction. This suggests that individuals' willingness to enroll may not be an accurate proxy for final enrollment, and that willingness to enroll may be inflated due to social desirability bias. Since there is scant evidence in the literature analyzing the transition between willingness to enroll and actual enrollment, the researchers cannot stress enough the importance of more research being done in this area. While ample research has been conducted on the reasons why individuals do or do not enroll into clinical trials, future research should use this knowledge to better understand how to

transition those that are willing to enroll to actual enrollment. The researchers found the largest proportional drop-offs at the stages where participants were asked to answer questions about themselves or provide contact information, and thus one recommendation is to limit the amount of personal data that interested participants must provide before the informed consent process takes place. Furthermore, at each interval in the workflow, participants were lost. It is unclear in this analysis if this loss was due to fatigue or due to the actual actions asked of the participants. Other recruitment studies tend not to have as many steps in the enrollment workflow process as this, and it is not advised to compare the results of this analysis to those with only one or two steps. However, this project found similar levels of enrollment despite the many workflow steps that individuals had to go through to enroll, suggesting that there is a possibility of increased enrollment if the workflow was limited. If replicated in the future, this study should limit the number of steps it requires to enroll into the study.

Finally, it is recommended that at the very least, enrollment is offered to all individuals equitably. Previous studies have shown that minorities are underrepresented in clinical trial research, yet they are also offered less enrollment opportunities than their Caucasian counterparts. This study lends credence to the theory that minorities will enroll at the same rates as Whites as long as enrollment is offered equitably and a reasonable effort is made to recruit them. This study found that there was no significant disparity in enrollment between African Americans and Whites, and the researchers credit this to automating enrollment to all eligible individuals. Future studies should see if this result holds true for other

minority groups as well. In addition, while it may be promising that African American and White enrollment did not differ significantly, both groups hovered at an enrollment fraction of only 3%. While low, this does not differ substantially from what is seen in the general population which is both concerning and promising. It is concerning in the fact that simply removing the access to enrollment barrier may not be enough to increase participation into clinical trials. Instead, stronger attempts to recruit individuals such as increased physician dialogue or recommendation may be necessary to improve clinical trial enrollment rates. However this study is also promising in that it suggests a low effort automated recruitment effort is enough to at least reach the typical enrollment standard seen throughout clinical trials. For organizations that lack time and resources for active recruitment, given enough time this type of recruitment could lead to minimal recruitment for small scale studies.

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# Appendix A

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**Tablet Screening**

Patient must give responses in bold to qualify.

1. Do you want to lose weight?

    **Yes**/No

2. Are you currently participating in a structured weight loss program or a weight loss study?

    Yes/**No**

3. In your lifetime, have you experienced any of the following:

    a. myocardial infarction (heart attack) Yes/**No**

    b. cancer Yes/**No**

    c. eating disorder Yes/**No**

    d. bariatric surgery Yes/**No**

4. Do you have a diagnosed thyroid condition and/or do you take thyroid medication?

    Yes/**No**

5. Are you pregnant, planning to become pregnant in the next 6 months, or breastfeeding?

    Yes/**No**

6. Are you willing and able to receive text messages as part of the study? Standard messaging rates for your phone will apply.

    **Yes**/No

7. Would you be willing to provide your email address and phone number to be contacted by a study staff person?

    **Yes**/No

8. Do you have access to the internet from a computer or smartphone?

    **Yes**/No

# Appendix B

## Comprehension Questions

Patient must give responses in bold to qualify.

1. For this study I will be asked to:

    a. exercise 5 times a week

    b. follow a specific diet plan

    **c. weigh-in when I receive a text and fill out an online questionnaire once a month**

2. All of my weights, questionnaire answers, and some health information my medical records will be available to the research staff.

