ONE IN A MILLION: NAVIGATING HEALTH INFORMATION AND ADVOCACY IN RARE DISEASE DIAGNOSIS AND TREATMENT

by

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Fairfax, VA

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DEDICATION

This work is dedicated to all patients, whether your disease is rare, common, or undiagnosed – may you find answers, peace, and health.

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LIST OF ABBREVIATIONS

A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 ..... ADAMST13
Acquired Immune Deficiency Syndrome ..... AIDS
Complete Blood Count ..... CBC
Comprehensive Health Enhancement Support Systems ..... CHESS
Electronic Health Communication ..... eHealth
Food and Drug Administration ..... FDA
General Practitioner ..... GP
Government Accountability Office ..... GAO
Health Significant Other ..... HSO
Hemolytic-uremic syndrome ..... HUS
Human Immunodeficiency Virus ..... HIV
Immunoglobulin A ..... IgA
Immunoglobulin G ..... IgG
Low-Literacy User Cancer Information Interface ..... LUCI
Microliter (one-millionth of one liter) ..... mcL
Mobile Health Communication ..... mHealth
National Cancer Institute ..... NCI
National Heart, Lung, and Blood Institute ..... NHLBI
National Organization for Rare Disorders ..... NORD
New Drug Application ..... NDA
New Molecular Entity ..... NME
non-governmental organization ..... NGO
Office of Information Technology ..... OIT
Office of Orphan Products Development ..... OOPD
Office of Rare Disease Research ..... ORDR
Orphan Drug Act of 1983 ..... ODA
protein molecular weight ..... kDa
Rare Diseases Europe ..... EURORDIS
Research and Development ..... R&D
Statistical Package for the Social Sciences ..... SPSS
Thrombotic Thrombocytopenic Purpora ..... TTP
ultralarge von Willebrand factor ..... ULvWF
Uncertainty Management Theory ..... UMT
Uncertainty Reduction Theory ..... URT

United States Centers for Disease Control..... CDC
von Willebrand disease.....vWD
von Willebrand factor .....vWF
World Health Organization.....WHO

ABSTRACT

ONE IN A MILLION: NAVIGATING HEALTH INFORMATION AND ADVOCACY IN RARE DISEASE DIAGNOSIS AND TREATMENT

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George Mason University, 2013

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Background: Rare diseases represent an important public health issue; prevalence is an estimated 30 million patients in the United States. Efforts from advocacy organizations and governmental outreach based on assumptions derived from mainstream diseases fail to address the unique challenges rare diseases present, resulting in alienation, isolation, stigmatization, and poor health outcomes. Methods: Current ehealth practices were compared with needs reported by patients and HSOs with a selected rare disease via 1. content analysis of threads (n=852) from a pre-eminent online advocacy community; 2. content analysis of advocacy, government, and non-scientific resources 3. Cross-sectional surveys (n=57); 4. In-depth interviews (n=28); 5. Focus Group Discussions (n=12). Findings: Analyzed qualitatively and quantitatively using *a priori* codes to evaluate Weick's model of organizing and Uncertainty Management Theory as well as codes emerging via Grounded Theory, the exemplar rare disease community fails to meet the

needs described by patients and HSOs. Interactions were low (mean = 1.81 responses, median and mode = 0) using the mainstream mechanism. Conversely, patients informally organizing reported a reduction in isolation and equivocality and were more equipped with strategies to manage their health. However, they lacked ability to advocate on a large scale and questioned information credibility. Conclusions: Rare disease patients rely on peers for social support and information. Leveraging the resources of well-known advocacy groups with a patient-centered model will enable peer-to-peer support and information sharing, leading toward the understanding of the pathogenesis and side effects associated with rare diseases.

Keywords: rare disease communication, health communication, Weick's model of organizing, UMT, eHealth communication, disease advocacy, message boards, online communities

CHAPTER ONE: STATEMENT OF THE PROBLEM

Introduction

Rare diseases collectively affect 30 million Americans (NORD, 2011), but it is challenging to find consistent information about specific rare diseases, especially in language that is understandable to most patients. Rare disease patients experience alienation and feelings of marginalization because of their limited ability to access information about their conditions, and encounter various obstacles throughout their diagnosis and treatment processes (Field & Boat, 2010; Brown, 2011). An examination of this problem from the perspective of health communication explores whether many of the factors that contribute to rare disease patients' difficulty in navigating the healthcare system and subsequent experiences of alienation may be eased with effective communication. Strategic and effective health communication can improve health outcomes, and patients who are able to consume accurate and clear information about their health are more likely to follow treatment regimens and receive treatment that is consistent with their symptoms (Kreps, 2005). Chronic disease patients participating in online communication forums have been found to achieve a collective wisdom as a result of communicating shared experiences, which can assist patients and their teams of physicians in reaching accurate diagnoses and in both understanding and responding to certain symptoms (Fox & Jones, 2008). Patients learning from each other's experiences

can help to build a sense of community and reduce feelings of alienation that stem from navigating life-threatening or changing illnesses (Macias et al, 2005). In addition to the benefits that patients see, inclusion of patients in the development of drugs and treatments has potential to improve productivity by decreasing value conflicts and associated scrutiny during the pharmaceutical development and approval process which has stagnated in recent years (Cohen et al, 2007).

Several interest groups and organizations have worked to improve the visibility of rare diseases with limited success. The current leading online repository for information about rare diseases (a partnership between the National Organization for Rare Disorders and Rare Diseases Europe, available at www.rareconnect.org) is working to develop online communities for individual rare diseases. It is still relatively young and thus extremely limited in scope; despite the fact that there are more than 7,000 rare diseases. There are online communities for only about 32 diseases on this website. NORD/EURORDIS follows a model that is similar to other health communication interventions for more mainstream diseases, through which interest and funding are garnered by demonstrating the number of people who are affected by the health problem. The more people affected, the stronger the rationale is for garnering attention and support. However, this model is problematic in an application to rare diseases because ignoring the many rare diseases that affect limited numbers of patients has the potential to further marginalize members of the communities whose diseases are not included due to relatively low numbers of individual diagnoses and because rare diseases are not a monolithic entity, but represent a range of often disparate health challenges.

In addition to the potential benefits that will be provided to the healthcare field as a result of informed and connected patients, there is a great deal to be learned from how patients communicate with one another to support their health-related information needs. Weick's model of organizing states that organizational actors require increasing help from others to gather relevant and revealing information as the problems they face become increasingly difficult to interpret and respond to (Weick, 1969). Weick contends that the process of organizing is a set of interconnected communication processes that are used to resolve equivocality of uncertain situations for problem solving and adaptation, and that organizing occurs in three phases: enactment, selection, and retention. This model can be fruitfully applied to healthcare situations, and in this context, health communication enables patients and healthcare providers to manage decision-making in times of high uncertainty (Kreps, 2009). Coupling Weick's model with Uncertainty Management Theory (UMT), which explores the complex relationship that patients have in coping with uncertainty and the roles that uncertainty can play at different periods, can lead to a study that will help to illuminate the organizational and information needs of people confronting health crises.

