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Research Participation Decision-Making Among Youth and Parents of Youth with Chronic Health Conditions: A Dissertation

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RESEARCH PARTICIPATION DECISION-MAKING AMONG YOUTH AND PARENTS OF YOUTH WITH CHRONIC HEALTH CONDITIONS

A Dissertation Presented

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TABLE OF CONTENTS

Abstract

The purpose and aims of this qualitative descriptive study were to describe how past experiences with research (including communication, information, values and support) may contribute to research fatigue among youth and parents of youth with HIV, CF, and T1D. Eighteen parents and youth were purposively recruited from outpatient subspecialty clinics at a major academic medical center. They took part in qualitative interviews, completed a demographics form, and the *Decisional Conflict Scale.* Youth participants also completed the *Erikson Psychosocial Stage Inventory*. Two major themes emerged: blurred lines and hope for the future. Research fatigue was not found in this sample. Results point to challenges with informed consent in settings where research and clinical care are integrated, and suggest that protective factors allow for continued participation without excess burden on youth and parents. Strategies to minimize research fatigue and support engagement in research are offered.

Research Participation Decision-Making and Research Fatigue among Youth and Parents of Youth with Chronic Health Conditions:

A Dissertation Proposal

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Introduction and Specific Aims

Clinical research is necessary to improve the care and treatment of individuals living with chronic health conditions (CHC). The National Institutes of Health (1998) require that children under the age of 21 be included in all human subjects' research. This underscores the importance of including of youth in clinical research agendas for CHC. HIV infection, cystic fibrosis (CF), and type 1 diabetes (T1D) are examples of CHC that have benefitted from pediatric-focused research funding by numerous private and governmental agencies (Cystic Fibrosis Foundation, 2014; National Institutes of Health, 2014; Type 1 Diabetes TrialNet, 2014) leading to significant advances in treatment and improved outcomes. These conditions share common features: the need for daily medications and frequent medical follow up, the potential for complications and reduced life expectancy, and the lack of available cure. Youth living with these CHC are likely to have been approached about participation in clinical research and may be asked to engage again as the research agendas in these areas are progressive and include the efforts to find a functional cure for HIV (Deeks et al., 2012), the use of mutation-specific drug therapy in CF patients (Pettit, 2012), and the use of continuous loop technology in the management of T1D (Larson & Pinsker, 2013; Phillip et al., 2012).

One challenge to enrollment is when eligible participants decline to take part. Failing to meet target accrual in a clinical research study negatively impacts power, internal and external validity (Burns, 2009), and the ability of the study to address its primary endpoints (Schroen et al., 2012). Enrollment refusal and attrition are high in studies of youth with chronic conditions, with rates of refusal averaging 37% and attrition 20-32% (Karlson & Rapoff, 2009). Slow recruitment can lengthen the data collection period resulting in excess cost and premature closure of the study (Muth, Yu, Alston, & Ellenberg, 2001; Peters-Lawrence et al., 2012).

Studies examining factors that influence youth participants and their parents have focused on motivations to participate in clinical research (Broome & Richards, 2003; Tait, Voepel-Lewis, & Malviya, 2003; Wynn et al., 2010). Reasons for declining research participation have been less thoroughly investigated; however children and adolescents are strongly influenced by relationships with adults, particularly their parents and research staff (Broome & Richards, 2003; Broome, Richards, & Hall, 2001).

For HIV-infected youth, it has been hypothesized that participation burn-out from repeated research engagements may be to blame for declining research participation (Pagano-Therrien, 2013). Research fatigue and related concepts have been described in a number of fields (Bradburn, 1978; Clark, 2008; Finau, 2011; Helgesson, 2011; Kolch et al., 2010; Maar et al., 2011; Odland & Nieboer, 2012; Sharp, 1983; Shue, 2011; Ulrich, Wallen, Feister, & Grady, 2005) but have not been explored in youth with CHC who have taken part in clinical research. Research fatigue is defined as apathy, indifference, or resistance to research (Clark, 2008)**.** Because further advances in science will help improve the health and well being of youth with HIV, CF, and T1D, the goal is to promote engagement in research**,** and to decrease the burden of participation and the incidence of research fatigue among youth with these targeted CHC.

The purpose of this qualitative descriptive study is to describe how past experiences with research may contribute to research fatigue among youth and parents of youth with HIV, CF, and T1D. Components of the *decisional conflict* framework (O'Connor, 1995, 2010) will guide this study. Youth and parents of youth with HIV, CF, and T1D who have previously participated in or declined participation in a clinical research study will be interviewed separately. The specific aims of this study are to:

1. Describe how communication and information about past clinical research participation informs decision-making about research participation among youth and parents of youth with chronic health conditions.

2. Describe how participant's values influence decision-making about engagement in clinical research among youth and parents of youth with chronic health conditions.

3. Describe what types of support youth and parents of youth with chronic health conditions perceive to be important to decrease participation burden and research fatigue.

4. Describe potential strategies to optimize support for decision-making about participation and for reducing burden and fatigue among youth and parents of youth with CHC taking part in clinical research.

The ability to engage these populations in research is critical to advance science and improve the health and well being of youth with CHC in general. The long term goal is to improve the overall approach to clinical research through the development of interventions to engage youth and their parents without over burdening families by providing necessary support and facilitating informed, collaborative decision-making.

Background and Significance

Factors Influencing Research Participation Among Youth

Studies of motivators and barriers to the engagement of youth in research have focused primarily on factors that influence parental attitudes and decision-making (Barratt, Levickis, Naughton, Gerner, & Gibbons, 2013; Buscariollo et al., 2012; Caldwell, Butow, & Craig, 2003; Hoberman et al., 2013; Rothmier, Lasley, & Shapiro, 2003; Sammons, Atkinson, Choonara, & Stephenson, 2007; Tait et al., 2003; Tait, Voepel-Lewis, Siewert, & Malviya, 1998; van Stuijvenberg et al., 1998; Woolfall et al., 2013; Wynn et al., 2010). Studies describing the

perspective of children and adolescents indicate that participation is highly influenced by relationships with adults, including parents and research staff (Broome & Richards, 2003; Broome et al., 2001). Communication between a child and parent may directly influence the parental decision to consent (Tait et al., 2003) and parental decisions may be impacted by their child's health status (Sammons et al., 2007), where parents with children who are acutely ill may be more likely to consent.

Table 1 summarizes the motivations and barriers to participation in clinical research as described by parents, children, and adolescents in a variety of qualitative and quantitative studies, including randomized controlled trials (RCT). The populations of youth under investigation in these studies represent a wide variety of pediatric conditions including, but not limited to: asthma, type 1 diabetes, surgery, pneumonia, obesity, vesico-ureteral reflux, sickle cell disease, neurodevelopmental and sleep disorders, and steroid induced osteopenia.

Table 1: Factors influencing research participation

Motivations, or reasons given by those who consent to participate	**Barriers, or reasons given by those who decline participation**
Parental perspective	
To contribute to science or medical knowledge (Rothmier et al., 2003; Sammons et al., 2007; van Stuijvenberg et al., 1998; Wynn et al., 2010) To benefit one's child (Buscariollo et al., 2012; Hoberman et al., 2013; Sammons et al., 2007; Tait et al., 2003; van Stuijvenberg et al., 1998; Woodgate & Edwards, 2010; Wynn et al., 2010) To gain more information (Caldwell et al., 2003; Rothmier et al., 2003; Sammons et al., 2007; van Stuijvenberg et al., 1998) Desire closer monitoring or follow up (Caldwell et al., 2003; Hoberman et al., 2013; Sammons et al., 2007; Wynn et al., 2010) Physician or staff trust and/or encouragement (Buscariollo et al., 2012; Caldwell et al.,	Fear of randomization, unknown, negative experiences (Barratt et al., 2013; Caldwell et al., 2003; Hoberman et al., 2013; Sammons et al., 2007; Tait et al., 2003; Wynn et al., 2010) Uncertainty • Due to placebo (Tait et al., 2003; van Stuijvenberg et al., 1998) • Due to risks, side effects (Buscariollo et al., 2012; Caldwell et al., 2003; Sammons et al., 2007; Tait et al., 2003; van Stuijvenberg et al., 1998; Wynn et al., 2010) Distrust of research (Buscariollo et al., 2012; Tait et al., 2003; Wynn et al., 2010) Child as "guinea pig" (Buscariollo et al., 2012; Caldwell et al., 2003; Tait et al., 2003)

2003; Hoberman et al., 2013; Rothmier et al., 2003; Tait et al., 2003; Woodgate & Edwards, 2010; Woolfall et al., 2013) Study and consent understandable, favorable risk versus benefits, adequate time to decide (Buscariollo et al., 2012; Caldwell et al., 2003; Hoberman et al., 2013; Tait et al., 2003)	
Shared parental and youth perspectives	
To benefit others (Broome et al., 2001; Buscariollo et al., 2012; Caldwell et al., 2003; Sammons et al., 2007; van Stuijvenberg et al., 1998; Wendler, Abdoler, Wiener, & Grady, 2012; Woodgate & Edwards, 2010; Woolfall et al., 2013) To access a new drug or treatment (Broome & Richards, 2003; Caldwell et al., 2003; Rothmier et al., 2003; Woolfall et al., 2013; Wynn et al., 2010) Financial benefit, incentives (Broome & Richards, 2003; Caldwell et al., 2003; Rothmier et al., 2003)	Invasive tests involving needles,(Sammons et al., 2007) extra bloodwork or diagnostic procedures (Broome & Richards, 2003; Wynn et al., 2010) Time commitment, convenience (Barratt et al., 2013; Broome & Richards, 2003; Buscariollo et al., 2012; Caldwell et al., 2003; van Stuijvenberg et al., 1998; Wynn et al., 2010)

Parents and youth agree to research participation when there is clarity about the potential benefits: accessing a new drug or treatment; receiving more intensive follow up; accessing new information about the condition; or potential financial compensation (Broome & Richards, 2003; Caldwell et al., 2003; Hoberman et al., 2013; Rothmier et al., 2003; Sammons et al., 2007; van Stuijvenberg et al., 1998; Woolfall et al., 2013; Wynn et al., 2010). Parents assess whether the benefits of a study outweigh potential risks, and the likelihood of participation is higher when parents perceive a study to be important (Tait et al., 2003) and low-risk (Hoberman et al., 2013; Tait et al., 2003). Parents and youth are also motivated by altruism, specifically, a desire to help others with the same medical condition (Broome et al., 2001; Buscariollo et al., 2012; Caldwell et al., 2003; Sammons et al., 2007; van Stuijvenberg et al., 1998; Wendler et al., 2012; Woodgate & Edwards, 2010; Woolfall et al., 2013), or more broadly, to contribute to scientific or medical

knowledge (Rothmier et al., 2003; Sammons et al., 2007; van Stuijvenberg et al., 1998; Wynn et al., 2010). This desire to help may be driven by a feeling of obligation on the part of parents (Caldwell et al., 2003; van Stuijvenberg et al., 1998).