    **True**/False

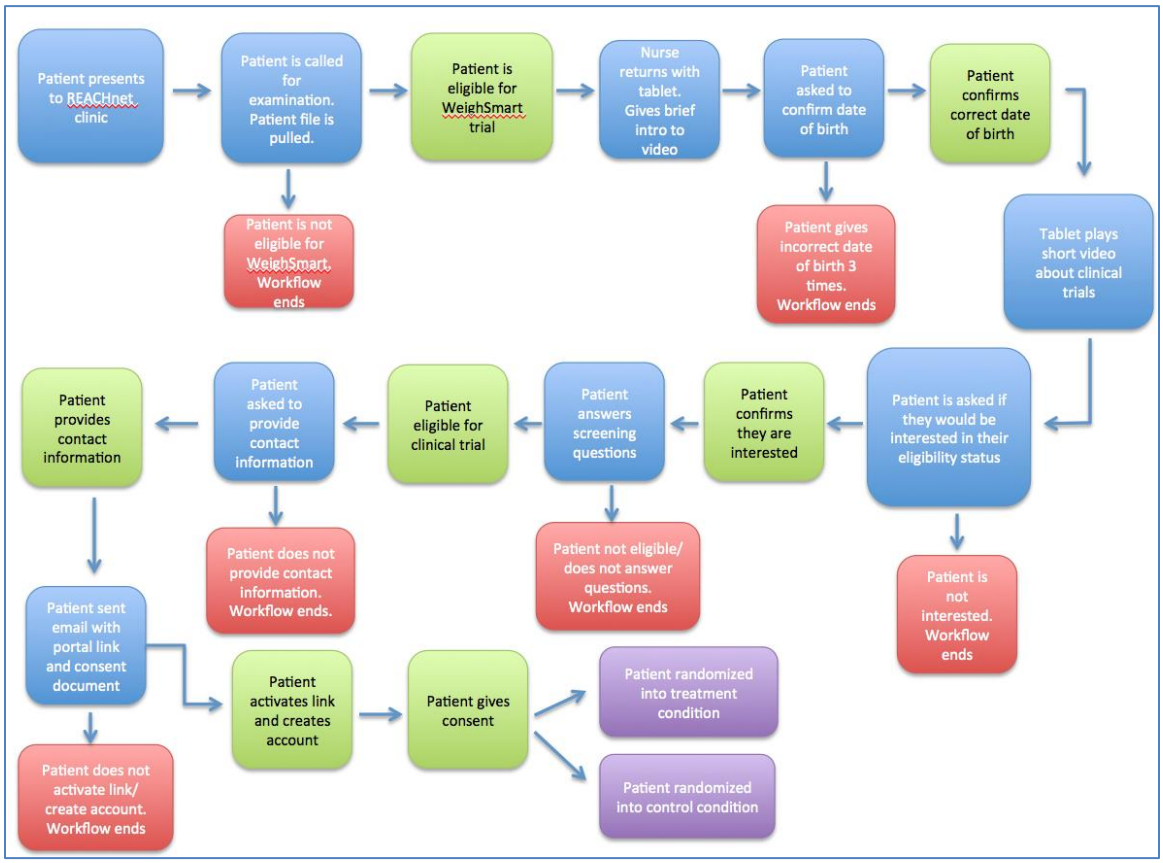
3. I understand that my data for this study are stored electronically and there is a very small risk that the security could be compromised.

    **True**/False

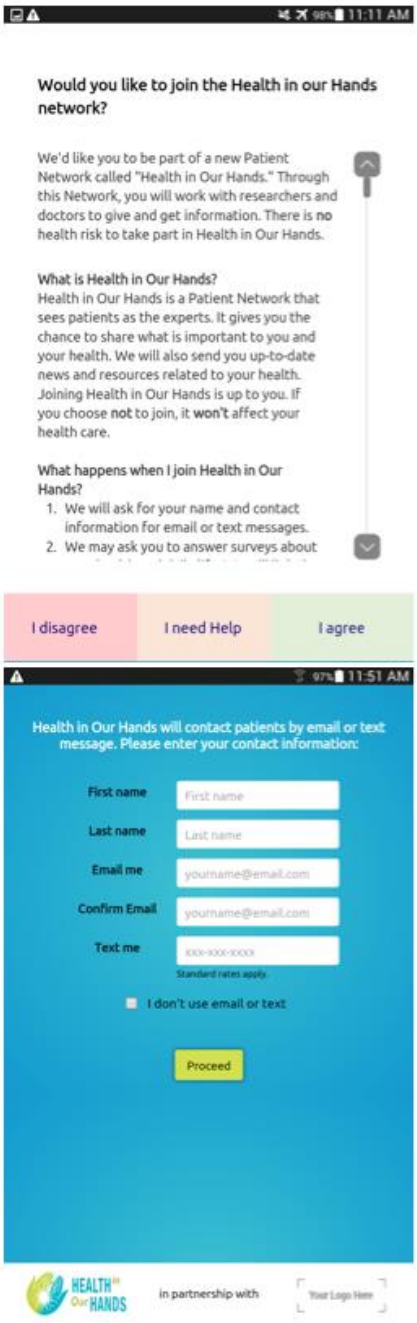
4. Once I enroll in the study I can choose to stop at any time.

    **True**/False

# Appendix C


Patient presents to REACHnet clinic
Patient is called for examination. Patient file is pulled.
Patient is not eligible for WeighSmart. Workflow ends
Patient is eligible for WeighSmart trial
Nurse returns with tablet. Gives brief intro to video
Patient asked to confirm date of birth
Patient gives incorrect date of birth 3 times. Workflow ends
Patient confirms correct date of birth
Tablet plays short video about clinical trials
Patient is asked if they would be interested in their eligibility status
Patient is not interested. Workflow ends
Patient confirms they are interested
Patient answers screening questions
Patient not eligible/ does not answer questions. Workflow ends
Patient eligible for clinical trial
Patient asked to provide contact information
Patient does not provide contact information. Workflow ends.
Patient provides contact information
Patient sent email with portal link and consent document
Patient does not activate link/ create account. Workflow ends
Patient activates link and creates account
Patient gives consent
Patient randomized into treatment condition
Patient randomized into control condition

# Appendix D





Would you like to answer 6 short questions about your health now? In the future, we may ask you to respond to health questions when you're at the clinic, but we will not contact you directly.