Instead of reliance upon the dominant model and mass outreach, this study posits that health communication that is informed by grassroots communication strategies is essential to reaching, informing, and enabling patients with rare diseases to advocate on their own behalf. A strategy that takes advantage of eHealth technologies, such as online message boards, websites and forums, smartphone apps, and social media, will be extremely beneficial in disseminating relevant health information to those confronting

rare diseases. The use of informal social networks can be empowering to patients, which is psychologically useful (Panth, 2010). By relying on patients to be the voices of their own communication campaign, a system could be designed to provide important resources and community-building to patients who have a rare disease. This could begin a discussion to empower patients to take a more active role in the healthcare process.

Statement of the Problem

The current established norm of communication about rare diseases appears to follow a model that is similar to more mainstream diseases; the number of people collectively affected by health care problems is touted, but actual advocacy or treatment for specific rare diseases is limited. Funding is more prevalent for health issues affecting larger numbers of people. However, this strategy limits the ability of many rare disease patients to participate in the community-building and information seeking that is described above and is necessary to help them achieve improved outcomes. This proposal is for a study that will explore the design of communication strategies to better address the specific needs of patients with rare diseases.

Purpose of the Study

This study will serve as a basis for guiding communication about rare diseases in the future and empowering healthcare actors, including patients diagnosed with rare diseases, their health significant others (who act as caregivers), and healthcare providers who interact with these patients. The study will evaluate the existence of social networks surrounding people navigating the healthcare system to cope with rare diseases. Levels of

personal information equivocality will be measured, as will the amount and quality of interactions to help manage high levels of equivocality. Exemplar rare disease communication venues will be analyzed as a control to determine how rare disease patients are currently using these fora, and actors will be interviewed to determine their existing information needs as they have experienced them. This study will be used to inform the creation of a set of recommendations and considerations that can be applied broadly across rare diseases support programs, but the product of this particular study will only be discretely applicable to idiopathic Thrombotic Thrombocytopenic Pupura (TTP), an autoimmune blood disorder affecting roughly 4 out of every million Americans.

Key Terms and Necessary Background Information

There are several non-technical terms with specific definitions that will be used throughout this dissertation. This section includes operational definitions of these terms.

Definition of key terms.

Rare disease: For the purposes of this study, a rare disease is defined as a disease affecting less than 200,000 Americans. There are more than 7,000 rare diseases, which collectively affect more than 30 million Americans.

Equivocality: Central to Weick's model of organizing, equivocality is the complexity or difficulty associated with navigating unknown or unfamiliar systems.

Actor: In this study, any person interacting with the healthcare system surrounding a rare disease will be referred to as an actor. This could include patients, healthcare consumers, family members and loved ones of patients, health care providers, and caretakers.

Patient: A patient, in this context, is anyone who has been diagnosed with a rare disease. They need not currently be undergoing treatment, but will have received a diagnosis and have at one point been under the care of a healthcare provider for their rare disease.

Healthcare Provider: A healthcare provider is an individual with professional training in the delivery of health care who is directly responsible for helping a patient to navigate information regarding their diagnosis, treatment, or prevention. This can include physicians, nurses, mental health providers, and medical technicians.

Health Significant Other (HSO): A health significant other is a person, commonly a family member or spouse, who is often responsible for caretaking, decision making, and treatment adherence for a rare disease patient. This person frequently takes the patient to appointments with their healthcare provider, and is tasked with making decisions for the patient when the patient is not able to.

Clinical information about TTP and communication implications. Thrombotic Thrombocytopenic Purpura (TTP) is a rare blood disease that affects fewer than 4 per 1 million people. TTP can be inherited or acquired, although the exact pathogenesis is somewhat contested within the scientific community (Lämmle et al, 2012; Peyvandi, Palla, & Lotta, 2010). Inherited TTP, also referred to as familial TTP, is usually diagnosed during infancy, whereas acquired (or idiopathic) TTP can occur at various points throughout one's lifetime (Levy et al, 2005). TTP was first diagnosed in 1924, and

was described as a generally fatal condition that occurs among patients who were previously healthy (Lämmle et al, 2012).

TTP is a form of thrombocytopenia, a condition in which platelets fall below the normal range of 150,000 to 450,000 platelets per McL, causing low circulating platelets (NHLBI, 2012). Upon discovery of thrombocytopenia, a patient must undergo a series of evaluations to determine the reason for their low platelet count and the appropriate steps for care. Thrombocytopenia is not necessarily serious, but extremely low platelet counts can result in bleeding (internal or external) and renal failure, which can be fatal.

Patients who are found to have TTP are often diagnosed through exclusion. Thrombocytopenia typically affects young women, with a female to male ratio of 3:2 (Levy et al, 2005). The protocol for patients who fall outside of this demographic category calls for healthcare providers to seek out alternative diagnoses (e.g. HIV/AIDS, non-Hodgkin lymphoma) (Provan et al, 2010). Patients who are found to have no alternate conditions and whose symptoms have a certain level of severity may ultimately receive a TTP diagnosis. TTP is clinically defined as the presence of a pentad of symptoms: microangiopathic hemolytic anemia, thrombocytopenic purpura, neurologic dysfunction, renal dysfunction, and fever; however, most patients do not exhibit all five characteristics (Vesely et al, 2003). The level of uncertainty in diagnosis and treatment is complicated by the high mortality rate: 95% of TTP cases that go untreated are fatal (Fischer Conner & Rajan, 2012). Once other diagnoses have been ruled out and TTP is diagnosed, treatment is largely experimental and catered to the specific presentation of symptoms by the patient. The goal of treatment is to restore the platelet count and must

target the cause of low platelets. Low platelet counts can occur because of low platelet production (i.e. the bone marrow does not produce enough platelets) or low circulation (i.e. enough platelets are produced but they are held in the spleen or the body destroys them or uses them too quickly) (NHLBI, 2012). There is a range of possible treatments, including some combination of plasma exchange, corticosteroid treatment, chemotherapy, transfusions (red cell and platelet), and splenectomy. Many of the treatments that have been found to be effective have not been tested in randomized controlled trials because of the rareness of the disease, and studies that represent substantial advances in treatment have very small sample sizes of between 1 and 4 patients (Lämmle et al, 2012; Furlan et al, 1998). The reason behind the variability of treatment effectiveness is not widely understood, and treatments often are attempted in the order of severity of potential complications (i.e. more risky treatments, such as organ removal, would be a last resort) (Michael et al, 2009; Lämmle et al, 2012). Seemingly minor changes in treatment have had huge influences so far. In the 1970s, a combination of plasma exchange and fresh frozen plasma (FFP) infusion replaced standalone FFP infusion as the standard treatment. The mortality rate is now 10-20%, compared to its previous characterization as "generally fatal" (Lämmle et al, 2012). Morbidity is still high, and one-third of patients with acquired TTP will experience chronic TTP (Levy et al, 2005). Relapses occur most frequently within one year of the initial episode, but can occur at any time during a patient's life (Lämmle et al, 2012).