Trust and positive communication between research staff, parents, and patients can influence the decision to participate (Broome & Richards, 2003; Rothmier et al., 2003; Tait et al., 1998; Woodgate & Edwards, 2010; Woolfall et al., 2013). Encouragement and support from care providers are motivators. Communication includes written information of study details, such as the understandability of the informed consent form. Poor communication is a potential barrier to participation. Putting pressure on families, by giving them insufficient time or space to consider the research, can lead to distrust of the researcher or the research process (Buscariollo et al., 2012; Tait et al., 2003; Wynn et al., 2010).

Burden is a major barrier to clinical research participation and includes the invasiveness of study procedures. Perceived burden varies based on the type and frequency of study evaluations, where procedures involving needles (e.g. blood tests and injections) were deemed particularly burdensome to families (Buscariollo et al., 2012; Caldwell et al., 2003; Sammons et al., 2007; Wynn et al., 2010). Burden also refers to the inconvenience of participation, including factors such as time commitment, travel and transportation arrangements, and the need to miss work or school. Fear and uncertainty of study safety and risk of side effects, both known and unknown, are barriers to participation. Higher levels of parental uncertainty and anxiety are associated with refusal to participate (Hoberman et al., 2013; Sammons et al., 2007).

Uncertainty is highest in studies that include placebos, randomization, and/or blinding (Tait et al., 2003; van Stuijvenberg et al., 1998). Parents who have a greater understanding of research (Tait et al., 2003) and the principles of randomization and blinding (Hoberman et al.,

2013) are more likely to consent for their child to participate. Parents who decline participation for their child often fear their child being used as a *guinea pig* (Buscariollo et al., 2012; Caldwell et al., 2003; Tait et al., 1998).

Respondent Burden and Research Fatigue

Respondent burden, defined as the research subject's perception of psychological, physical, or economic hardship associated with participation in research (Ulrich et al., 2005), can present a significant challenge to study enrollment and can negatively impact data quality. Interviews that require significant time and effort, involve the collection of sensitive information, or necessitate multiple sessions to complete add to burden (Bradburn, 1978; Sharp, 1983). Measurement scales that involve a large number of variables and are lengthy or time consuming are also burdensome (Strickland, 1996). Minimizing the burden of study procedures is noted to be an important safeguard (Kolch et al., 2010) for children who are considered to be a vulnerable population requiring special protection as research subjects (National Institutes of Health, 1998).

Research fatigue manifests as apathy, indifference, or resistance to research and arises from subjects who are unable to recognize changes as a result of previous research participation, or who become overwhelmed by practical issues related to repeated research participation, such as time, financial strain, or transportation (Clark, 2008). Research fatigue has been documented among small, vulnerable, or under-represented groups (Finau, 2011; Maar et al., 2011; Odland & Nieboer, 2012). Contributing factors include: perceptions of helplessness and the research as overly investigator-driven; failure to consider the value of community input to ensure culturally and contextually relevant studies; perceptions that previous research is being duplicated or results are not being translated; utilized research methods do not engage the participants or are not preferred by a given population; lack of communication resulting in feelings that nothing has

changed or that no feedback was given to participants based on prior research findings (Finau, 2011; Maar et al., 2011; Odland & Nieboer, 2012). Avoidance of research fatigue is important for successful recruitment and retention to studies in populations that may have repeated opportunities for research participation. Research fatigue has not been formally studied in children, but has been suspected in a small group of research-experienced HIV infected youth (Pagano-Therrien, 2013), but the proposed study will be the first to formally explore research fatigue in a population of youth who have participated in research for various chronic illnesses.

Chronic Health Conditions in Youth

Conditions such as asthma, which may only require episodic care, and obesity, which can be reversed with lifestyle interventions, are increasingly common, but are driven by social and ecological causes (Halfon & Newacheck, 2010) that place these conditions in a different category from HIV, CF, and T1D. These conditions are similar in the need for daily medication, frequent medical appointments, and the potential for complications and reduced life expectancy. These three CHC are set apart from many others because there are currently no cures available. Each has the potential to be immediately life threatening, but with treatment, individuals can be stabilized, altering the clinical course from acute to chronic. The advancement of care and treatment for youth with HIV, CF, and T1D can be directly attributed to clinical research.

Current Research in HIV, CF, and T1D

Several recent reports in the HIV literature have generated excitement at the prospect of achieving an HIV cure (Hutter et al., 2009; Hütter & Thiel, 2011; Persaud et al., 2013; Saez-Cirion et al., 2013; Taylor, Wilkin, Shalev, & Hammer, 2013). These reports highlight the importance of examining HIV reservoirs in working towards a functional or sterilizing HIV cure, and the potential role of perinatally HIV-infected youth as subjects of investigation. Nursing

research on the aging perinatally infected population is ripe for investigating issues of self efficacy (Erlen, Cha, Kim, Caruthers, & Sereika, 2010) and related issues in the transition from pediatric to adult care (Pearlstein et al., 2013). Improving medication adherence (Robbins et al., 2013), HIV prevention (Fisher, Lee, & Boudreau, 2014), as well as management of depression and other mental health issues (Brawner, 2012) in youth with HIV also require further study.

Although initially promising, gene therapy for treatment of CF has proven challenging and there are currently no ongoing human clinical trials involving gene therapy for CF (Hoffman & Ramsey, 2013). However, improvement in quality of life remains a priority with current research focusing on the CF model, including impaired mucociliary clearance, airway obstruction, inflammation, and infection (Hoffman & Ramsey, 2013). The first CF transmembrane regulator (CFTR) modulating drug (Ivacaftor [Kalydeco]) was recently approved to treat the G551D mutation which is present in 5% of individuals with CF (Hoffman & Ramsey, 2013). CFTR modulators improve pulmonary function, increase body weight, and decrease the number of pulmonary exacerbations, all of which contribute to improved quality of life (Davies et al., 2013; Pettit, 2012). Research focusing on a similar drug to treat the more common CF mutation, F508del, represents a shift to personalized medicine, aiming to directly treat the underlying mutation based on an individual's genotype (Pettit, 2012). Nursing research to address medication adherence, physical activity, and nutrition (Bradley, Madge, Morton, Quittner, & Elborn, 2012) will also benefit overall quality of life. Like youth with HIV, there is also much to be learned about self efficacy (Mickley, Burkhart, & Sigler, 2013) and the transition of care from pediatric to adult CF providers (Al-Yateem, 2012).

Immune system modulation in individuals with T1D has been a focus of research over the past decade. The Immune Tolerance Network (ITN), a multi-centered, NIH-funded group, has

been responsible for multiple clinical trials of immune modulating agents (Ehlers & Nepom, 2012) including anti-CD20 monoclonal antibody (Rituximab) and anti-interleukin-1 beta monoclonal antibody (Gan, Albanese-O'Neill, & Haller, 2012), although the results of these trials have been mixed. Continuous glucose monitoring (Larson & Pinsker, 2013; Phillip et al., 2012; Tansey et al., 2013) in youth with T1D is a newer technology that was recently approved for use in children and adolescents (Food and Drug Administration, 2014). Adherence and quality of life (Mlynarczyk, 2013) are important areas of nursing research that will be important to re-examine in light of this new technology. Nursing research on diabetes self management (Hanna et al., 2013) is critical as these youth also move towards transition to adult care.

As research in these areas moves ahead, researchers must be cognizant of research fatigue and the burden placed on youth and their families from participation in multiple studies. Because every encounter with research can influence decisions about future engagement, it is vitally important to assess whether research fatigue may be present in these populations, and whether this phenomenon affects decision-making about research participation among youth and parents of youth with CHC.

Conceptual Framework

The decisional conflict framework has been used to guide decisions about treatment and may be adaptable for decision-making by youth and their parents about research participation. Youth with CHC and their parents or caregivers face decisions related to their heath care that may include deciding whether to take part in clinical research. Decisional conflict is present when there is uncertainty about the course of action to take (O'Connor, 1995) or when opposing tendencies are present that interfere with decision-making (Janis & Mann, 1977). Uncertainty in decision-making is highest when the decision involves risk, challenges personal values, results in

significant gains or losses, or when the potential implications of the decision are unclear (Keeney, 1982; O'Connor, 1997). Decisional conflict manifests prior to decision-making (Janis, 1959) and may be related to a lack of information about options, lack of experience with decision making, perceived external influence such as that of a health care provider or family member, and lack of an adequate support system (O'Connor, 1997).

Literature suggests that research fatigue manifests primarily as apathy, indifference, or resistance to research (Clark, 2008). The contributing factors usually involve practical issues like excessive burden or hardships of some kind that might be relieved with adequate *supports*. Other contributing issues relate to the perceived *value* of research, and communication of *information* between investigators and participants.

This study aims to explore whether youth and parents of youth with CHC report features of research fatigue as factors that contribute to their uncertainty and decision-making conflict about clinical research participation. An adapted decisional conflict framework will be used to explore the common factors that contribute to decision-making uncertainty and to research fatigue (Figure 1).

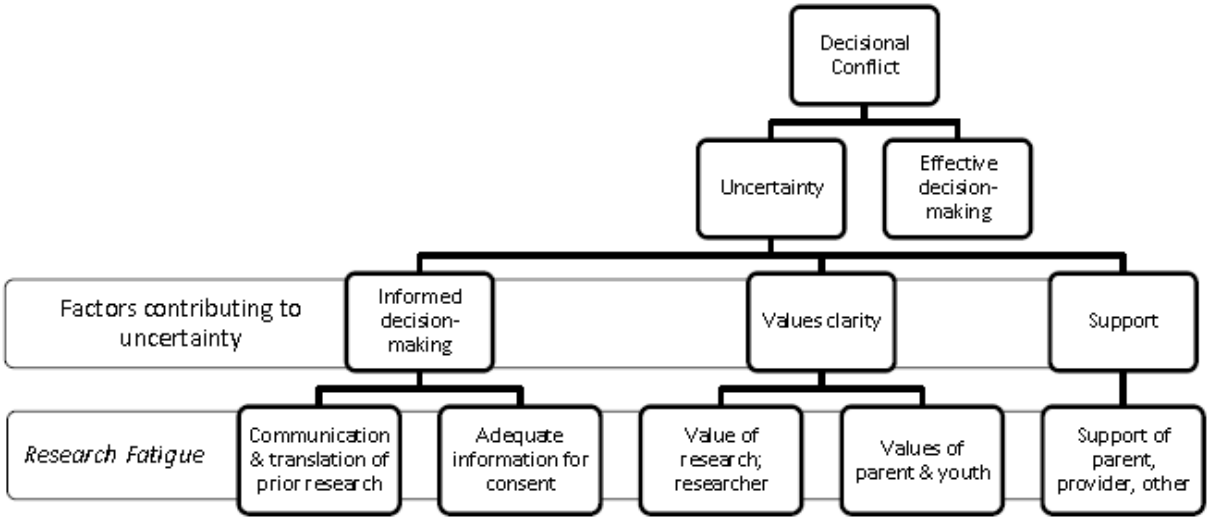

Figure 1: Decisional Conflict framework applied to research decision-making and research fatigue.