No, Thanks | Continue

# Appendix E.

**Tulane University Human Research Protection Office**
***Increasing Knowledge and Access to Clinical Trials on Clinical Trial Enrollment***

**Principal Investigator:** E. Cannon Ledford
**Study Title:** ***Increasing Knowledge and Access to Clinical Trials on Clinical Trial Enrollment***

**Why is this study being done?**

We are conducting this research study to determine what information is important to share with patients in order to increase their knowledge, understanding, and comfort with clinical trials. Previous research has shown that many people are uncomfortable with clinical trials and do not have a good understanding on why they are necessary and how they work. While there are great educational videos out there describing clinical trials, most of these resources are either very short and do not give much information or are quite long and in depth, often clocking in at 30 minutes or longer. The researchers in this study are attempting to uncover the most important themes and topics from these longer videos that will improve a persons knowledge and comfort with clinical trials in order to develop a short (around 5 minutes) video that can be given to patients as they wait to see a doctor during a regular health care visit.

**What are the study procedures? What will I be asked to do?**

If you agree to take part in this study, you will be asked to be interviewed by a researcher. The interview will begin by you filling out a questionnaire asking about your familiarity with clinical trials as well as a few questions about yourself. After filling out this section of the questionnaire, you will then answer questions assessing your knowledge and understandings of clinical trials. After answering these questions, you will then be asked to watch the "About Clinical Trials" video series produced by the American Cancer Society. After watching the series, you will be asked to answer the same knowledge and understanding questions in order to see how the video series affected your previous answers. After answering these questions, the researcher will ask you about your satisfaction with the video series and if there were any topics and themes that should have been covered more in depth or if there were any that could have been cut out. After answering these questions, you will be asked to list the important topics and themes that a video attempting to improve understanding and comfort of clinical trials should cover. After listing all of these topics and themes, you will be asked to sort these topics and themes in terms of importance. After sorting these topics and themes, you will be asked to re-sort them in terms of importance if you were to develop a video that was only 5 minutes long that was to be shown to patients in a health care setting as they wait to be seen by a health care provider.

The interviews will take place in the Fall of 2018 and Spring of 2019 at the Louisiana Public Health Institute (1515 Poydras St. Suite 1200, New Orleans, LA 70112) or at the interviewees location of choice. Interviews will be conducted until a minimum of 25 unique interviews have been completed. Each interview will be anonymous and last

between an hour to an hour and a half. The audio from the interviews will be recorded and transcribed in order to ensure answers are accurately reported.

**What are the risks or inconveniences of the study?**

We believe there are minimal risks associated with this research study. There is a slight risk of a breach of confidentiality, however all interviews will be conducted anonymously and all recordings will be kept in a locked safe and destroyed when the study is complete. Furthermore, there will be a possible inconvenience in the time it takes to complete the study and the travel to get to the study site. A final risk is that due to the subject matter, participants may feel more concerned about their health after participation that they otherwise would have had they not participated.

**What are the benefits of the study?**

Direct benefits to the participant from their involvement in this study include an increased knowledge and understanding of clinical trials, which could positively affect their health in the future. In addition to these direct benefits, participation in this study will increase knowledge surrounding clinical trial enrollment as well as inform future studies in the development of educational materials that may be given to patients at the point of care. These future educational materials could have a direct impact on the health of individuals in the future by encouraging individuals to participate in clinical trials.

**Will I receive payment for participation?**

Participants will be given a $20 gift card at the conclusion of the interview for their participation.

**Are there costs to participate?**

The only costs to this study are transportation fees. Participants will be compensated for their parking costs when they arrive at the interview location.

**How will my personal information be protected?**

The following procedures will be used to protect the confidentiality of your data. The researchers will keep all study records (including any codes to your data) locked in a secure location. In addition, all records will be identified by a unique code and names will remain anonymous. A master key that links names and codes will be maintained in a

separate and secure location. All electronic files containing identifiable information will be password protected. Any computer hosting such files will also have password protections to prevent access by unauthorized users. Only the members of the research staff will have access to the passwords. All audio files will be given a unique code and names will not be used throughout the recording. At the conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations. Audio recordings will be destroyed as soon as they are properly transcribed. Transcriptions and other data described in this paragraph will have all identifying data removed and be kept for 3 years to ensure publication of the data. All other information will be maintained in accordance with the security provisions of this paragraph and destroyed at the conclusion of the study.

You should also know that the Tulane University Human Research Protection Office, Social/Behavioral Institutional Review Board (IRB) and/or the Office of Research Compliance may inspect study records as part of its auditing program, but these reviews will only focus on the researchers and not on your responses or involvement. The IRB is a group of people who review research studies to protect the rights and welfare of research participants.

## Can I stop being in the study and what are my rights?

You do not have to be in this study if you do not want to. If you agree to be in the study, but later change your mind, you may drop out at any time. There are no penalties or consequences of any kind if you decide that you do not want to participate. In addition, you do not have to answer any question that you do not want to answer.