There are certain epidemiological similarities that represent genetic or biological predisposition to TTP; however, it appears that in practice, these are not yet understood

well enough to be applied broadly or uniformly. For example, von Willebrand factor (vWF) has long been recognized to play a role in TTP, but new findings have emerged toward an application of the specific role and its implications for appropriate treatment. vWF is a blot-clotting protein (specifically, a plasma glycoprotein) whose functions include acting as the primary adhesive link between platelets and the subendothelium and carrying and stabilizing a coagulation factor in the blood (Levy et al, 2005). vWF multimers are most active when they are initially released, at which point they are large. As they mature, they reduce in size substantially (from about 20,000 kDa to about 300 kDa) or cleaving enzymes break them into fragments. Smaller vWF multimers are less active. Numerous studies of TTP patients' plasma (including patients with familial and acquired TTP) have found unusually large vWF (ULvWF) multimers, which cause platelet aggregation (Furlan et al, 1998). It is thought that the ULvWF multimers remain in circulation due to a lack of ADAMTS13, which is a cleaving enzyme that is also referred to as vWF-cleaving protease (vWFCP). In fact, a test for ADAMTS13 activity is one of the very few diagnostic instruments used for TTP. However, estimates on the prevalence of severe ADAMTS13 deficiency in acute TTP patients vary from 30 – 60% (Vesely et al, 2003 and Lämmle et al, 2012, respectively). For example, Peyvandi et al's (2012) discussion of the treatment TTP, which deals specifically with TTP in the cases of severe ADAMTS13 deficiency that is either genetically caused or caused by autoantibodies, states that "it should also be mentioned that there are idiopathic cases of TTP with only slightly deficient or even normal ADAMTS13 levels at presentation, but these cases are not object of the present article in which idiopathic and autoantibody-

mediated TTP are used as synonyms" (p. 1444). Therefore, while this is a useful diagnostic device, it has a limited reach in terms of application (Vesely et al, 2003), and causes confusion about treatments and the epidemiology of the disease within the scientific and lay communities. Patients who do not show severe ADAMTS13 deficiency may still receive a TTP diagnosis and undergo treatment accordingly. Beyond the initial ADAMTS13 screening, additional screening is not generally part of follow up (Vesely et al, 2003). Some online resources acknowledge that ADAMTS13 screening results will rarely change the treatment protocol (e.g. NHLBI, Wikipedia, WebMD); otherwise, there is inconsistent mention of ADAMTS13 screening in the literature that has been created to be accessible to the lay-person.

Unlike the health information materials or testing protocols mentioned above, the scientific literature focuses sharply on elements and biological processes that affect ADAMTS13 function, noting important implications for understanding and treating TTP. Decreased or completely deficient ADAMTS13 has been associated with low platelet count and recurrent TTP in longitudinal studies. In a seminal study of a patient with chronic recurrent TTP, complete ADAMTS13 deficiency was found during the first acute TTP manifestation. This patient's protease activity increased during remission and their platelet count stabilized; the ADAMTS13 subsequently disappeared and platelet count declined twice, each time leading up to TTP reoccurrence (Furlan et al, 1998). Lämmle et al (2012) (citing Peyvandi et al, 2008) note that persistent recurring severe ADAMTS13 deficiency and/or the presence of ADAMTS13 antibodies during remission was found to be a predictor of TTP recurrence in a study of 109 TTP patients followed over the course

of 12 years. Patients in this study who had ADAMTS13 antibodies or deficiency were more than three times more likely to experience reoccurrence than patients with normal protease activity. Access to this information could seriously affect decisions made by patients who are in remission as they negotiate follow-up protocols with their health care providers.

TTP is treated as an autoimmune disease regardless of the outcomes of ADAMTS13 screening. This can be seen by the NHLBI's attribution (above) of TTP to destruction of platelets in the spleen in cases of adequate platelet production but low platelet circulation (2012). Current scholarship builds on this hypothesis, notably the recent discovery that inhibitory antibodies target ADAMTS13 epitopes in the spacer domain, which is a part of the ADAMTS13 protein that is necessary for vWF-cleaving (Lämmle et al, 2012). Depleted or decreased vWF-cleaving has been attributed to the presence of immunoglobulin G (IgG) inhibitors, so studies on the effect that these agents have on the ADAMTS13 structure offer promise for TTP treatment and would aid in predicting and potentially avoiding reoccurrences (Furlan et al, 1998; Levy et al, 2005).

Many acquired TTP patients with chronic episodes have confirmed presence of autoantibodies that inhibit ADAMTS13 and vWF-cleaving activity. However, in addition to autoantibodies that specifically target ADAMTS13 (such as IgG antibodies inhibiting protease activity), antibodies that are directed at other molecules with a physiological interaction with ADAMTS13 could also inhibit its functional activity (Klaus, 2004). Lämmle et al (2012) argue that these findings must be investigated; the foundational

studies have limitations, such as retrospective sampling, but could seriously influence what is currently known about TTP and how it is treated.

> If a high titer inhibitor, a combination of several Ig isotypes, and/or persistence of severe ADAMTS13 functional deficiency during remission do indeed sensitively predict disease relapse, interventional strategies…should be evaluated for their prophylactic efficacy (Lämmle et al, 2012, p. 175).

For example, splenectomy had been established as an acceptable treatment method because of the role that the spleen plays in autoimmune responses, and has been part of treatment protocol for some time. Schaller et al (2011) offer a deeper understanding of the reason that splenectomy is an effective treatment for chronic, recurrent TTP, suggesting that anti-ADAMTS13 B cell clones are produced in the spleen. B cells play an important and complicated role in autoimmune function, and their role in ADAMTS13 function must be further examined (Siegel, 2009). Further, Lämmle et al (2012) suggest that the seemingly random success or failure of treatments across patients could mean that what is currently considered to be TTP could actually be multiple diseases that have similar symptoms but distinct causes (e.g. deficiency of ADAMTS13 vs. ADAMTS13 activity inhibited by other biological functions). Further exploration of these processes could reduce ineffective and unnecessary treatments, enable a departure from the current, often experimental approach to treatment approach, allow efficient and appropriate treatments, and reduce likelihood of relapse. Effective communication, especially between patients and physicians, could be crucial to this process, such as in cases where minor symptom differences would suggest distinct conditions.

It is also possible that treatment for other diseases and disorders is exposing patients to risks for TTP. von Willebrand Disease (vWD) is the most commonly inherited coagulation disorder, characterized by low quantity or poor quality vWF. It is treated by supplementing vWF or stimulating its production (Kessler et al, 2012). Mannucci et al (2004) have found that there is a negative association between vWF and ADAMTS13 (i.e. injecting healthy patients with vWF significantly decreased their ADAMTS13 levels).