Methods

Design

This study will use *qualitative description* (Sandelowski, 2000, 2010) to describe the experience of youth and parents of youth with CHC with clinical research participation, the factors that influence their decision-making, and whether research fatigue plays a role.

Sample/Sampling

Stratified purposive sampling will be used to recruit both youth and parents of youth with each of the targeted CHC (Table 2) who have previously made decisions about clinical research participation in order to obtain a rich description of their experiences. Recruitment of parent-child dyads was considered. However, given that this study will recruit youth and parents of youth with past research experience, it was decided that dyad recruitment could result in bias if only the parent or youth agreed to participate while the other declined, or if the parent was not available or deceased, as may be the case with many HIV infected youth who would otherwise be eligible to take part in this study. Dyad recruitment would likely result in a more homogeneous population of parents and youth who are very enthusiastic about and experienced with research. Enrolling individual participants will allow for a description of the unique experiences of the intended heterogeneous population. Disparate as well as concordant youth/parent decision-making processes will be described. All study participants will be interviewed separately and analysis of youth and parents data will be conducted separately. For the purpose of this study, a parent is defined as a natural or adoptive parent or legal guardian. Maximum variation sampling will ensure that participants vary in the number and types of studies for which they were approached or in which they participated. Participants who have declined participation will also be included.

A target sample size of 30 participants falls within the recommended range for qualitative studies, which is anywhere from 10-50 participants, depending on the specific type of qualitative method being used (Sandelowski, 1995). Because the sample will be heterogeneous, both in terms of the type of chronic health condition and prior research experience, the target sample size falls on the higher end of this acceptable range. The final sample size will be determined by the number of participant interviews required to reach informational redundancy (Lincoln & Guba, 1985), which will be achieved when no new ideas emerge from the interviews and the categories of ideas are fully explored (Creswell, 2013). The final sample size will be determined during the conduct of the study in consultation with qualitative research mentors.

Table 2: Intended sample N=30	**HIV**	**Cystic Fibrosis**	**Type 1 Diabetes**
Youth	n=5	n=5	n=5
Related or un-related parents/legal guardians of youth	n=5	n=5	n=5

Inclusion and Exclusion Criteria

Inclusion criteria for youth participants include: diagnosed with HIV, CF, or T1DM; current age 13-21; prior participation or invitation to participate in at least one clinical research study at any point through age 21; English speaking. The upper age limit of 21 was chosen for this study to coincide with the age at which transition from pediatric to adult health care settings is typically accomplished (American Academy of Pediatrics, American Academy of Family Physicians, American College of Physicians, & Transitions Clinical Report Authoring Group, 2011). Parental inclusion criteria include: parent or legal guardian of a youth with HIV, CF, or T1D who participated or was invited to participate in at least one clinical research study through age 21 (youth does not need to participate in this study); English speaking, took primary responsibility for providing consent for past clinical research participation. All participants must

demonstrate willingness to participate in the interview by reviewing and signing the informed consent or assent documents.

Cognitive impairment that would prevent a participant from responding meaningfully to interview questions will be an exclusion criterion and determined in consultation with the referring care providers. Therefore, clinical care providers from the HIV, CF, and T1D clinics will be asked to carefully consider referring candidates demonstrating dementia, psychosis, abnormal behaviors, confusion, forgetfulness, or difficulty communicating (Jeste et al., 2003).

Individuals with mild cognitive impairment will not be excluded. However, candidates must be able to provide their own consent or assent by demonstrating adequate capacity for decision-making (University of California San Francisco, 2010). Decision-making capacity is the ability to make a meaningful decision about participation, including the ability to: 1) understand the study's purpose, procedures, risks, and benefits; 2) appreciate the significance of the study and implications of the risks and benefits to the individual; and 3) engage in reasoning about the risks and benefits of participation (Jeste et al., 2003). For this minimal-risk study, understanding of these elements of informed consent will be evaluated through an Evaluation to Sign Consent (ESC) (Appendix I) (DeRenzo, Conley, & Love, 1998; Sturman, 2005). The principle investigator (PI), a nurse with 10 years of experience, will assess each candidate's alertness and ability to communicate. Candidates scoring 12 out of 12 possible points will be permitted to provide their own consent or assent to participate; all others will be excluded.

Setting

The setting for this study will be the outpatient subspecialty clinics, specifically, the pediatric HIV, pulmonary, and endocrinology clinics at a major academic medical center. Five youth and five parents of youth will be recruited from each of the clinics for participation. The

pediatric HIV clinic currently serves 38 infected youth. Parents or guardians accompany a majority of youth to clinical visits and will be easily accessible for recruitment. The pediatric HIV clinic has been involved in clinical trials, including phase I, II, and II drug studies, long term follow up, pharmacokinetic, and vaccine studies, for over 20 years. At any given time, as many as ten or more studies have been ongoing. The number of studies has decreased significantly in the past year; however, most patients have been involved in at least one, and as many as 16 studies over the course of their lives. The diabetes clinic serves 571 children, and approximately 60 new youth with T1D enter the clinic each year. The clinic is active in clinical trials of new drugs, behavioral intervention studies, and T1D screening studies. On average, there are 5 studies ongoing at a given time. The CF clinic currently serves 96 pediatric patients. Approximately 7 studies are currently being conducted, including phase II and III drug studies, and long-term observational and prospective outcomes.

Procedures

Thirty participants will be recruited purposively from the Pediatric HIV, CF, and T1D clinics. Clinical care providers and study coordinators based in these clinics will assist with recruitment by distributing a flyer detailing the study. This document will emphasize the importance of understanding the reasons why individuals have declined past clinical research studies and that their input will allow researchers to learn how make studies less burdensome and support potential participants in their decision-making. Individuals meeting inclusion criteria will give permission to be contacted by the PI by phone to further discuss details of the study. Participants will then be scheduled for the study visit, where informed consent and assent will be obtained prior to individual interviews and completion of a demographics form and three instruments.

Data Collection

Interviews will be conducted by this PI during face-to-face, audio-recorded, individual interviews using a semi-structured interview guide (Appendix II). Youth and parents will be interviewed separately in order to describe their unique perspectives on research participation. Interviews will take place in a private conference room or office at the medical center at the convenience of the participant. Field notes will be written immediately following each interview to document what was done and to summarize the interviewers' observations and reflections. The interviews are anticipated to last approximately one hour. Interviews will be audio recorded and then professionally transcribed. In addition to interviews, participants will be asked to complete a demographics form (Appendix III). To triangulate interview data, the Decisional Conflict Scale (DCS) and the Pediatric Research Participation Questionnaire (PRPQ) will be administered prior to the interview (Appendix III). Completion of these instruments will contribute to this study's trustworthiness.

The decisional conflict scale.

The DCS is a 16-item, 5 category response scale measuring personal perceptions of uncertainty, modifiable factors contributing to uncertainty, and effective decision-making. The DCS will be preceded by a comment asking participants to complete the DCS considering their past experiences with decision-making about a research study. Internal consistency (Cronbach's Alpha) for the scale ranges from 0.78 to 0.92 (O'Connor, 1995). Validation studies report less than 1% missing responses, contributing to face validity (O'Connor, 1995). In evaluating construct validity, statistically significant ($p<0.0002$) differences were found between individuals with high and low DCS scores, supporting the scale's validity (O'Connor, 1995). Divergent

validity has also been assessed, with a weak but statistically significant inverse correlation ($r=-0.16$; $p<0.05$) found between high DCS scores and low levels of knowledge (O'Connor, 1995).

The pediatric research participation questionnaire.

The PRPQ is a measure designed to aid in understanding decision-making about clinical trials participation among pediatric patients with CHC (Barakat et al., 2013). This questionnaire will be used to capture motivators and barriers to participating in clinical research for their (or their child's) CHC. Three versions have been newly developed: a 12 item, yes/no response questionnaire for children ages 8-15 years; a 21 item, agree/disagree questionnaire for adolescents and young adults ages 16-39 years old; and a 21 item, agree/disagree questionnaire for caregivers. Internal consistency coefficients for these recently developed scales have not yet been reported. This scale will be utilized only if Cronbach's alphas become available and are >0.7.

Data Management

Electronic data will be stored on a secured research drive on the University server that is backed up nightly. Access to this drive will be limited to the PI and dissertation chairperson. Every transcript will be reviewed against the original audio recording to ensure accuracy of transcription. NVivo (version 10) software will be utilized to prepare interview summaries. SPSS (version 22) will be used to manage demographic information and quantitative data generated from the DCS and PRPQ. To minimize missing data, the paper instruments will be reviewed for completion prior to the participant leaving the interview session. Double entry of data will be performed to ensure accuracy.

Data Analysis

Qualitative Content Analysis (Miles, Huberman, & Saldana, 2013) will be used to analyze the interview data. Transcripts will be read and summarized as the study progresses. Data reduction will be achieved by reviewing one section of data at a time. Transcripts will be examined for similarities and analysis will be done across cases. NVivo software will then be utilized to accomplish coding. Data will be placed in code folders, documenting coding rationale in the field notes. Rebuilding of data will be accomplished through the development of categories by looking for links between codes. The interview guide will be revised, as needed, during the conduct of the interviews as the transcripts are analyzed across cases. To ensure maximum variation across participants, purposive sampling will take place as the study unfolds to attempt to vary the number and type of studies participants. Field notes will document the analysis process.

Analysis will include within and across-participant comparisons of DCS scores and interview responses. In particular, the interview transcripts will be examined for participants with high DCS scores, representing a high level of decisional conflict, for common themes. Similarly, thematic analysis of transcripts will be done for participants with low DCS scores, which represents a low level of decisional conflict. The themes generated from high and low scoring participants will then be compared. The PRPQ yields dichotomous (yes/no, or agree/disagree) responses to understand the perceived benefits and barriers to research participation. Within-participant PRPQ responses will be examined and used to validate qualitative interview responses to questions about benefits and barriers to participation. Across-participant PRPQ responses will be analyzed against the qualitative interview themes. Thematic analysis of qualitative data will also take place across-participants with similar PRPQ responses with high and low DCS score.

If elements of research fatigue emerge from the qualitative data, further analysis will take place to compare within-participant descriptions of research fatigue to DCS scores and PRPQ responses to make an assessment as to the utility of these scales in future studies on research fatigue. However, the intended sample size is too small to draw statistical conclusions.

To ensure trustworthiness, the following techniques will be employed: peer debriefing, member checks, purposive sampling, rich description, triangulation, reflexive journaling, field notes, and an audit trail (Lincoln, 1985). Through regular, modified peer debriefing meetings, the PI will benefit from the insight of dissertation committee members, who are experts in conducting qualitative research. Interview proceedings, audio tapes, transcripts, and preliminary data findings will be discussed. At least 2 youth and 2 parents who are willing to take part in member checks will be contacted to review de-identified transcripts and the PI's preliminary data interpretations to ensure their ideas were accurately captured. Transferability of findings from this study will be enhanced through purposive sampling to achieve a rich description of the participant's experiences with research.