## Who do I contact if I have questions about the study?

Take as much time as you like before you make a decision to participate in this study. We will be happy to answer any question you have about this study. If you have further questions about this study, want to voice concerns or complaints about the research or if you have a research-related problem, you may contact the principal investigator, Cannon Ledford at (228) 623-1545 or eledford@tulane.edu.

## Disclosure of Potential Conflict of Interest

The investigator in this study has no conflicts of interest that would affect this study.

# Appendix F

Development of a Short Video to Improve Patient Knowledge, Understanding, and Comfort Surrounding Clinical Trials Questionnaire.

You are about to participate in a survey of knowledge and understanding of clinical trials. The survey should take between 10-15 minutes to complete. The purpose of the survey is to gain understanding of public knowledge and understanding of clinical research so that future educational materials about clinical trials can be developed and shown to patients during a visit to a healthcare center. All responses that you give will remain confidential and you will be assigned a randomized number in order to ensure your anonymity. Demographic questions such as race, age, and gender are asked only for research purposes and will not be tied with your name in any way. You do not have to answer any question you do not feel comfortable with.

**Demographics**

Id number_____ Gender_____

Age_____ Race/Ethnicity_____

Highest level of education_____

**Trial Experience**

| Questions | Response options (circle one) | | |
|---|---|---|---|
| 1. Have you ever heard about clinical trials? | Yes | No | Don't Know/Not sure |
| 2. Have you ever participated in a clinical trial? | Yes | No | Don't Know/Not sure |
| 3. Do you know anyone who has participated in a clinical trial? | Yes | No | Don't Know/Not sure |

**Trial Knowledge**

| Questions | | Response options (circle one) | | |
|---|---|---|---|---|
| 1. | One reason clinical trials are run is to improve the treatment of future patients. | True | False | Don't Know/Not sure |
| 2. | One of the major purposes of a clinical trial is to compare the effects (good and bad) of two or more different ways of treating patients in order to see which is better. | Yes | No | Don't Know/Not sure |
| 3. | One of the major purposes of clinical trials is to test the safety of a new drug or treatment. | Yes | No | Don't Know/Not sure |
| 4. | If I participate in a clinical trial, it is possible that the study sponsor, various government agencies, or others who are not directly involved in my care can review my medical records. | Yes | No | Don't Know/Not sure |
| 5. | There may not be direct medical benefit to me from my participation in this clinical trial. | Yes | No | Don't Know/Not sure |
| 6. | After I agree to participate in a clinical trial, my treatment may be chosen randomly (by chance) from two or more possibilities. | Yes | No | Don't Know/Not sure |
| 7. | If I had not wanted to participate in a clinical trial, I could have declined to sign the consent form. | Yes | No | Don't Know/Not sure |
| 8. | I have to remain in the clinical trial even if I decide someday that I want to withdraw. | Yes | No | Don't Know/Not sure |

## Trial comfort

| Questions | | Response (Circle one) | | | | |
|---|---|---|---|---|---|---|
| 1. | I have a good understanding of how clinical trials work | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 2. | If I had the option, I would definitely consider joining a clinical trial | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |

## Understanding

How well do you feel you understand the following aspects of clinical trials? If you don't understand the item at all, please circle 1. If you understand it very well, please circle 5. If you understand it somewhat, please circle a number between 1 and 5 (the higher number representing more understanding).

| Questions | | Response (Circle one) | | | | |
|---|---|---|---|---|---|---|
| 1. | Clinical trials involve research | 1 | 2 | 3 | 4 | 5 |
| 2. | What the researchers are trying to find out in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 3. | The treatments and procedures you could undergo | 1 | 2 | 3 | 4 | 5 |
| 4. | The possible risks and discomforts of participating in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 5. | The possible benefits to you of participating in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 6. | The alternatives to participation in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 7. | The effect of the clinical trial on the confidentiality of your medical records | 1 | 2 | 3 | 4 | 5 |
| 8. | Clinical trial participation is voluntary | 1 | 2 | 3 | 4 | 5 |

# Appendix G.

Development of a Short Video to Improve Patient Knowledge, Understanding, and Comfort Surrounding Clinical Trials Questionnaire After Video.

**Trial Knowledge**

| Questions | | Response options (circle one) | | |
|---|---|---|---|---|
| 1. | One reason clinical trials are run is to improve the treatment of future patients. | True | False | Don't Know/Not sure |
| 2. | One of the major purposes of a clinical trial is to compare the effects (good and bad) of two or more different ways of treating patients in order to see which is better. | Yes | No | Don't Know/Not sure |
| 3. | One of the major purposes of clinical trials is to test the safety of a new drug or treatment. | Yes | No | Don't Know/Not sure |
| 4. | If I participate in a clinical trial, it is possible that the study sponsor, various government agencies, or others who are not directly involved in my care can review my medical records. | Yes | No | Don't Know/Not sure |
| 5. | There may not be direct medical benefit to me from my participation in this clinical trial. | Yes | No | Don't Know/Not sure |
| 6. | After I agree to participate in a clinical trial, my treatment may be chosen randomly (by chance) from two or more possibilities. | Yes | No | Don't Know/Not sure |
| 7. | If I had not wanted to participate in a clinical trial, I could have declined to sign the consent form. | Yes | No | Don't Know/Not sure |
| 8. | I have to remain in the clinical trial even if I decide someday that I want to withdraw. | Yes | No | Don't Know/Not sure |