TTP patients can fully recover while remaining severely deficient in ADAMTS13, which implies that low ADAMTS13 may not cause TTP. Instead, an acute condition such as an illness or infection, coupled with a low ADAMTS13 level could spur an acute TTP episode (Lämmle et al, 2012). This is consistent with the assertion made by Furlan et al (1998) that ADAMTS13 deficiency predisposes patients to chronic acquired TTP. It is not yet understood why some otherwise healthy people develop autoimmune reactions that target or affect ADAMTS13, but there is some evidence that genetic factors may contribute (Studt et al, 2004), and more evidence that a triggering event causes the onset of acute TTP (Shah & Sarode, 2013). An exploration of this connection seems to be extremely important in the understanding of TTP, diagnosis, treatment, and continued care post-clinical remission.

Pending the results of continued studies and acceptance of the implications into treatment protocols, patients may begin to interact with ADAMTS13 screening results much more than they currently are. Because of the current limited availability of this information, it is unlikely that many patients are aware of the significance and body of

research that is being done regarding the various potential causes of ADAMTS13 deficiency, ULvWF multimer presence, platelet aggregation, and TTP. Patients would benefit from having some level of awareness about current scholarship on ADAMTS13 activity and their disease. There is reason to believe that some widely used screening tools for ADAMTS13 may not accurately capture *in vivo* function (defined as function as it would occur naturally, as opposed to *in vitro* function, or function in a controlled environment), particularly where static assays are used instead of flow based assays (Lämmle et al, 2012). Flow based assays, which yield more detailed information and offer a more physiologically accurate understanding of vascular processes, are more challenging to conduct (Butler et al, 2009). Patients could be well served to advocate for this more detailed evaluation, especially in the event that physicians without much experience with this particular rare disease do not closely follow the latest ADAMTS13 research. Promising research advances signal potential for positive future directions, but relatively few scientists engage in this work because of the rareness of TTP. Researchers who recognize the limitations of ADAMTS13 as a defining characteristic of TTP have also turned toward antibody and antigen testing, especially in the interest of determining treatment and prognostic protocols (Shah & Sarode, 2013). Formative research suggests that patients are typically unable or too overwhelmed to parse this information, which appears in especially specialized scientific journals, precluding the likelihood for self-advocacy for further research or more appropriate screening and monitoring methods. Further, "there is clinical overlap with hemolytic uremic syndrome (HUS), autoimmune disease, and a spectrum of pregnancy-related problems" (Scully, et

al., 2012), which makes diagnosis difficult and also has implications on patients' understanding of what disease they actually have.

I have selected TTP as a case study for rare disease communication for multiple reasons. My initial introduction to the uniquely extreme complexity of navigating information and communication about a rare disease came from a personal relationship with a patient who had been diagnosed with acquired idiopathic TTP. As a result of this relationship, I have my own experience as an HSO and have an in-depth understanding of some of the processes involved in coping with this particular disease. In addition to my personal familiarity, I also note that many rare diseases are autoimmune, which results in a certain kind of complexity and rhetoric; one's body is attacking itself. Patients with TTP experience many of the challenges that occur across rare diseases, including difficulty achieving diagnosis, limited clear treatment options, variable and dramatic prognoses, and a possibility for recurrence.

CHAPTER TWO: REVIEW OF THE LITERATURE

This chapter is an exploration of the available literature pertaining to health communication about rare diseases, relevant medical and pharmaceutical processes and products, and communication strategies. A rare disease is defined in this paper as a disease affecting less than 200,000 people in the United States (Pariser, 2011). These rare diseases collectively affect 30 million Americans (NORD, 2011). A confluence of factors makes health communication for rare diseases a very challenging endeavor. These factors include the limited availability of health information to patients; the way that information is made available to patients; the nature of rare diseases; and the process of drug and treatment development in the United States. In this literature review, I will present information available on rare disease communication and will consult literature from other disciplines to supplement the information in my review. My review of the literature will demonstrate the unique challenges presented by rare diseases and will point toward a need for the development of specific communication strategies to address these needs.

Importance of Health Information

Access to information about one's health is essential to maintaining a healthy lifestyle, understanding and making sense of what is going on with one's body, and making sound, rational decisions related to healthcare. Access to health information is a key element of many of the social movements that call for a deviation from the traditional

biomedical model of medicine, which enforces a strict delineation between patient as consumer and physician as expert (Low & Schuiling, 2005).

The *biomedical model*, which is what many people picture when they think of Western medicine, reinforces a divide between physician and patient. Even under ideal circumstances, a patient must grapple with a cumbersome process to receive medical care. Assuming that they have access to medical insurance and a physician, patients must schedule appointments, rearrange their schedules, arrange for transportation to physicians' offices, frequently waiting and enduring multiple rounds of screening before even seeing a physician. The physician may have only limited time to spend with the patient, generally separates from the patient by dress (white coat), name and honorific (Dr. Jones), and language (technical and Latin terms indiscernible to the lay person). Once the patient leaves the physician's office, the divide is further reinforced by a patient's challenges in gaining access his or her own medical records, more waiting, difficulty accessing treatment, and so on.

According to the biomedical model of healthcare, health is "the absence of disease" (Low & Schuiling, 2005). Neither the human nor the community is the focus of physicians or researchers ensconced in the biomedical model. Rather, symptoms, organs, and disease incidence are the primary areas of focus. This is problematic because it is alienating to patients, which creates turmoil in the face of indecision. It is dangerous because this model frequently excludes patients from or limits their access to the decision making process, which is an issue because patients are often best suited to monitor what is occurring with their own bodies.

While it is not a goal to eliminate or even diminish the role of the physician in healthcare, it is necessary that the patient have an active role. This assertion is prevalent in many of the healthcare models that have arisen from social movements seeking to address the inadequacies of the biomedical model. For example, the *social model* of healthcare specifically addresses the critique of the biomedical model stating that it focuses too much on symptoms and not enough on psychological and environmental factors surrounding an individual's health (or the health of many individuals). The social model pays attention to preventative and recuperative care. It acknowledges the influences of environmental factors on public and individual health, and the role of the community on an individual's health (Wade & Halligan, 2004). The social model gives equal consideration to living and working conditions, the environment, a person's access to healthcare, health habits, and lifestyle conditions. The thesis of this model is that all of these factors must be taken into consideration to evaluate, care for, and improve the health of an individual. A clear deviation here from the biomedical model is the importance of the patient's participation in his or her healthcare, both by providing information and also by taking part in a holistic approach to care (Bond & Bond, 1994).

The social model of healthcare is in line with the World Health Organization (WHO) definition of health: "a complete state of physical, mental, and social well-being and not merely the absence of infirmity" (WHO, 1946). Dissemination of accurate, clear health information that is easily accessible is very important in the social model of healthcare. In this framework, if someone lacks access to health information or

knowledge of their options, that person lacks a resource that will assist in achieving positive health outcomes.

The *feminist model* of healthcare, like the social model, advocates for a holistic approach involving the individual and the community. The feminist model is also deeply critical of the biomedical model's gatekeeping functions and lack of agency afforded to patients (Low & Schuiling, 2005). This model has foundations in the feminist social movement and is particularly focused on addressing structural gender inequities in healthcare through grassroots mobilization, information gathering and dissemination that is accessible to ordinary people (Hoffman, 2003). The feminist model notes that many vulnerable populations are not taken into consideration in medical research, which has serious consequences. One example of this is with heart disease, which had long been classified as a men's disease, but which in fact is the leading cause of death among American women (NHLBI, 2002).