The PI will take part in reflective journaling throughout the study to record personal feelings and reflections, and all study activities and interview observations will be recorded in field notes. These documents will be considered part of the audit trail and will be reviewed in the peer debriefing meetings and at the request of the dissertation committee members.

Human Subjects Involvement

Participants will be male and female youth or parents of youth with HIV infection, CF, or T1D recruited from the pediatric clinics at UMMC-CMC. To gain the perspective of children who have been involved in clinical research, inclusion of this vulnerable population is necessary in the effort to improve research procedures in the future that minimize burden and support

informed decision-making among children and families. Pregnant women may be involved in this study if they are a youth with HIV, CF, or T1D, or if they are already the parent of a youth with HIV, CF, or T1D. Pregnant women will not be excluded because this study does not pose harm or seek to collect information about the pregnancy or the fetus. Prisoners and institutionalized individuals will be excluded from participation. Youth participants will be between 13 and 21 years of age, and their ability to contribute meaningfully to the interview will be determined in consultation with their clinical care providers who will assess referred participants for severe cognitive deficits including dementia, psychosis, abnormal behaviors, confusion, forgetfulness, or difficulty communicating (Jeste et al., 2003). Parents or legal guardians will be at least 18 years of age. Subjects will reflect the socio-demographic composition of the clinics, which is variable across these three populations (Table 3). Ethnicity and gender will not be used as criteria in determining eligibility. Recruited participants will be asked to take part in a single interview and data collection session. A $25 gift card to a local retail store will be provided to participants as a gesture of gratitude for their participation. Member checks to validate study data will be conducted with at least 2 youth and 2 parents who will be selected based on their willingness to be re-contacted and their potential to provide meaningful review of the study data. An additional $25 gift card will be provided to participants who take part in member-checks.

Table 3: Racial and ethnic composition of available clinical populations	Caucasian	Hispanic	Black	Asian	Other race	Not reported/unknown
HIV	24%	50%	21%	5%	0%	0%
CF	88%	2%	0%	0%	3%	7%
T1D	84%	2%	3%	1%	6%	4%

Potential Risks and Protections

There are no anticipated physical risks to participants. However, there is the rare chance that participants may become upset when talking about their/their child's chronic health condition or their past research experience. This psychological risk will be included in the informed consent and discussed with participants in advance. Before participating in research interviews, participants will be assured of their confidentiality and will be reminded that they have the right to terminate the interview or decline to answer specific questions, or terminate their participation at any point in the research process.

The PI has extensive experience recruiting and interviewing children and parents in highly complex clinical trials, and is sensitive to the emotions that can emerge during study visits. If at any time during the interview or data collection procedures a participant become too physically or emotionally tired or upset, they will be reminded that they have the option to stop the interview or data collection. The PI will attempt to comfort the participant and provide any explanations that would be helpful. If a child becomes upset, the parent will be notified, along with members of the clinical care team so that arrangements can be made for appropriate follow up with a mental health provider as needed. If a parent becomes upset, the child's clinical care team will also be notified so that support staff (i.e. licensed social worker) can be engaged as needed. Participants exhibiting extreme distress will be escorted to Emergency Mental Health Services at the Emergency Department at UMMC, which serves children and adults.

There is no anticipated financial risk, as the PI will work with participants to schedule interviews at a time when participants will not miss work. There is always the potential for a loss of confidentiality when study instruments and data forms are completed, but every precaution will be taken to ensure that all data are kept strictly confidential. Participant names

will not be used during the audio-recorded interviews. Only the PI will have access to identifiable data (a list that links the study ID with participant names), which will be stored in a locked file cabinet in the PI's locked office. Personal identifiers will be stripped from the data and kept separately in a locked file available only to the PI. All information provided by participants will be referenced to unique participant ID numbers and will be kept in a locked file cabinet. The participants ID numbers could be connected to the participant's names only through a single master file, accessible only to the PI. Passwords and protection codes will be used to protect data files against inadvertent changes or unauthorized access. All data files will be backed up nightly. Documentation of the data management procedures will be carefully maintained. Results will never be reported in a personally identifiable matter; only grouped or de-identified data will be presented in publications or presentations. The usual standards for medical confidentiality will be observed.

As a vulnerable population, the protection of children in this research study will be ensured by obtaining informed consent from one of the child's parents or guardians. Consent of only one parent or guardian will be required as this study is considered to present no greater than minimal risk. Children will have the opportunity to affirm their agreement to the study by providing their assent. Children whose parent/guardian provides informed consent, but who do not themselves provide assent will not be included in the study.

Recruitment and Informed Consent

Participants will be recruited from the UMMC Children's Medical Center outpatient pediatric HIV, pulmonary and endocrinology clinics. Prior to recruitment, an informational meeting at each outpatient clinic will be conducted to explain the study in detail to clinical care providers including physicians, nurse practitioners, and clinic nurses, as well as clinic-based

study coordinators. Study coordinators in the HIV, CF, and T1D clinics will be crucial to the recruitment process. The PI will request lists of active and inactive studies involving participants in these three clinics from the IRB and will then work with the study coordinators and principle investigators to identify potential participants who are developmentally capable to contribute meaningfully to the interview. Study coordinators, or clinical care providers will be asked to provide an informational fact sheet explaining the study and a permission-to-contact form to potential participants as they attend clinic visits or by mail if there is no clinical visit scheduled during the data collection time period. They will ask interested patients and parents to complete the permission-to-contact form. This form will be approved by the UMMS IRB and will request that interested patients or parents provide basic contact information (name, phone number, and/or email address) and the most convenient day and time to have a discussion by phone. The PI will contact all interested patients and parents by telephone to discuss the study in more detail. Potential participants will be given the PI's phone number in the event they prefer to call rather than be contacted. Patients and parents who remain interested in participating after learning details about the study will be scheduled for the study visit at a convenient time, and will have the option to receive a copy of the Informed Consent Form (ICF) by mail in advance of the visit.

Prior to any data collection on the day of the study visit, the PI will meet with the study candidate and parent, if appropriate, in a private room to conduct the informed consent and/or assent processes. It is anticipated that this will take approximately one-half hour. Given the diversity of literacy rates in this population, the PI will then explain the ICF and assent form (AF) to every candidate/parent, reading the forms aloud for those who indicate that preference, and engaging in discussion about the content to ensure comprehension. The participant/parent and minor participant aged 16 or 17 will be asked to read the ICF in full, or carefully consider

the contents read to them. Minor participants aged 13-15 will be asked to read the AF in full, or carefully consider the contents read to them. The PI will provide the candidate/parent with paper and pen to record any questions that arise as the ICF and AF are read or considered. The PI will explain that participation in the study is voluntary and that their participation or lack of participation will not influence their/their child's medical care. The candidate/parent will be reminded that they can leave the study at any time and for any reason. The PI will exit the room allowing the candidate/parent to review and consider the ICF and/or AF without feeling rushed or pressured. The candidate/parent will indicate readiness to proceed with the informed consent and/or assent process by opening the door to the private room. The PI will then answer any remaining questions. Before the ICF and AF are signed, the ESC will be used to document the participant's knowledge of the contents of the ICF. Participants must score 12 out of 12 possible points to ensure adequate cognitive capacity to sign his/her own informed consent or assent.

Informed consent will be provided by participants 18 years of age and older. Informed consent for minor participants, defined for this study as a participant between the ages of 13 and 17, will be provided by one parent or legal guardian of the minor participant. Minor participants aged 13-15 will provide their assent to participate and will complete the assent form (AF). Minor participants aged 16 and 17 will indicate their consent, along with a parent or guardian, by co-signing the ICF, which is a standard procedural requirement of the University IRB.

Potential participants/parents agreeing to participate will be asked by the PI to sign the IRB-approved written ICF and/or AF. Consent and/or assent will only be obtained from each participant/parent after he/she acknowledges an understanding of the study and expresses a willingness to participate, and after the ESC is completed and passed. The ICF will address the purpose of the study, study procedures, risks, confidentiality of materials, right to withdraw from

the study at any time, and the names of study contacts (i.e., the PI and IRB) in case of any concerns or questions. The assent will address, in simpler terms, the same components as the ICF. Two copies of the ICF, and AF if appropriate, will be signed by the participant/parent, of which one copy will be retained by the PI and the other given to the participant/parent.

If at any point the participant/parent decides not to take part in the study, they will be asked to allow documentation of their reason for refusal. This includes youth under 18 years of age who are willing to provide assent, but whose parents or guardians decline to give consent. Permission to collect basic de-identified demographic information (age, gender, race, ethnicity, highest level of education, marital status, and employment status for all participants and youth of parent participants; number of years since youth's diagnosis; number and type of prior research studies participated in) will be requested. There will also be a free text area for the participant or parent/guardian to describe in more detail the reason for refusal.

Potential Benefits

There may be no direct benefit to individual subjects in this study. However, participants could derive benefit from being able to express their feelings about their/their child's past research experiences. Further, information gained from this study could benefit future participants with chronic illness by allowing the PI to learn how to better approach parents and youth, and support their decision-making about research studies. Participation in this study presents no greater than minimal risk. It is reasonable to suggest that the potential benefits outweigh the minimal risk posed by this study.

Potential Challenges

There are three main challenges associated with this study. It may be difficult to recruit participants who have already participated in multiple studies or previously refused research

participation. To manage this challenge and promote recruitment of previous decliners, potential participants will be reminded that this study is different from other clinical studies; it is low risk and the time commitment is minimal. Every attempt has been made to keep the research burden low by being flexible in scheduling study visits, limiting the number of questionnaires, and requesting only one interview session. Participants will be reminded that data obtained in this study may be helpful in the future to improve the approach to engaging youth and parents in clinical research while minimizing burden and research fatigue. Data about prior research participation refusal will be collected as a part of this study. This data will be considered in the analysis of interview data, and will be reported in the results.

A second potential challenge is that youth recruited for this study represent two different developmental levels. According to Erikson, the goal of adolescence is to explore independence and work to develop a sense of self (identity versus role confusion); the focus of young adults is on exploring personal relationships and making commitments (intimacy versus isolation) (Erikson, 1950). The *identity* and *intimacy* subscales of the Erikson Psychosocial Inventory Scale (EPSI) (Appendix III) will be used to classify youth participants by developmental level. Each subscale contains 12 randomly ordered items, half of which reflect successful resolution of the crisis associated with that developmental stage, and the other half unsuccessful resolution. The Likert responses range from 1-*hardly ever* true to 5-*almost always true.* The scale is suitable for participants 13 years of age and older. Alpha reliability coefficients from two test samples range from 0.71-0.78 for the identity subscale and 0.63-0.73 for the intimacy subscale (Rosenthal, Gurney, & Moore, 1981). Analysis of data for youth participants will be undertaken with consideration for the developmental stages. Between-subject comparisons will only be made between participants of similar age and developmental level.