**Trial comfort**

| Questions | | Response (Circle one) | | | | |
|---|---|---|---|---|---|---|
| 1. | I have a good understanding of how clinical trials work | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 2. | If I had the option, I would definitely consider joining a clinical trial | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |

**Understanding**

How well do you feel you understand the following aspects of clinical trials? If you don't understand the item at all, please circle 1. If you understand it very well, please circle 5. If you understand it somewhat, please circle a number between 1 and 5 (the higher number representing more understanding).

| Questions | | Response (Circle one) | | | | |
|---|---|---|---|---|---|---|
| 1. | Clinical trials involve research | 1 | 2 | 3 | 4 | 5 |
| 2. | What the researchers are trying to find out in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 3. | The treatments and procedures you could undergo | 1 | 2 | 3 | 4 | 5 |
| 4. | The possible risks and discomforts of participating in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 5. | The possible benefits to you of participating in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 6. | The alternatives to participation in a clinical trial | 1 | 2 | 3 | 4 | 5 |
| 7. | The effect of the clinical trial on the confidentiality of your medical records | 1 | 2 | 3 | 4 | 5 |
| 8. | Clinical trial participation is voluntary | 1 | 2 | 3 | 4 | 5 |

# Appendix H

**Satisfaction**

| | Questions | Response (Circle one) | | | | |
|---|---|---|---|---|---|---|
| 1. | The video contained too much information | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 2. | The video contained too little information | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 3. | My knowledge of clinical trials has increased after watching this video | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 4. | Patients should receive information like this before deciding whether or not to join a clinical trial | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 5. | This material helped me better understand clinical trials | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 6. | This material would help me in making a decision about joining a clinical trial | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 7. | I would recommend this material to a friend who needed information about clinical trials | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 8. | The information was easy to understand | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 9. | I feel more comfortable with clinical trials after watching this video | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |
| 10. | I feel better prepared to discuss clinical trials with my physician after watching this material | Strongly Disagree | Disagree | Neutral | Agree | Strongly Agree |

## Appendix I.

| Development of short–form video | | |
|---|---|---|
| V1 | What, if anything, did you find helpful in the video? | Open ended response |
| V2 | What, if anything, did you find unhelpful in the video? | Open ended response |
| V3 | What topics or ideas (if any) in the video would you have wished the video focused more on to help you decide on participating in a clinical trial? | Open ended response |
| V4 | What topics or ideas (if any) presented in the video do you view as unnecessary when discussing clinical trial participation? | Open ended response |
| V5 | Which topics or ideas (if any) presented in the video helped you feel more comfortable with clinical trials? What about [topic] made you feel more comfortable? | Open ended response |
| V6 | Which topics or ideas (if any) presented in the video made you feel less comfortable with clinical trials? What about [topic] made you feel less comfortable? | Open ended response |
| V7 | The total length of time of these videos clocks in at over 28 minutes. Using this video as a reference, what topics and themes should be covered in order to increase patient comfort and knowledge of clinical trials? | Free listing response |
| V8 | Why is it important that [topic] should be covered? | Open ended response |

## Appendix J

**Code Report**

Selected codes (76)

---

- **Awareness of CT**
- **Benefits**
- **Breaking up video series**
- **Bring a caregiver**
- **Can be cut**
- **Cancer**
- **Car wash**
- **Comfort**
- **Connecting with doctor/team**
- **Create additional resources**
- **CT knowledge**
- **Dialogue promotion**
- **Distrust**
- **Diversity**
- **Doctor patient relationship**
- **Doctor prospective**
- **Engaging/enjoyable**
- **Extra costs**
- **Fears**

○ **General video**

○ **Graphics**

○ **Guinea pig**

○ **Help with condition**

○ **Helpful**

○ **Important**

○ **In depth**

○ **Informative**

○ **Informed consent**

○ **IRB**

○ **Jargon**

○ **Learned about**

○ **Legal**

○ **Length**

○ **Like aspect**

○ **More likely to enroll**

○ **Music**

○ **Need to include**

○ **Negative**

○ **Negative feedback**

Comment: by ecled

> *Any statement made by participants that represented something the patient disliked about the video series or something that the patient was not happy with in the series. Examples of negative feedback included "not realistic" "I didn't like," "I would not," and "too long." Any item coded "too long," "too general," or "repetitive" was automatically coded negative feedback.*

- **Nurse**
- **Overwhelm**
- **Patient prospective**
- **Placebo**
- **Play in background**
- **Positive**
- **Positive feedback**