The feminist model of healthcare is of particular interest to health communicators. Its call to reject many of the problematic foundational elements of the biomedical model stems not only from the criticism of exclusion of women and other vulnerable groups, but also the gatekeeping and separation of physician and patient performed under the biomedical model. The feminist model spurred the women's health movement, which began in the 1960s and sought to make healthcare more accessible. This occurred by educating women and making information available outside of a traditional medical establishment. Perhaps the best-known example of this is the publication of *Our Bodies, Ourselves* by the Boston Women's Health Collective in 1970. This book served as an

encyclopedia of women's health information and enabled women to be advocates for their own health. Prior to this movement, women were incapable of getting information about their bodies, even from health professionals.

Today, electronic health communication has largely replaced the consumption of books like *Our Bodies, Ourselves*, and the internet exists as a powerful health information dissemination mechanism. However, there still remain major gaps in health information availability. The WHO states that much of the burden of global disease stems from avoidable lifestyle decisions and Neuhauser and Kreps (2010) suggest this results from lack of information and understanding by the public. This is applicable in scenarios for prevention (such as HIV) or in care for a chronic illness (e.g. strategies for healthier living after cancer). Neuhauser and Kreps (2010) point out health communication is most effective when it has both the reach of a mass media campaign and the feel of interpersonal communication. The internet is especially useful in this regard because it allows for increased access in comparison to traditional health communication media (pamphlets, books, journals, face-to-face interactions, etc.) and allows for personalized interpersonal communication in addition to mass levels of dissemination.

The U.S. Centers for Disease Control (CDC) and the National Cancer Institute (NCI) define health communication as "the study and use of communication strategies to inform individual decisions that enhance health" (CDC, 2011). Electronic health (eHealth) communication is the use of emerging technology, especially the internet, to improve or enable health and healthcare (Atkinson & Gold, 2002). The addition of eHealth technologies allows for additional channels through which the intended

audiences may be reached. Traditional health communication channels, such as television, radio, large-scale print media (e.g. billboards, posters), and smaller-scale print media (e.g. pamphlets, newspaper ads, and Op Eds) take advantage of existing mass communication platforms to transform them into mechanisms of public health information dissemination. Health communication can also occur at a more interpersonal level, such as between physicians and patients. Often, aids such as posters and pamphlets are designed by health communicators in an effort to catalyze discussion between patients and doctors, or commercials encourage patients to speak with their doctors about certain symptoms, concerns, or medications. Health communicators may have interventions with physicians to encourage communication about health, or they may work at the community level to educate about or advocate for certain health behaviors.

EHealth communication has the same goals as health communication, but it makes use of online and digital technologies. Environments such as online message boards, websites and forums, smartphone applications, and social media (e.g. Facebook, Twitter, blogs) are utilized by eHealth communicators. In settings where digital, Web 2.0 technologies are not as prevalent (such as developing countries or other areas that remain heavily affected by the digital divide) eHealth can also be adapted. In these settings, eHealth is sometimes also referred to as mHealth, or mobile health, and can include texting or paging patients to remind them of medical appointments or to keep them engaged in a particular dialogue or cause; replacing venues such as drop-in centers with anonymous or confidential call-in hotlines; and other cell phone- or internet-based platforms. The common theme of eHealth interventions is a use of available technology

to deliver messaging on a personal level, such as to patients' cell phones or home computers.

The ability for many to become a part of health communication dialogues from anywhere in the world is one advantage of eHealth communication technologies. Building on Fox and Jones' (2008) assertion, chronic disease patients not only can establish a collective wisdom thanks to online communities – in some cases, the information gained through these collectives is more insightful than the knowledge and conclusions drawn by an individual patient/physician dyad. Patients who have access to information about their healthcare often cannot only make better decisions in their day-to-day lives, but they also can assist their healthcare team in providing medical care (Fox & Jones, 2008). A patient who is aware of, and engaged with, his or her condition may be able to more fully provide important information to his or her healthcare providers to make better decisions. Traditional health communication has championed this, but eHealth communication channels provide additional points of access and are unique in their ability to engage the target audience as users – instead of someone seeing a public service announcement or a poster, he or she can go online and talk about the issues with engaged others, read about the issues, view educational media, or play relevant digital games to personally gather relevant health information.

When designing behavior change communication interventions, a targeted approach that uses multiple venues appropriate for the intended audience must be considered and used, and messaging must be created that addresses the critical beliefs maintained by the target audience that influences their attitudes, norms, and self-efficacy

beliefs and, ultimately, their behaviors (Fishbein et al, 2002). EHealth communication platforms offer promising opportunities to expand the reach of health communicators, but these campaigns must be designed strategically and appropriately for the target audience. Fishbein et al (2002) analyze mass media campaigns that had little effect on health behavior, and in some cases, the effect of these campaigns was the opposite outcome of what was intended. This is called the boomerang effect. In one such example, youth that had been exposed to an anti-drug public service announcement reported that they were more likely to try marijuana or inhalants after watching the public service announcement (Fishbein et al, 2002). Most failures of health communication campaigns are attributable to inadequate formative research, and inadequate message testing (Kreps, in press). Preparatory research must be conducted to determine which beliefs influence the attitudes, norms, and feelings of self-efficacy that influence health behaviors (Ajzen & Fishbein, 1980). By beginning with this information, implementers may design campaigns that resonate with their intended audience to achieve the greatest influences. Additionally, messages must be crafted strategically, be clear and consistent, and should avoid vague suggestions. Brooks (2011) defines strategic communication as communication designed with the receiver in mind, and as a result of listening, planning, and consultation with the target audience. Strategic communication must also be practical and measurable within the context of the organization undertaking the initiative (Hallahan, 2007; Tatham, 2008; Argenti et al, 2005). Finally, ad placement cannot be left to chance - the mechanism and timing of delivery must be intentional to most effectively reach the target audience (Ajzen & Fishbein, 1980).

Because of the divergent needs of different communities, eHealth communication can (and should) be adapted and channels carefully selected as part of the message development and delivery strategy. Underlining the importance of delivery in eHealth interventions, NCI funded four pilot projects with innovative eHealth applications that specifically addressed the digital divide (Kreps, 2005). The populations included those who are particularly hard to reach through health communication because of different levels of access to the internet and different levels of health and technological literacy, as well as general literacy, including low-literacy seniors, underserved women who had recently been diagnosed with breast cancer, lower income minority groups and providers serving these groups, and low-income families (Kreps, 2005). The pilot projects employed various eHealth technologies to reach these groups and meet their specific needs. For example, the Computerized Health Education and Support System (CHESS) Project utilized multiple information formats in an internet-based delivery to address a digital-divide pitfall related to getting people access to health communication software. The Low-Literacy User Cancer Information Interface (LUCI) is a multi-level project whose innovation includes an expanded multimedia use of computers to adapt messaging for the target audience in the form of an interactive soap opera (Kreps, 2005). In those examples, eHealth technologies were adapted to specifically meet the needs of very narrowly defined, and hard to reach, communities.