Third, there is potential for recruitment bias as assenting youth under 18 years of age will not be permitted to participate without parental consent. All participants who decline will be asked for permission to be added to a recruitment log. This log will include basic demographic information and a free-text area to describe the reason for refusal. Brief analysis of eligible participants who did not enroll will be described in the study results.

Potential Contributions

Knowledge gained from this proposed qualitative descriptive study has the potential to greatly improve how youth with CHC, a vulnerable population, are approached to engage in clinical research. Advances in scientific and nursing knowledge to improve the health and well-being of youth with CHC depend on the ability to recruit and retain participants in clinical research studies, which can be challenging when participants are faced with repeated requests. The perception of burden can be a significant barrier to research participation and this study will elucidate factors affecting that decision.

The qualitative data collected during this study will set the stage for a research trajectory that will include: (a) development of a scale to measure research fatigue; and (b) intervention studies to evaluate how to best engage youth with CHC and their parents in clinical research using innovative strategies to minimize burden and prevent research fatigue by providing adequate support and facilitating informed decision-making.

Appendix I: EVALUATION TO SIGN CONSENT (OR ASSENT) FORM (ESC)

Name: _____

Date of birth: _____ **Score**

1) Is the patient alert and able to communicate with the evaluator? ___ Yes **(=2)** ___ No **(=0)** _____

2) Ask the participant to name two (2) potential benefits of participating in the study.
0=not able to list potential benefits, 1=able to list one benefit, 2=able to list two benefits _____

_____

3) Ask the participant to name two (2) potential risks incurred as a result of participating in the study.
0=not able to list potential risks, 1=able to list one risk, 2=able to list two risks _____

_____

4) Ask the participant to name two (2) things that will be expected of him/her in terms of patient cooperation during in the study.
0=not able to list expectations, 1=able to list one expectation, 2=able to list two expectations _____

_____

5) Ask the participant to explain what he/she would do if he/she decided that they no longer wish to participate in the study.
0=doesn't know, 1=answers but not appropriate response, 2=talk to PI or clinical provider _____

_____

6) Ask the patient to explain what he/she would do if he/she is experiencing distress or discomfort.
0=doesn't know, 1=answers but not appropriate response, 2= talk to PI or clinical provider _____

_____

Total score _____

I hereby certify that the above participant is alert, able to communicate and able to give acceptable answers to items 2, 3, 4, 5, and 6 above.

_____

Evaluator Date

Appendix II: Interview Guide

For youth participants

Question	Probes	Conceptual Areas
1. Can you tell me a little bit about your experiences when you have participated in a research study (or studies)? *{Start here for those who have participated in a study in the past.}*	a. How many studies have you participated in? b. What kinds of studies were they? c. What were these studies like for you? d. How prepared were you for all of the requirements involved in the study? e. Did you have enough information about the study before you started it? If not, what information would have been helpful to know? f. Do you remember how you first learned about the study and what you and your parent(s) talked about? g. What was the consent process like for you? h. Who supported you through this study? i. Did you have enough support or could you have used more support? j. What type of support did you find most helpful? What types of support would be helpful in the future? k. Did you ever get information about the results of any research studies you were in? Would that information help you to decide if you were invited to do another research study?	General experience with research Informed consent Support Communication of information
2. Can you talk a little bit about how you made the decision to participate (or not participate) in a research study? *{Start here for those who have never participated in a study.}*	a. How did you make the decision? b. How much was your parent(s) involved in the decision-making process? c. Was anyone else involved in helping you make the decision? d. Did you experience any conflict with others or in your own mind about whether to participate in the study or not? e. What were some of the things that motivated you to participate (or not)? f. What were some of the barriers that you experienced when trying to decide whether to participate or not? g. How certain where you that this study was the right (not right) thing for you to do?	Decision-making Support Uncertainty General motivators to participation General barriers to participation Values clarity (of research/youth)
3. Can you talk about how interested you are now in participating in future studies?	a. Have you ever felt “tired” of being approached to be in these studies? Why?	Research fatigue Values clarity (of

	b. How important is participating in research to you personally?	research)
4. If you could teach the doctors and nurses who run these studies the best way to approach young people, like yourself, about research – what would you tell them?	a. What are the things they should or should not do? b. How important is it that the research staff listens to your suggestions about research?	Strategies for improving how we approach youth about research studies Values clarity (of youth)
5. Is there anything else that you would like to add?		

For parents/guardians

Question	**Probes**	**Conceptual Areas**
1. Can you tell me a little bit about your experiences of having your child participate in a research study (or studies)? *{Start here for those who have participated in a study in the past.}*	a. How many studies has s/he participated in? b. What kinds of studies were they? c. What were these studies like for you? d. How prepared were you, as a parent, for all of the requirements involved in the study? e. Did you have enough information about the study before s/he started it? If not, what information would have been helpful to know? f. Do you remember how you first learned about the study and what you and your child talked about? g. What was the consent process like for you and your child? h. Who supported you and your child through this study? i. Did you have enough support or could you have used more support? j. What type of support did you find most helpful? What types of support would be helpful if your child participates in the future? k. Did you ever get information about the results of any research studies your child took part in? Would that information help you to decide if your child was invited to do another study?	General experience with research Informed consent Support Communication of information
2. Can you talk a little bit about how you made the decision to allow your child to participate (or not participate) in a research study?	a. How did you make the decision to allow your child to participate? b. How much was your child involved in the decision-making process? c. Were any other people involved in helping you and your child make the	Decision-making Support

{Start here for those who have never participated in a study.}	decision? d. Did you experience any conflict with others or in your own mind about whether to let your child participate in the study or not? e. What were some of the things that motivated you to allow your child to participate (or not)? f. What were some of the barriers that you experienced when trying to decide whether to allow your child to participate or not? g. How certain where you that this study was the right (not right) thing for your child to do?	Uncertainty General motivators to participation General barriers to participation Values clarity (of research/parent)
3. Can you talk about how interested you are now in allowing your child to participate in future studies?	a. Have you ever felt "tired" of your child being approached to be in these studies? Why? b. How important is it to you for your child to participate in research?	Research fatigue Values clarity (of research)
4. If you could teach the doctors, nurses, and research staff the best way to approach young people about research – what would you tell them?	a. What are the things they should or should not do? b. How important is it that the research staff listens to your suggestions about research?	Strategies for improving how we approach youth about research studies Values clarity (of parent)
5. Is there anything else that you would like to add?		

Appendix III: Data Collection Instruments

Demographics

Date of visit: _____ Participant ID #: _____

Age: _____

Participant Status:

_____ Youth

_____ Parent/legal guardian

Year of youth diagnosis: _____

Diagnosis:

_____ HIV

_____ CF

_____ T1D

Gender:

____ female

____ male

Race:

_____ Caucasian

_____ Asian

_____ Black of African American

_____ American Indian

_____ Other

If other, please list: _____

Ethnicity:

_____ Hispanic or Latino

_____ Not Hispanic or Latino

_____ Unknown or not reported

Level of Education:

_____ Some High School

_____ High School diploma or GED

_____ Some college

_____ Associates degree

_____ Bachelors degree

_____ Masters degree

_____ PhD or post-doctorate

Marital Status:

_____ Single

_____ Married

_____ Unmarried partners

_____ Divorced

_____ Separated

_____ Widowed

Employment Status:

_____ Full time

_____ Part time

Occupation (please list):

_____

_____ Unemployed

_____ Retired

_____ Student

How many studies have you (your child) been invited to participate in since the time of diagnosis? _____

How many studies have you (your child) **declined** to take part in? _____

What types of studies were these? _____

How many studies have you (your child) **agreed** to take part in? _____

What types of studies were these? _____

Traditional Decisional Conflict Scale (DCS) Participant ID #: _____

Directions: Please think back to the last time you were (your child was) invited to participate in a research study. Please answer the following questions as you think about all the options you considered and how you made the decision to participate or decline.

	Strongly Agree [0]	Agree [1]	Neither Agree Nor Disagree [2]	Disagree [3]	Strongly Disagree [4]
1. I know which options are available to me.	☐	☐	☐	☐	☐
2. I know the benefits of each option.	☐	☐	☐	☐	☐
3. I know the risks and side effects of each option.	☐	☐	☐	☐	☐
4. I am clear about which benefits matter most to me.	☐	☐	☐	☐	☐
5. I am clear about which risks and side effects matter most to me.	☐	☐	☐	☐	☐
6. I am clear about which is more important to me (the benefits or the risks and side effects).	☐	☐	☐	☐	☐
7. I have enough support from others to make a choice.	☐	☐	☐	☐	☐
8. I am choosing without pressure from others.	☐	☐	☐	☐	☐
9. I have enough advice to make a choice.	☐	☐	☐	☐	☐
10. I am clear about the best choice for me.	☐	☐	☐	☐	☐
11. I feel sure about what to choose.	☐	☐	☐	☐	☐
12. This decision is easy for me to make.	☐	☐	☐	☐	☐
13. I feel I have made an informed choice.	☐	☐	☐	☐	☐
14. My decision shows what is important to me.	☐	☐	☐	☐	☐
15. I expect to stick with my decision.	☐	☐	☐	☐	☐
16. I am satisfied with my decision.	☐	☐	☐	☐	☐

Research Participation Questionnaire – Child (8-15 years old) Participant ID #: _____

Directions: While you go to the doctor or hospital to make you feel better, "research" asks you to participate in certain activities in order to learn things that will hopefully help others.
Please check YES or NO to answer these questions. We want to know what you think about medical (e.g., taking medicine, getting blood drawn) and psychosocial (e.g., thoughts and feelings about illness, coping with illness) research studies; there are no right or wrong answers.

	Yes	No
1. I would do research if it was to learn more about my illness.		
2. Doing a research study will cause me more problems like having to take more pills, getting poked, and answering upsetting questions.		
3. I do research because my doctors and nurses take good care of me.		
4. Doing research gives my family and me a chance to help.		
5. I am willing to do research when I know exactly what I will be asked to do.		
6. Research will help my illness get better.		
7. I participate in research when my parent tells me to do it.		
8. The hospital has people to review studies to make sure they are safe.		
9. I don't like doing research because I spend too much time at the hospital/clinic already.		
10. More people would do research if they got gift cards or gifts.		
11. Researchers sometimes hide facts from the people who do the studies.		
12. These people want me to be in research: 12a. My healthcare team(doctor, nurse and social worker)		
12b. My family		
12c. My friends		
12d. My religious leader		

Research Participation Questionnaire – AYA (16-39 years old) Participant # _____

Directions: While the goal of going to the doctor or hospital is to get care that is meant to benefit the patient and his/her family, "research" asks patients and families to participate in certain activities in order to learn things that will hopefully help future patients and families.
Please check AGREE or DISAGREE to reflect your agreement or disagreement with each of the following statements. We are interested in YOUR opinion about medical (e.g., taking medication, blood samples drawn) and psychosocial (e.g., thoughts and feelings about illness, coping with illness) research studies; there are no right or wrong answers.