Comment: by ecled

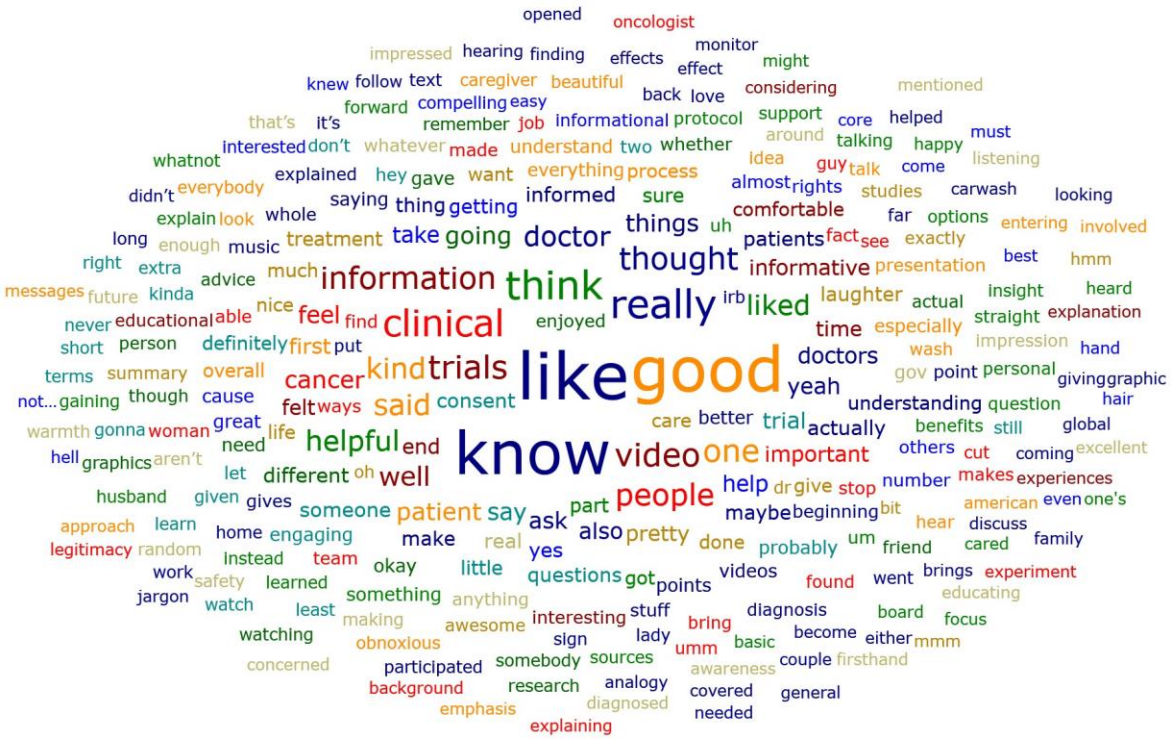
> *Any statement made by participants that represented something "good" or something the patient liked about the video series. Examples of positive feedback included "Good" "I liked," "Important," and "Helpful." Any item coded "like aspect," "helpful," "important," "informative" "useful" and "engaging/enjoyable" was automatically coded positive feedback.*

---

- **Pull out at any time**
- **Quesitions about**
- **Questionnaire issues**
- **Ranking**
- **Reliable information**
- **Repetitive/redundant**
- **Representative**
- **Risks**
- **Roadmap**
- **Safeguards**
- **Safety**
- **Side effects**

- **Specific condition/disease**
- **Standard of Care**
- **Summaries at end**
- **Things to add**
- **Too general**
- **Too long**
- **Trust**
- **Understanding**
- **Understanding difficulty**
- **Useful**
- **Video 1**
- **Video 2**
- **Video 3**
- **Video 4**
- **Video 5**
- **Video 6**
- **Warm**
- **Website/additional resources**

## Appendix K.


opened
oncologist
impressed
hearing
finding
effects
monitor
effect
might
knew
follow
text
caregiver
beautiful
back
love
considering
mentioned
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compelling
easy
that's
it's
remember
job
informational
protocol
support
core
helped
around
talking
happy
must
interested
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whatever
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understand
two
whether
idea
guy
talk
come
listening
whatnot
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hey
gave
want
everything
process
almost
rights
studies
carwash
looking
didn't
everybody
saying
thing
getting
informed
sure
comfortable
far
options
entering
involved
explain
look
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treatment
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nice
feel
find
clinical
really
irb
liked
laughter
actual
insight
heard
never
educational
able
enjoyed
time
especially
straight
explanation
short
person
definitely
first
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impression
hand
terms
summary
overall
cancer
kind
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like
good
doctors
wash
gov
point
personal
giving
graphic
not...
gaining
though
cause
felt
ways
said
consent
yeah
understanding
question
hair
warmth
gonna
woman
great
life
care
better
trial
actually
benefits
still
global
need
helpful
end
know
video
one
important
others
cut
coming
excellent
hell
graphics
aren't
let
different
oh
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husband
given
gives
someone
patient
say
ask
part
people
help
dr
give
stop
number
makes
experiences
approach
learn
home
engaging
make
real
also
pretty
maybe
beginning
bit
american
even
one's
hear
discuss
legitimacy
random
yes
done
probably
um
friend
cared
family
work
instead
team
okay
little
questions
got
points
videos
found
went
brings
experiment
safety
learned
educating
jargon
watch
least
something
anything
stuff
diagnosis
board
focus
making
awesome
interesting
bring
watching
obnoxious
sign
lady
umm
basic
become
either
mmm
concerned
participated
somebody
sources
awareness
couple
firsthand
background
research
analogy
covered
general
emphasis
diagnosed
needed
explaining