When done well, eHealth communication has very exciting potential (Neuhauser & Kreps, 2010). In 2011, 78% of adults reported regularly searching for information online (Pew, 2011). Eighty percent of internet users have searched for health information

online (Akinson et al, 2007; Pew, 2011). Two-thirds of those who search online for health information go offline and discuss what they learned with friends, neighbors, or health professionals (Fox & Jones, 2008). Phrased differently, access to health information does not replace the doctor; it supplements traditional channels for health information acquisition, creating a more educated and more empowered patient. Access to health information is not only empowering, it aids in healthcare (Francis, 2010). Patients with access to clear and accurate information regarding their healthcare make better decisions in their daily lives and can assist their health care providers in delivering medical care. A properly educated patient knows what to look for and what to discuss with his or her physician. This, in turn, can help the physician provide more complete care.

Drug Therapy Development

The care that physicians can provide and the information available to patients are mitigated by treatment availability. The mechanisms through which treatments are developed and approved in the United States have been of concern to policy makers and industry analysts in recent decades. In November 2006, the Government Accountability Office (GAO) released a Report to Congressional Requesters on new drug development to explore claims by the Food and Drug Administration (FDA) and analysts that suggested that drug development had not increased or, in some cases, had decreased since the mid-1990s despite scientific advances and increased funding during that same time period (GAO, 2006). Of particular concern was the stagnation of the development of new molecular entities (NMEs), which contain ingredients that had not previously been

available in the United States and represent a potential for innovation and promise for prevention, care, or treatment of serious illnesses.

GAO (2006) reported an inflation-adjusted increase in research and development (R&D) expenses of 147% between 1993 and 2004 ($16 billion - $40 billion), while new drug applications (NDAs) increased by 38%, and NDAs for NMEs increased by 7%. The average yearly number of FDA approvals also declined during this period, but the percentage accepted was high (76%), which indicates that the decline of approvals is consistent with the decline in NDAs submitted.

Examining these figures in more detail provides a picture that shows more decline than is represented at first glance – the 38% NDA increase from 1993-2004 is the result of a gradual increase followed by a sharp decrease; between 1993-1999, the annual number of NDAs increased by 74% (74 – 129) but declined between 2000 – 2004. The NME numbers show similar trends – NDAs for NMEs actually declined by 40% from 1995 – 2004, but when the numbers from 1993 – 1995 are included, the overall figure from 1993 – 2004 shows a 7% increase in NDAs submitted for NMEs (GAO, 2006).

Most recent data available from the FDA (2010) show a continuation of this declining trend. From 2001 – 2010, an average of 22.9 NDAs for NMEs were approved annually (range: 17 – 36, and it should be noted that the 36 approvals occurred in 2004 and were thus represented in the GAO report). A close examination of 2005 – 2010 figures shows even less variation in approvals, with a mean of 21.8 NME NDAs approved annually and a range of 18 – 26. The FDA confirms that submission of NME NDAs have decreased from 1996 – 2010, and the second lowest number of submitted

NME NDAs was in 2010 (23 submitted); the lowest (22) was in 2002. From these data, we can infer that this is a well-established trend.

Analysis of data from The Pharmaceutical Research and Manufacturers of America (PhRMA) 2009 (Scannell et al, 2012) annual report further illustrates the declining R&D productivity based on NMEs developed per $1 billion R&D, which is illustrated in the graph below:

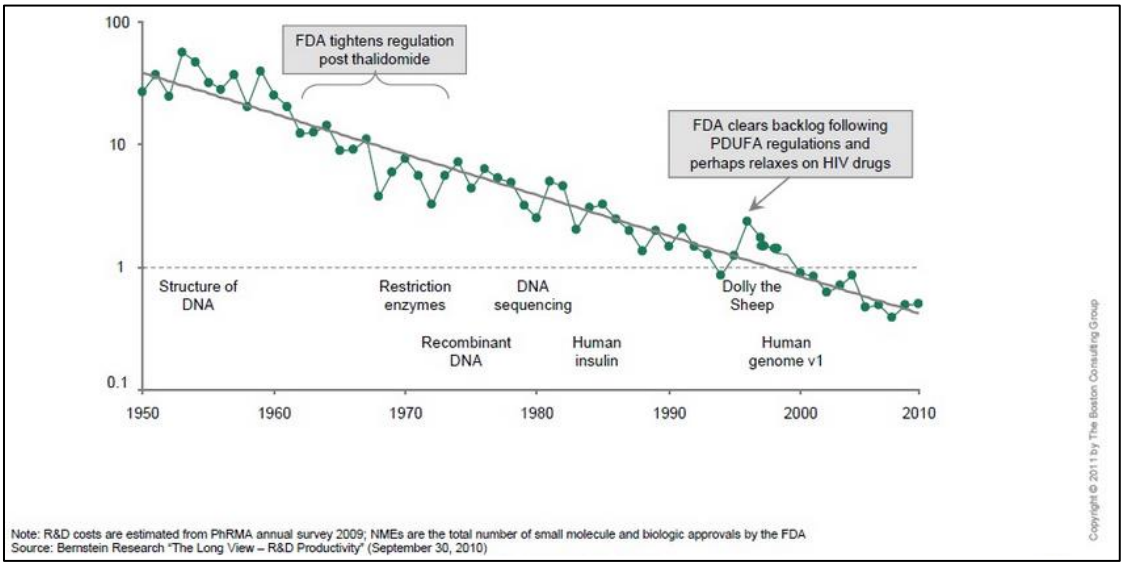


Figure 1 New drugs developed per $1 billion R&D

Some reports that examine the industry pipeline are optimistic that this trend may be shifting with an increase expected from 2012 – 2016 due to treatments that are currently in late stage development (Berggren et al 2012). However, the same reports acknowledge continued decline in revenues generated from these products, and the optimistic projected average for NDAs approved annually is expected to be 35; the yearly average for NDA approvals in the 1990s was 31. Therefore, the potential improvement

contained in this projection should be understood in proper context, especially considering the continued increased research and development investment since the 1990s. Furthermore, the report does not indicate a deluge of innovations within the pipeline, but rather, the conclusion of development and trials that began in the early 1990s (LaMattina, 2012). Projections made by Berggren et al come amid continued hand-wringing by others who are watching the industry, including pharmaceutical executives. Hewitt et al (2011) acknowledge the same pipeline findings referenced by Berggren et al, and their findings indicate that productivity will remain at a level consistent with the trend. Hewitt et al (2011) hold that this trend will persist until the method for developing drugs and bringing them to market is realigned to reflect and accommodate for current realities. Consensus reasons for this trend, which is frequently referred to as the productivity crisis, include increased costs, business decisions by pharmaceutical companies, intellectual property issues, and uncertainty about the approval process and how to translate scientific discoveries into safe and effective treatments (FDA, 2010; GAO 2006; Cohen et al, 2007).