	Agree	Disagree
1. I would participate in research that helps me directly if: 1a. It gives me more contact with the healthcare team.		
1b. I learn more about my illness.		
1c. I get tests/medicine and equipment that my insurance won't cover.		
1d. I get tests/medicine and equipment that are not available to the public.		
2. Research will cause me discomfort in the following ways: 2a. Require increased procedures.		
2b. Ask personal or upsetting questions.		
3. I participate in research because the healthcare team takes good care of me.		
4. The government sometimes exposes research participants to medicine and procedures known to be harmful to one's health.		
5. Participating in research gives me a chance to "give back."		
6. Research is part of a conspiracy to harm minority groups.		
7. I am willing to participate in research when I know exactly what I will be asked to do.		
8. I would not participate in research that does not benefit me because: 8a. The study does not meet my medical or psychosocial needs.		
8b. The study involves randomization (i.e. there is a chance that I may not get the treatment).		
8c. The study could provide information about my health that I would rather not know about.		
8d. The study may cause me physical harm.		
9. Research studies will eventually lead to a cure or improved treatments for those who participate in them.		

10. It makes me uncomfortable when my healthcare team wants to do research with me because: 10a. The healthcare team will view me only as a “research participant” if I enroll.		
10b. The healthcare team will treat me differently, if I do not enroll.		
11. The hospital has researchers and community members review studies to make sure they are safe.		
12. Researchers sometimes undermine the power of God and God’s will.		
13. When the researcher is of the same race, I am more likely to participate.		
14. It is difficult to find time to participate in a research study because: 14a. The study site is too far away.		
14b. I can’t take time off work.		
14c. I spend too much time at the hospital/clinic already.		
15. If my healthcare team is doing the research then I trust that it is good.		
16. Researchers sometimes hide information from participants prior to research.		
17. If researchers provided the following, it would lead to more participation in research: 17a. Childcare		
17b. Money or gifts		
17c. Transportation costs		
17d. Telephone or internet participation		
18. Researchers often ask for financial information that may get back to the government and cause me to lose my check/benefits.		
19. Personal information given in research does not stay private and might hurt me or people I care about.		
20. Researchers are motivated by their own career goals and not the welfare of the people who participate in their studies.		
21. The following people would support my decision to participate in research: 21a. My healthcare team (doctor, nurse and social worker)		
21b. My family		
21c. My friends		
21d. My religious leader		
21e. My community agency		

Research Participation Questionnaire - Caregiver Participant ID #: _____

Directions: While the goal of going to the doctor or hospital is to get care that is meant to benefit the patient and his/her family, "research" asks patients and families to participate in certain activities in order to learn things that will hopefully help future patients and families.
Please check AGREE or DISAGREE to reflect your agreement or disagreement with each of the following statements. We are interested in YOUR opinion about medical (e.g., taking medication, blood samples drawn) and psychosocial (e.g., thoughts and feelings about illness, coping with illness) research studies; there are no right or wrong answers.

	Agree	Disagree
1. We would participate in research that helps my child directly if: 1a. It gives us more contact with the healthcare team.		
1b. We learn more about my child's illness.		
1c. We get tests/medicine and equipment that my child's insurance won't cover.		
1d. We get tests/medicine and equipment that are not available to the public.		
2. Research will cause my child discomfort in the following ways: 2a. Require increased procedures.		
2b. Ask personal or upsetting questions.		
3. We participate in research because the healthcare team takes good care of my child.		
4. The government sometimes exposes research participants to medicine and procedures known to be harmful to one's health.		
5. Participating in research gives my family and me a chance to "give back."		
6. Research is part of a conspiracy to harm minority groups.		
7. We are willing to participate in research when we know exactly what we will be asked to do.		
8. We would not participate in research that does not benefit my child because: 8a. The study does not meet my child's medical or psychosocial needs.		
8b. The study involves randomization (i.e. there is a chance that my child would not get the treatment).		
8c. The study could provide information about my child's health that I would rather not know about.		
8d. The study may cause my child physical harm.		
9. Research studies will eventually lead to a cure or improved treatments for those who participate in them.		
10. It makes me uncomfortable when my healthcare team wants to do research with my child because: 10a. The healthcare team will view my child only as a "research participant" if I enroll.		
10b. The healthcare team will treat my child differently, if I do not enroll.		

11. The hospital has researchers and community members review studies to make sure they are safe.		
12. Researchers sometimes undermine the power of God and God's will.		
13. When the researcher is of the same race, I am more likely to participate.		
14. It is difficult to find time to participate in a research study because: 14a. The study site is too far away.		
14b. I can't take time off work.		
14c. We spend too much time at the hospital/clinic already.		
15. If my child's healthcare team is doing the research then I trust that it is good.		
16. Researchers sometimes hide information from participants prior to research.		
17. If researchers provided the following, it would lead to more participation in research: 17a. Childcare		
17b. Money or gifts		
17c. Transportation costs		
17d. Telephone or internet participation		
18. Researchers often ask for financial information that may get back to the government and cause me to lose my check/benefits.		
19. Personal information given in research does not stay private and might hurt me, my child, or people I care about.		
20. Researchers are motivated by their own career goals and not the welfare of the people who participate in their studies.		
21. The following people would support my decision to participate in research with my child: 21a. My child's healthcare team (doctor, nurse and social worker)		
21b. Our family		
21c. Our friends		
21d. Our religious leader		
21e. Our community agency		

Erikson Psychosocial Stage Inventory (EPSI) Participant ID #: _____
Identity and Intimacy subscales

Directions: Please circle the number that corresponds to how true the following statements are for you.

	Hardly ever true				**Almost always true**
1. I get embarrassed when someone begins to tell me personal things	1	2	3	4	5
2. I change my opinion of myself a lot	1	2	3	4	5
3. I'm ready to get involved with a special person	1	2	3	4	5
4. I've got a clear idea of what I want to be	1	2	3	4	5
5. I feel mixed up	1	2	3	4	5
6. The important things in life are clear to me	1	2	3	4	5
7. I've got it together	1	2	3	4	5
8. I know what kind of person I am	1	2	3	4	5
9. I'm warm and friendly	1	2	3	4	5
10. I can't decide what I want to do with my life	1	2	3	4	5
11. It's important to me to be completely open with my friends	1	2	3	4	5
12. I keep what I really think and feel to myself	1	2	3	4	5
13. I have a strong sense of what it means to be female/male	1	2	3	4	5
14. I think it's crazy to get too involved with people	1	2	3	4	5
15. I like myself and am proud of what I stand for	1	2	3	4	5
16. I don't really know what I'm on about	1	2	3	4	5
17. I care deeply for others	1	2	3	4	5
18. I find I have to keep up a front when I'm with people	1	2	3	4	5
19. I don't really feel involved	1	2	3	4	5
20. I'm basically a loner	1	2	3	4	5
21. I have a close physical and emotional relationship with another person	1	2	3	4	5
22. I prefer not to show too much of myself to others	1	2	3	4	5
23. Being alone with other people makes me feel uncomfortable	1	2	3	4	5
24. I find it easy to make close friends	1	2	3	4	5

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Executive Summary

Original proposal	**Modification and rationale**
Recruitment	
Clinical care providers and research staff will distribute the *Informational Fact Sheet* and *Permission to Contact Form* to eligible participants during their clinical visits.	Due to slow recruitment and feedback from clinical staff members who were assisting with recruitment that they were not remembering to distribute the study information; the study plan was modified such that these documents could be mailed to potentially eligible participants at home.
Methods	
Informed consent/assent procedures	Given the minimal risk nature of this study, a waiver of written documentation of informed consent/assent was requested and granted. Verbal informed consent and assent was obtained from youth and parents as applicable.
To evaluate understanding of informed consent, participants will complete an Evaluation to Sign Consent (ESC).	All participants were administered and passed the ESC. Due to word limitations imposed by the publishing journal, the final manuscript does not include a description of this process.
Interviews will take place in a private conference room or office at the medical center at the convenience of the participant.	In-person interviews also took place on the inpatient ward for patients with Cystic Fibrosis (and their parents) who were admitted for routine CF care. Clinical providers and research staff from the CF clinic suggested this approach to relieve burden on these families. Interviews also took place by phone for interested participants who could not travel to the Medical Center campus. These modifications were made to promote participation when recruitment was very slow.
Interview guide	Revisions were made to the interview guide to add probing questions to ask more directly about assent and research fatigue, and how participants were supported during past research participation.
To triangulate interview data, the Decisional Conflict Scale (DCS) and PRPQ will be administered prior to the interview.	The DCS and PRPQ were administered after the interview. This order was recommended in order to prevent obtaining bias responses to the qualitative interview.
Participants to complete the Pediatric Research Participation Questionnaire (PRPQ) to capture motivators and barriers to participating in clinical research, but internal consistency not reported at the	The PRPQ was not analyzed because data were incomplete due to a missing page and thus internal consistency could not be assessed. Internal consistencies for the questionnaire were not reported elsewhere in the literature.

time of proposal defense. Questionnaire to be administered but analyzed only if Cronbach's alphas become available and are >0.7.	
NVivo software was to be used to prepare and analyze the interviews.	Data analysis was conducted using hand coding due to the small sample size.