# Appendix L.


course couldn't certainly
defining beginning become banging average comes
delete bucolic authority ethnicity especially aspects bullet around check
couple believe experiences luck age entire educated slide anything... assume
billion general gold coast come bus effects drug directly somebodies charts
darker... affects guy all... fear double points that's aspect
focus first confusing white population whole will two caucasian says ...there comics
boston granddaughter different consent diversity summary background anybody's
charcoal help ages anything somebody guess everything best repetitive another three children
though impression experience desk may probably find make big time certain patient terms found agents
conversations inaudible next rather trying might well doctors family ordinary talked doesn't adults
crazy include lots base learn seem everybody feel bad getting
cover none thinking disease don't ask felt even clinical think irb remember sort building anymore
mocking face definitely medical good much hit videos didn't physician else table deleted
aside now least hear benefits woman doctor just know long us lot trial care legal open makes reading chronic
bus..."you investigational explain something okay cancer kind dog trials thing said look diagnosis carwash
patients love likely boats either put going information friend tell common black decide
convince necessary back language try see people one little take need away color caregiver anyway
warm nothing heck involved person really video can say yeah bit maybe better watch quite
scene last side pick mind cant helpful treatment want end support words sure question caring
almost rush daughter boring pretty music go understand high whatever things level college ummm crisp
seems bobblehead there's definition second speak read use looking standard instead crossing putting care...well
thoughts part someone talking saying talk cause five african overall stuff went demographics breathe clearly
bring won't ask... honestly way american show minutes important made bill
y'all window know... speaking asian community sometimes camera spoke beautiful
alone adopted realistic needs always blind current playing regular bunch cut
aspirin afraid wonder oncologists opinion placebo change
client along you're particular baby beach
coffee attack adoption arms call attribute comfortable
bullets... choppy
consideration

# Appendix M.

## Appendix N.

| Subject | Most important | Important if there's time | Can be cut |
|---|---|---|---|
| 1 | What is a clinical trial?<br>Why are clinical trials conducted and what is their purpose?<br>Why should I participate?<br>Scientific rigor behind clinical trials.<br>Always receive at least standard of care.<br>Option to withdraw.<br>How will information be protected/who has access to records?<br>How to find more information about clinical trials. | Side effects/risks/adverse events.<br>How will they be addressed?<br>Benefits.<br>Costs (tests, transportation, etc.). | What to ask my physician.<br>Will I get to know test results.<br>Follow up/contact with research team.<br>Why is this being done.<br>Procedure/Protocol.<br>How long is the study? |
| 2 | Risks<br>Safety | Where to find clinical trials<br>Research resources (where to find more info)<br>Cost (time, $) | Process/what will happen<br>Types of treatments (placebo) |
| 3 | Can I quit anytime<br>What to expect<br>Personal benefits<br>Protocol/procedure<br>Risks<br>Purpose | Informed consent<br>Time commitment<br>IRB<br>Global benefits<br>Confidentiality | Exclusionary criteria<br>Talking to team of caregivers<br>Relying on reputable sources<br>Personal anecdotes |
| 4 | Learn all you can about your condition from your doctor (what kind is it, what stage, what treatment).<br>Be an active part of treatment.<br>Which people should I consider to be on my treatment team.<br>Am I eligible to | What is a clinical trial?<br>How do I find out about trials on my disease area?<br>Do you offer participation in a clinical trial? Why or why not?<br>If no, does someone else offer?<br>participation? | What is informed consent? How does it protect me?<br>Are there drawbacks to quitting the trial?<br>If I cant to quit the trial, can I? |

| | | | |
|---|---|---|---|
| | participate in a clinical trial? | How do clinical trials work?<br>Am I protected? How?<br>Risks.<br>Benefits.<br>Time commitment.<br>Expenses.<br>Do I get paid for participation?<br>Is CT part of my treatment or is it a broader study?<br>What is placebo?<br>Can I opt out?<br>Who to talk to about making a decision to participate.<br>Who can explain the trial and who can I ask questions? | |
| 5 | Be careful of use of language.<br>What is a clinical trial?<br>Reason for the clinical trial.<br>Everything will be explained to you.<br>Benefits.<br>Risks.<br>Use of real people.<br>You will be cared for.<br>Ask questions.<br>Care won't be taken away<br>Time involved.<br>Where to find resources | Include a nurse in video. | |
| 6 | Informed consent gives the participant the right to withdraw from the trial at anytime for any reason.<br>Risk.<br>Even if the trial does not help the individual in | | |