Various initiatives have been established to address these limiting factors, including the Critical Path Initiative in 2004, which is FDA's national strategy to increase innovation in drug development (FDA, 2010). Alternately, Cohen et al (2007) suggest that this evident breakdown of the current therapy development model should be taken as an opportunity to overhaul the system and implement a patient-centered paradigm. In the current model, the patients' role is limited to consumer and voluntary participant in clinical research trials. The patient-centered model advocates for the inclusion of

educated patients during the entire clinical trial process, including bringing patient advocates and representatives to research policy and ethics discussions, based on the premise that patient collaboration will result in more effective drug therapy and treatment development. The patient-centered paradigm would increase efficiency because it "will promote a better understanding of the differences between people and laboratory animals and the role of self-awareness, hopes, expectations, attitudes, and advocacy (self-help) in treatment. This will help build trust, recruit clinical trial participants, and promote more effective development of new therapies" (Cohen et al, 2007, p. 537). Patient involvement under the current model is problematic because of conflicting core values of the various stakeholder groups, outlined by Cohen et al, consisting of scientists, clinical care providers, the pharmaceutical industry sponsors, and patients (2007). For example, the importance placed by scientists on objectivity and data may be at odds with clinical care providers whose goal is to provide their patients with the best care possible, which can become complicated when the patient is enrolled in a randomized double blind clinical trial and is in the control group. A patient's core values may prize innovation to attain access to treatment or cures, but the sponsors' competing core value of cost effectiveness and profit as part of prudent business decisions may prevent research in an area where costs will not be recovered. These conflicting values can lead to distrust, inefficient production, and unethical behavior. Competition between values that may be at odds, such as profit maximization versus treatment developments creates a negative perception, bad publicity, scrutiny, and suspicion. These discursive occurrences have material consequences, namely increased scrutiny of the pharmaceutical industry and resultant

increased regulations. Testifying before Congress in July 2011, a pharmaceutical industry executive noted that "many factors have contributed to the escalating cost, time, and risk of new drug development, [but] a changing regulatory environment at the FDA is the most significant" (Leff, 2011, quoted by Hewitt et al, 2011, p.8).

There is no indication that government scrutiny of drug development will decrease, so any strategy aimed at improving innovation and ending the productivity crisis must address the elements that are within the control of the industry. Bioethicists advise government officials when they are making policy considerations, including calls for increased regulation, and "bioethics is predicated on the premise that public and patient values matter – that physicians, scientists, and government officials should not hold complete control as to how medicine and research are practiced" (Dresser, 2003, as quoted in Cohen et al, 2007). This is part of the motivation behind the overhaul suggested by Cohen et al (2007) toward a patient-centered model, which should be given serious consideration for its ability to ease obstacles by signaling an adoption of accepted ethical principles. In addition to improving acceptability of treatment from the initial stages, fostering innovation, and increasing the effectiveness of developed treatments, a shift to a patient-centered model could help to reduce scrutiny that results from competitive core values. Ensuring the incorporation of patients' core values and rights during all parts of the clinical trial process is vital to balancing all stakeholder interests and efficiently making new treatments available.

What is a Rare Disease?

A rare disease is defined by the FDA as a disease affecting less than 200,000 people in the United States (Pariser, 2011). There are more than 7,000 rare diseases influencing Americans and cumulatively, more than 30 million Americans are living with one or more of these diseases (NORD, 2011). A rare disease can be chronic or terminal, can cause pain or go unnoticed. This loose definition is a testament to the fragmented nature of these diseases.

People with rare diseases are an especially marginalized community. By virtue of the fact that they suffer from something that is uncommon, treatment and information are difficult to secure. The Orphan Drug Act: Public Law 97-414 was passed in 1983 to help combat this (FDA, 2011; Field & Boat, 2010). Because of the privatization of drug manufacturers and pharmaceutical companies in the West, there is little incentive for the development of treatment or care for rare and orphan diseases. Because of this, promising orphan drugs may not be developed, despite their apparent effectiveness. The Orphan Drug Act (ODA) was developed to reduce the cost to develop drugs for rare conditions and to provide financial incentives for doing so (FDA, 2011). The Office of Orphan Product Development (OOPD) was established under the FDA. This office endeavors to advance the evaluation and development of products demonstrating promise in treatment of rare diseases and conditions. This office also works on issues related to rare diseases.

The Orphan Drug Designation Program exists within the OOPD to characterize drugs that are specifically intended for treatment of rare diseases. Specifically, this program provides financial incentives for the development and testing of drugs that will

be used to treat a disease or disorder affecting less than 200,000 people in the United States, or that affects more than 200,000 people but where there is no reasonable expectation that the investment will be recovered (Pariser, 2011; Field & Boat, 2010). This was put in place because of a clear lack of financial incentive for private pharmaceutical companies to devote significant resources to developing and testing treatments for which there is only a very small market. There is a further designation for the development of treatment to reach fewer than 4,000 people called the Humanitarian Use Device (FDA, 2011).

These designations resulted from a 30-year U.S. government interagency collaborative effort seeking to address the difficulty in research aimed at treatment options for truly rare diseases (Field & Boat, 2010). Anne Pariser was brought on to fill a newly created position of Associate Director for Rare Diseases at the FDA in 2010, under their initiative to expand the commitment to this fragmented, underserved population (FDA, 2010). Development is still slow-going, which is attributable in part to the general stagnation of drug development discussed above. Where specialized treatments are not available, or have not been developed, treatment for other diseases (frequently cancer) is administered. While this can be successful in treating a particular rare disease, there are often unnecessary side effects, especially in cases where chemotherapy or other invasive treatments are used in the absence of targeted drugs. Additionally, because treatment is being administered for something other than the primary designation, this can be costly for patients, as insurance companies are frequently unsupportive of off-label treatment (Field & Boat, 2010; Brown, 2011).

In addition to the lack of treatment options available for a rare disease, the isolation experienced by patients can have debilitating physical and psychological consequences. Frequently, as a result of the fragmented nature of these diseases and their low prevalence, it can take substantial time to reach a diagnosis. Often, this is because physicians are unfamiliar with the symptoms with which they are presented. This could be avoided by taking a more holistic approach through which the patient is educated and consulted, but would also require better communication between physicians, including the sharing of health records of an individual patient who has a team of doctors (Mayo, 2011).

To address these needs, especially the feelings of isolation and patients' difficulty in finding information, a few interest groups have made use of traditional and contemporary communication and community building techniques. The National Organization for Rare Disorders (NORD) is an American organization whose mission is to provide education, advocacy programs, research grants, and medical assistance targeting rare diseases (NORD, 2011). NORD takes a similar approach as mainstream health information sharing. NORD lumps all rare diseases together to demonstrate the major influences felt on the U.S. population because of rare diseases. Their goal is to improve the lives of individuals and families affected by rare diseases. They do this through education, policy advocacy, research grants, and medical assistance. Additionally, NORD has partnered with their European counterpart, EURORDIS, to create a website that provides an online community in which people with rare diseases and their family members or caretakers may share information – RareConnect.org.