RESEARCH PARTICIPATION DECISION-MAKING AMONG YOUTH AND PARENTS OF YOUTH WITH CHRONIC HEALTH CONDITIONS

Dissertation Defense

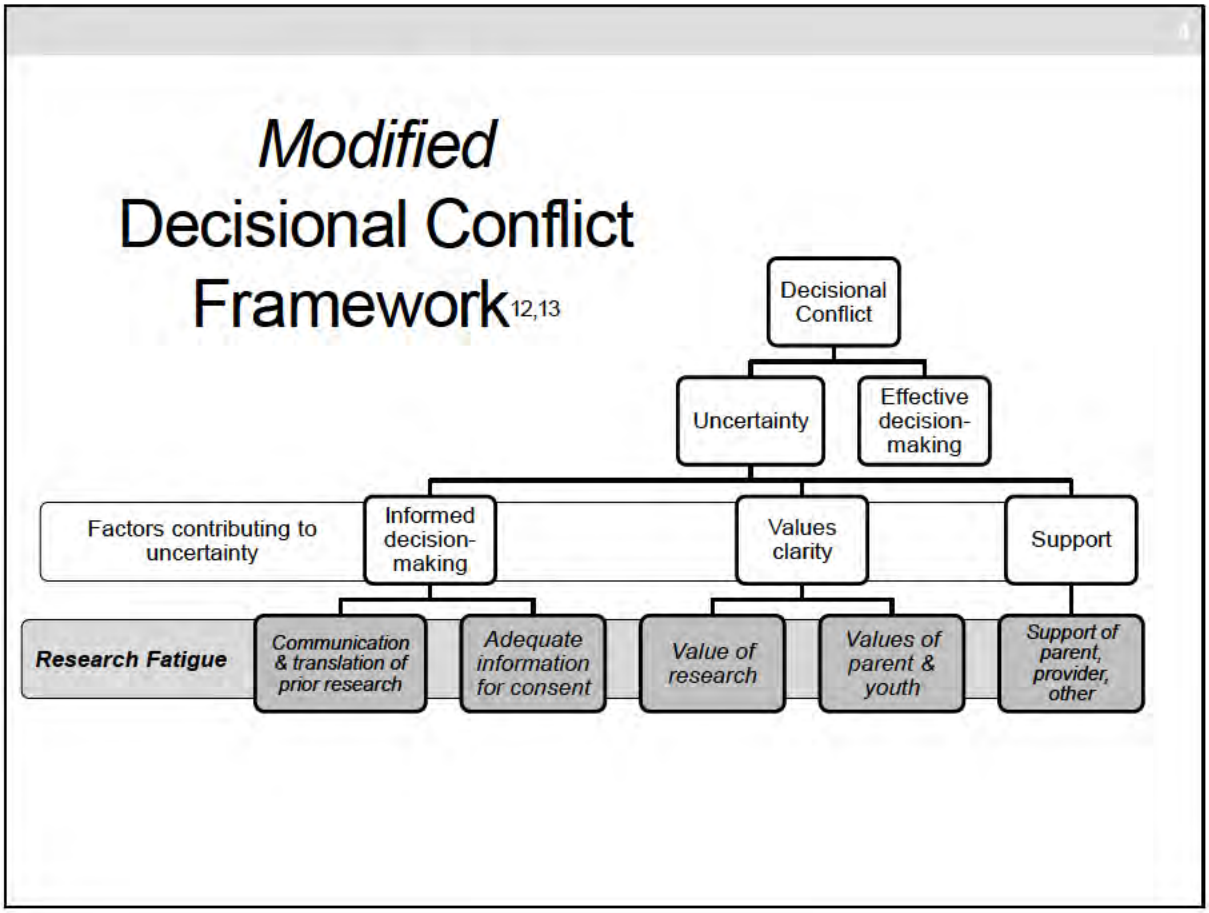
Jesica Pagano-Therrien, MSN, RN, CPNP
University of Massachusetts, Worcester

Background and Significance

- Clinical research has improved the care & treatment of youth with chronic health conditions (CHC)[1-3]
- Pediatric-focused agendas for HIV, cystic fibrosis (CF) and type 1 diabetes (T1D) research present many opportunities for participation[4-7]
- Important to understand factors impacting recruitment and retention:
  - Burden of study requirements
  - Research fatigue from repeat participation[8-11]

Purpose

- This study explored whether youth with HIV, CF, and T1D and parents of youth with the same conditions describe features of research fatigue as factors that impact decision-making about research participation.


Modified
Decisional Conflict Framework[12,13]
Decisional Conflict
Uncertainty
Effective decision-making
Factors contributing to uncertainty
Informed decision-making
Values clarity
Support
Research Fatigue
Communication & translation of prior research
Adequate information for consent
Value of research
Values of parent & youth
Support of parent, provider, other

5

Specific Aims

- Among youth with HIV, CF, and T1D, and parents of youth with the same conditions, to describe:
  1. How *communication* and *information* impact decision-making about research
  2. How participant's *values* influence decision-making about research
  3. What types of *support* are perceived to be important in order to minimize participation burden and research fatigue
  4. Potential strategies to optimize support for decision-making and reduce research-related burden and fatigue

METHODS

Design, Sample and Setting

- Qualitative description[14,15]
- Purposive sampling
  - Youth with HIV, CF & T1D and parents of youth with these CHCs who have made prior decisions about research participation
- Recruitment:
  - Outpatient subspecialty clinics at an academic medical center where research activities are robust
  - Assisted by clinical care providers & research staff

Inclusion Criteria

Youth	Parents
Diagnosed with HIV, CF, or T1D	Parent or legal guardian of a youth with HIV, CF, or T1D
Age 13-21	Primary responsibility for providing consent for past study participation
Prior participation or invitation to participate in at least one study	Child with prior participation or invitation to participate in at least one study
English speaking	English speaking
Able to respond meaningfully to interview questions	Able to respond meaningfully to interview questions

9

Procedures

- Study was approved by University IRB
- Recruitment: May- December 2015
- Minimal-risk
  - Waiver of written informed consent
  - Informational "*Fact Sheet"* for consent and assent
- Retail gift card provided as gesture of gratitude

Data collection

Interviews

Decisional Conflict Scale[12,13]

(Cronbach's alpha 0.78 to 0.92)

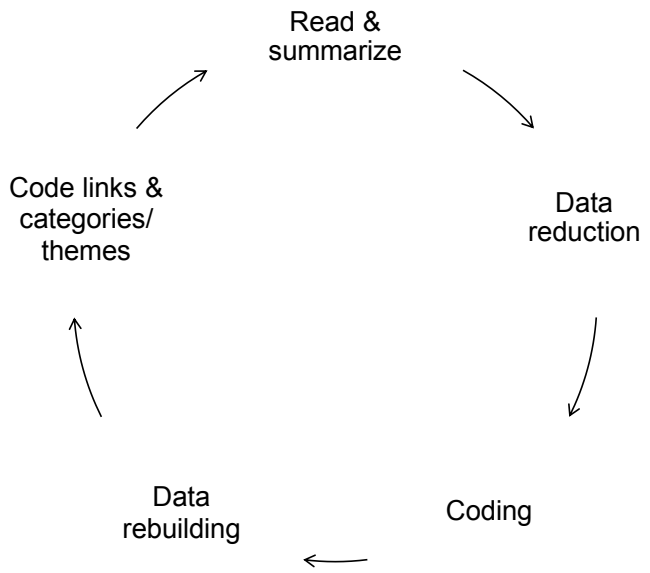
Demographics

Erikson Psychosocial Stage Inventory[16]

(Cronbach's alpha 0.71-0.78; 0.63-0.73)

11

Data analysis: Qualitative Content Analysis[17]



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Data analysis: Comparisons of interview responses & DCS

Within-participant	Across-participants
• DCS will validate interview responses	• Themes derived from those with high v. low DCS scores

Ensuring Trustworthiness[18]

Credibility	Transferability	Dependability	Confirmability

• Triangulation
• Modified peer debriefing
• Member checks
	• Purposive sampling → rich description	• Audit trail
		  • Field notes
		  • Reflexive journaling
			• Audit trail
			• Triangulation

RESULTS

15

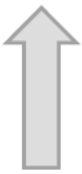
Subject Demographics

	n	%
HIV	8	44
CF	5	28
T1D	5	28

	Parents, N=8	**Youth, N=10**
	M (range)	**M (range)**
Age	48.75 (33-61)	18.5 (14-21)
Number of Past Studies		
Invited to participate	7.3 (1-20)	4.4 (1-12)
Agreed to participate	6.9 (1-20)	3.3 (1-6)
Declined to participate	0.2 (0-1)	0.8 (0-6)
	n (%)	**n (%)**
Gender		
Male	0 (0)	6 (60)
Female	8 (100)	4 (40)
Race		
Caucasian	7 (87.5)	8 (80)
Other	1 (12.5)	2 (20)
Ethnicity		
Non-Hispanic/Latino	7 (87.5)	7 (70)
Hispanic/Latino	1 (12.5)	2 (20)
Not reported	0 (0)	1 (10)

16

Differences in youth scores on the EPSI subscales were not statistically significant



p=.835

Themes

- "A part of life."
- Fundamental Trust
- Informed Consent
- "A two-way thing."
- "Think beyond ourselves."
- Transitions

18

Blurred Lines

- Blurred line between clinical care and research
- Clinicians serving in research roles
- Conveniences and challenges with this model

19

Blurred Lines: "A part of life."

- Parent:

  "I guess I had so much else going on in life that participating in the study was kind of 'behind the scenes.' And I guess because we participated in a number of them, it just became routine as part of clinic..."

20

Blurred Lines: "A part of life."

- Youth:

  "My day consists of doing two, twenty-minute sessions on a percussion machine, inhalers, antibiotics…so it's just a part of my life. You can't really get tired...I understand the necessity and when there's an offer [to take part in research] being put out to me that could help, I'm gonna take it."

21

Blurred Lines: Fundamental Trust

- Youth:

  "I've known these people forever so if they didn't have my best at heart then they wouldn't be doing it."

22

Blurred Lines: Fundamental Trust

- Parent:

  "We have the most contact with the nurse. I think the person I feel most comfortable with is really who it should be…I wouldn't say it should be a stranger."

- Parent:

  "I feel so comfortable with her [social worker]. That's the only person that I trusted enough."

23

Blurred Lines: Informed Consent

- Parent:

  "I think it can be confusing at that moment because we are in clinic anyways and you don't really have the time to sit and absorb what is actually happening and I think especially like with him, he was always a busy kid, so you were trying to rein him in and I mean, honestly, I probably didn't even read three quarters of it, I just signed it. When I knew that it wasn't going to take more time than our normal clinic visits I was like 'this has to be important' and I signed it."

24

Blurred Lines: Informed Consent

- Youth:

"I'll do anything that they want me to do so long as it doesn't have a major negative side."

25

Hope for the Future

- Hopeful and optimistic about the future
- Progress fosters hope and enthusiasm for additional research
- Cure, contributing to the greater good are factors that drive motivation to participate
- Transitions

26

Hope for the Future: "A two-way thing."

- Youth:

  "Like when I was born, [I was] not expected to live more than a few years and that makes me really think…I have to repay her…[research is] to help the scientists and [the doctor] so it's kind of a two way thing, it's helping her, helping research and finding a cure one day."

27

Hope for the Future: "A two-way thing."

- Parent:

  "I always got that faith, you know that hope, that the more they study the more they learn and one day maybe they get the cure. So that's my motivation all the time."

28

Hope for the Future:
"Think beyond ourselves."

- Youth:

  "I'm never gonna say no unless it's like super high risk. Because it's not only about me it's about a lot of other people."

29

Hope for the Future:
"Think beyond ourselves."

- Parent:

  "'I know it might bother you for that little bit of time while you are in there having those additional blood draws but…we kind of have to think beyond just ourselves for that short time…because a long time ago somebody else participated in a study for these medications you're taking, you've had such a great outcome so whatever we can do to help somebody down the road is better.'"

30

Hope for the Future: Transitions

- Youth:

  "If I wanted to do it I would just say 'I want to do it.' They never really pushed me to do anything…it was all my decision even before I was 18. They signed off but they would ask me if I wanted to do it and in the end, my decision was the final one."