| | | | |
|---|---|---|---|
| | the trial, it may positively impact future participants.<br>Length of trial.<br>Benefit.<br>Safety. | | |
| 7 | Privacy.<br>Informed consent.<br>Who should participate.<br>Importance of clinical trials. | Safety of study.<br>More intense personal care.<br>Different types of trials. | Downfalls of participating in trials.<br>What the trial is looking for. |
| 8 | Standard of care.<br>Study undergoes IRB review.<br>Can be casual/light (not about life threatening things).<br>Personal info/data safety.<br>Withdraw. | Protocol<br>Monitoring/ongoing IRB review/oversight.<br>Awareness of commitment (could involve extra visits or tests). | IRB<br>Informed consent. |
| 9 | Patients' expectation.<br>Side effects.<br>Who does it benefit.<br>Higher lever of care and monitoring during study. | | Background of studies in general/short history.<br>Procedure.<br>Location of study.<br>Renumeration.<br>Duration of trials.<br>Trial sponsors. |
| 10 | Bringing your prescriptions/telling about other conditions.<br>Patients can say something if they don't understand/patient voice matters.<br>Trusting relationship.<br>Empowering the participant.<br>Brochures for those w/out internet.<br>Transportation. | | |

| | | | |
|---|---|---|---|
| 11 | Introduction to CT's.<br>What CT's are.<br>Why you should participate. | Who is involved/funds.<br>Potential benefits.<br>Potential risks/harms. | Additional information/resources.<br>Questions and Answers.<br>Support.<br>Ending survey. |
| 12 | What CT's are<br>Reasons to have CT's.<br>Why participation is important.<br>Benefits to participation.<br>Risks to participation.<br>Standard of care.<br>Government involvement/protection.<br>Opt out at any time.<br>Benefit to society. | | |
| 13 | What is a CT.<br>Benefits.<br>Risk.<br>Standard of Care.<br>Placebo.<br>Treatment options.<br>Dropping out of trial.<br>Privacy. | Accessing more info.<br>Communication with doctor.<br>Cost. | What trial is studying.<br>Length of trial.<br>Health Safeguards.<br>Informed consent. |
| 14 | Giving consent.<br>All possible treatments.<br>Doctor/healthcare team as your ally.<br>Before you see doctor, what info do you need.<br>Your particular diagnosis.<br>Diversity in presentation.<br>Informed consent.<br>Bring a friend. | How we develop CT's.<br>Safeguards.<br>Extra costs/time.<br>Extra testing.<br>Who pays for CT.<br>Standard of care.<br>What is a CT. | How CT will affect your life.<br>Placebos. |
| 15 | What is a CT.<br>Gather information yourself.<br>Extra resources available. | What will CT mean to me as a patient? | Trust in doctor. |

| | | | |
|---|---|---|---|
| | Informed consent.<br>Other patient perspectives. | | |
| 16 | Is the trial reputable?<br>Doctor knowledge of trial.<br>Expected results.<br>Risk factors. | Is the trial right for you (cost/benefit analysis)?<br>Success rate of trial. | Relationship with your doctor. |
| 17 | More information.<br>Risks.<br>Better clarification. | Benefits.<br>What is a CT? | |
| 18 | Risks.<br>Benefits.<br>Your rights as a patient.<br>Informed consent. | What CT's do for future medical treatment/how CT's can help those in future or test new medications<br>(Additional) Costs of joining a trial.<br>Confidentiality. | Questions patients should ask/Asking questions. |
| 19 | What goes into a CT/Safety testing of CT.<br>Still get Standard of Care in addition to treatment.<br>What is consent and it's protections. | CT's aren't just sugar pills/Don't use placebos.<br>Extra time/costs of CT's. | Benefits for everyone/Altruism.<br>Remember to ask questions. |
| 20 | Homelessness.<br>Poverty. | Recovery. | |
| 21 | What a trial is.<br>Mental health issues.<br>Abuse and where to turn<br>Going to the doctor is good.<br>Addiction.<br>Benefits of CT. | | |
| 22 | How CT's work.<br>Materials/resources.<br>Care/Safety. | | |

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| 23 | Risks and Benefits.<br>Speak directly to camera.<br>Website/phone number for extra resources.<br>Can leave at anytime.<br>Laughter.<br>Show warm relationships between Dr. and Patient.<br>Patients navigating the system.<br>Emphasize altruism.<br>Happy voice encouraging participation.<br>Diversity of subjects<br>Compensation.<br>Roadmap diagram for a CT journey.<br>Show the ease of enrollment.<br>Patient testimony. | Links to available trials.<br>Warm interaction between family and doctors.<br>Smiling actors.<br>Animation/Graphics.<br>The birthday cake scene.<br>Couples having fun.<br>Subjects being examined.<br>Bright clothing.<br>Actors speaking directly to camera. | Equal minority family representation.<br>Safety of trials.<br>Upbeat music. |