31

Hope for the Future: Transitions

- Parent:

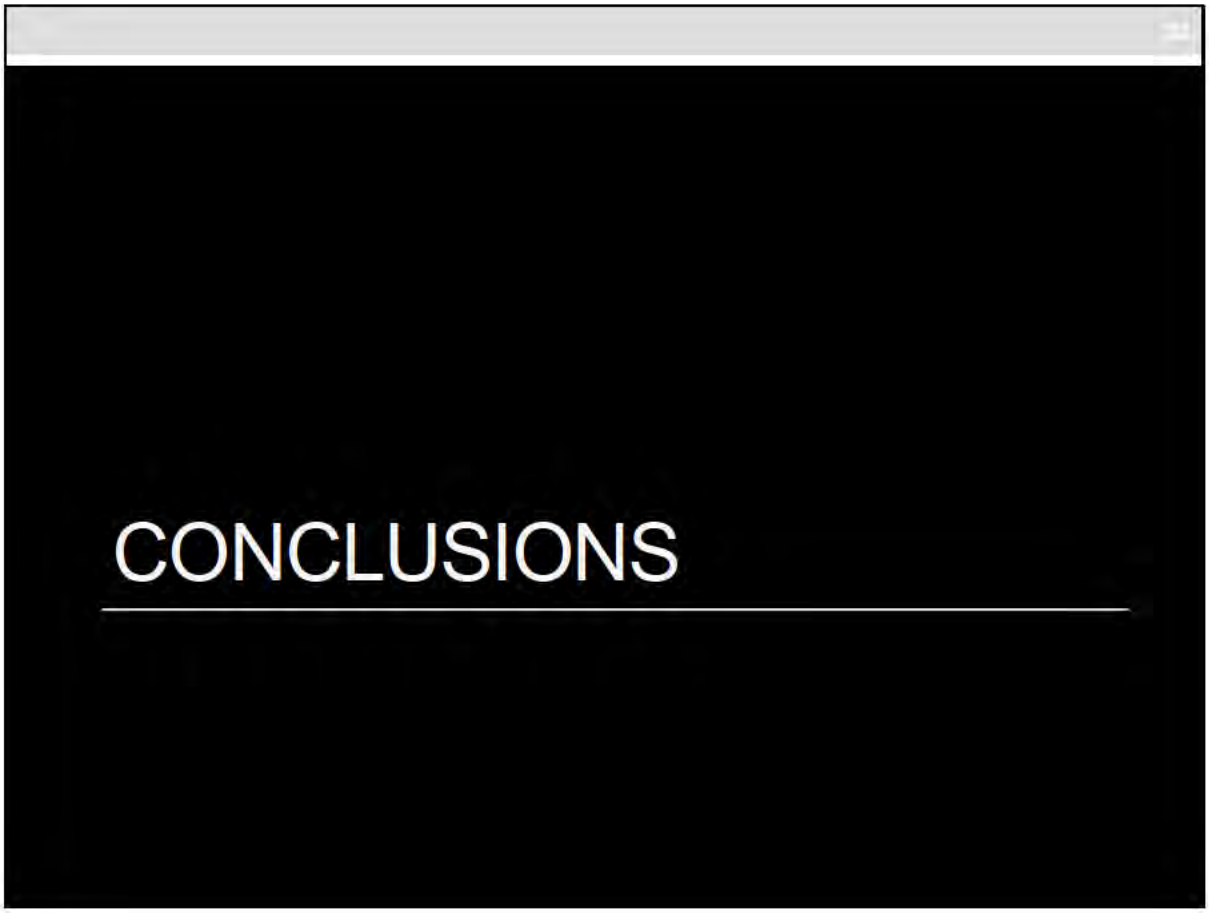
  "[It will be important for her to have] someone to talk to about it. I know she will come to me and ask to do it or not, if she should do it… I would be here to help her whenever she needed it."

32

Both youth and parent scores on the Decisional Conflict Scale were low

	Youth	Parents
Scale	M (range)	M (range)
Total	10.3 (0-31)	12.1 (0-33)
Uncertainty	9.8 (0-33)	9.4 (0-33)
Informed	10.6 (0-25)	12.5 (0-25)
Values clarity	14.4 (0-50)	18.9 (0-67)
Support	8.3 (0-33)	10.4 (0-25)
Effective decision-making	8.5 (0-31)	10.1 (0-25)

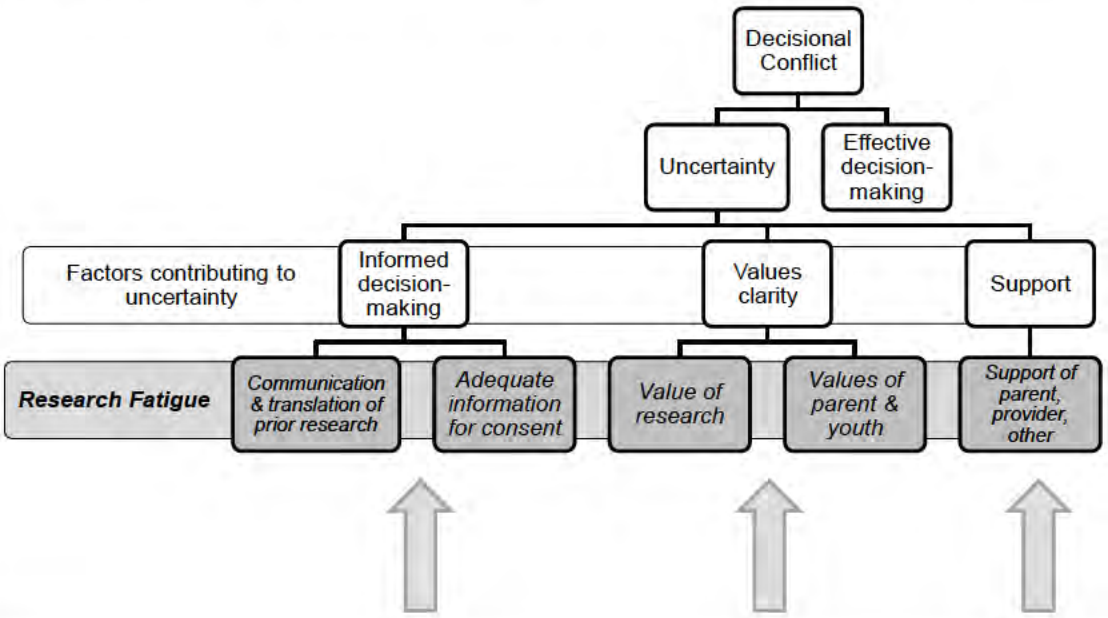
Note. Scores range from 0 [no decisional conflict; feels extremely certain/informed/clear about personal values/supported; good decision] to 100 [extremely high decisional conflict; extremely uncertain/uninformed/unclear about personal values/unsupported; bad decision.]


CONCLUSIONS

Limitations

- No participants who had only said no to a study
- Possible recall bias
- Sample was largely Caucasian and non-Hispanic/Latino
  - Lack of diversity specific to HIV group
- Parents were all mothers/female guardians

Fit of the *Modified* Decisional Conflict Framework



Implications

Fundamental Trust

- Awareness of competing interests of dual role
- Impact on Informed Consent
- Strategies:
  - Simulation scenarios
  - Input from Research Subject Advocates (RSA)

Transitions

- Supporting independent decision-making
- Research literacy skills as part of transition preparation

37

Conclusions

- Integrated model of clinical care and research maximizes convenience and alleviates research fatigue
- Pearl for supporting decision-making and promoting engagement of youth in research:
  - Show gratitude by sharing study results/outcomes with participants whenever possible

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39

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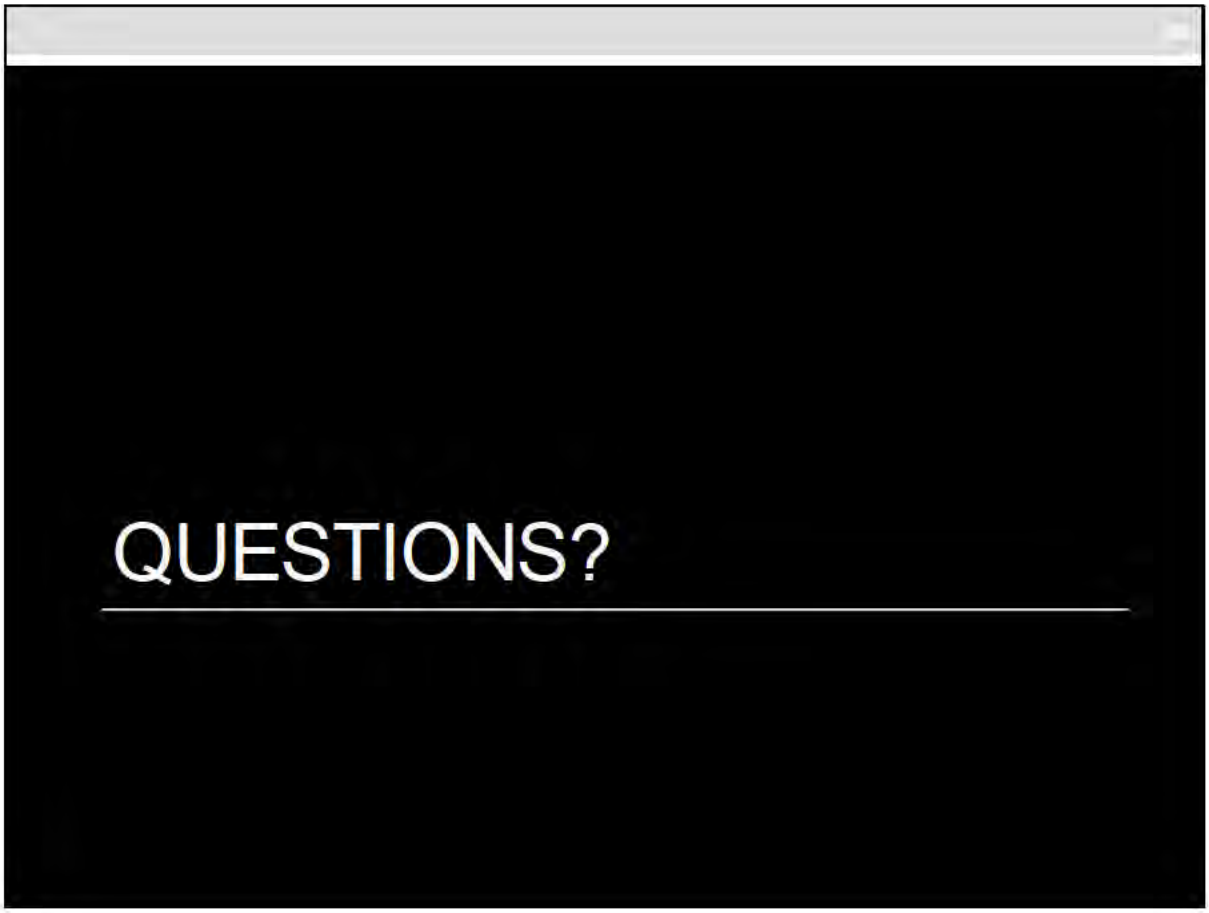
QUESTIONS?

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