However, because of the nature of rare diseases, this approach is somewhat problematic. NORD acknowledges on their website that there are 7,000+ rare diseases, but they have online communities for only 32 rare diseases. Those diseases without an online community have a link to a search feature, and communities are created upon request. Unfortunately, even though the goal is to provide a community of inclusion where support and information can be shared, the opposite is true: those with a rare disease not included in the 32 communities are even more alienated than before. Patients who imagined that they found a community and answers were confronted with another dead end. This model of inclusion with subsequent exclusion among the most rare of rare diseases further alienates and stigmatizes. If Goffman's (1963) theory of stigma separates the normals from the stigmatized, this places those suffering from the rarest of diseases one step further: normals → those afflicted who have a community within the rare disease communities → anyone suffering from one of the 6,068 or more excluded rare diseases. The intramarginalizing influence of this spoiled identity is legitimate and damaging, particularly when facing situations that are already life changing, if not life threatening.

Rare Disease Day, USA is a non-profit organization, with private, frequently pharmaceutical industry corporate sponsors, existing to raise awareness about the influences of rare diseases in the United States. Much like World AIDS Day, they host events strategically to garner press, raise awareness, and create community. Their goals (yet unreached, but outlined on their website) include creating a video encyclopedia of rare diseases, creating a social networking blitz, creating a database of physicians

specializing in rare diseases, and sharing patient stories (Rare Disease Day, USA, 2011). Much like with NORD, this one size fits all approach is problematic. In an effort to create a sense of community, those with the rarest of diseases are alienated. Additionally, the events are disconnected and often geared toward a target audience of medical professionals, despite the stated goal of fostering community and gathering patient stories. The messages lack coordination, and while the goals are admirable and necessary, it is not possible to have a focused, consistent messages pertaining to more than 7,000 diseases.

Alternative Health Communication Strategies

Top-down social mobilization strategies can useful for issues with single or concentrated interests, including health communication for mainstream diseases. However, successful communication strategies must account for the motivations and needs of relevant actors (Obregón & Waisbord, 2010). Hoffman (2003) contrasts top-down campaigns and movements, which are frequently run by elites on behalf of the target population, with movements concentrated on creating change from below, or grassroots movements. Grassroots movements are characterized by popular mobilization of ordinary people demanding change on their own behalf, with a goal of immediate improvement to the current situation instead of total system transformation (Hoffman, 2003).

An initial search for health communication programs that were built on grassroots social movement strategies returned surprisingly meager results, but they give good insights into the state of these movements. There are a number of news stories about

grassroots health efforts internationally. In one such article, the Chinese practice of building government and public hospitals in rural areas, accessible to the public but lacking medical staff is chronicled (Wang, 2011). Wang reports that the government hopes to have at least one qualified general practitioner in each of these locations within two years, but the rhetoric within the article belies a favorable opinion of grassroots interventions. Another example is Grassroots Health, a Canadian-based non-profit public health organization working to elevate public health messages from science into practice about Vitamin D advocacy and its relationship with breast cancer (Grassroots Health, 2011). Grassroots Health works with Vitamin D scientists to aggregate and disseminate knowledge and best practices to medical practitioners and individuals to change public opinion and create healthier life choices and prevent disease (Grassroots Health, 2011). Based on the description, this organization sounds like a perfect example of a single-issue grassroots cause; however, it does not provide a model to use for rare disease communication. It is difficult to identify where the "grassroots" element of this intervention is. According to their website, Grassroots Health is sponsoring a study among women maintaining target Vitamin D serum levels (Grassroots Health, 2011), but they seem to only focus on this specific study, which has one specific target population (women over a certain age), for an already well-publicized disease (breast cancer). While it stands to reason that individual organizations and doctors focus on specific issues, this is demonstrative of many of the issues surrounding rare disease communication. Grassroots health is not encompassing of a larger community of people confronting a

range of health issues, and while it hints at other issues, Grassroots Health is mainly just a research study for a specific treatment for breast cancer.

Outside of explicit "health" interventions, grassroots communication techniques are more prevalent. Panth (2010) discusses a Nepalese civil society intervention aimed at women's literacy and empowerment. Through this strategy, women were trained and learned basic literacy concepts. They then submitted written stories about their successes and challenges to the project staff, who compiled the stories along with transcriptions of oral lore. These groupings were gathered in newsletter form and circulated to the women in the target audience. This was a self-reinforcing initiative, since reading the stories improved literacy, gave women a voice, and increased their empowerment by fostering a sense of community. This example is in a vastly different context than rare disease communication in the United States, but it is adaptable, especially with the inclusion of updated technologies.

These communication techniques are applicable across a spectrum of needs and fields. This can be seen by comparing an institution-level example of a creative and practical use of (what were then) emerging technologies to improve uptake of resources and empower people to use them with the Nepalese civil society example discussed above. North Carolina State University's Office of Information Technology (NC State OIT, 2008) had a similar challenge in technical reach, but concerning a major difference in practice and audience. In trying to empower students and faculty to use new technological resources, OIT determined that those with the most knowledge of the new technologies were inadequately skilled at communicating them. OIT combated this via

Twitter, which enabled widespread dissemination of information to those who needed it, in a forum that increased users' technological uptake and fostered an online community. By enabling users to interact with the technology developers, uptake increased and desired behavior changes were reinforced.

One of the greatest strengths of grassroots communication is the use and reach of informal networks (Riano, 1994). This is especially true among communities who are disenfranchised in some way such that they are not easily accessible. This demonstrates the potential of online resources. These resources can help to disseminate information and foster community. In 2010, a panel convened to discuss the influence of technology on grassroots communication; they determined that effects are rippling throughout grassroots communication strategies employed in politics, NGOs and non-profits, and across health and democracy (Bivings Report, 2010). With this in mind, social media can be used to connect users. Debra Ruh, one of the panelists, states that the use of grassroots communication and technology can allow anyone to be a conversation leader, and eliminates the need for a centralized conversation held by a few empowered opinion leaders (Ruh, 2010).

Effective health communication serves two distinct goals that reinforce each other: 1. Disseminating information that allows patients to advocate for themselves, take better care of themselves, supplement the information that their physician has, and make informed decisions about their health; and 2. Fostering a sense of community to enable shared information and resources, gains in emotional and psychological support, and establishment of a collective identity (Fox & Jones, 2008). NORD/EURORDIS has

attempted to promote research and funding for rare diseases with some success, and has done so by utilizing the collective numbers. However, I have demonstrated that the reach of this approach is limited and problematic. The goals of effective health communication align with the strengths of grassroots movements, particularly as applied to communities with similar struggles but disparate specific needs, such as patients with rare diseases.

An analysis of the current online community offerings and in-depth consultation with members of a rare disease community is an important next step toward the creation of a resource for effective rare disease communication. Rare disease patients will benefit from access to information, the ability to participate actively in health decisions, and availability of a community that could reduce alienation and increase self-advocacy. Further, the promise of the patient-centered model and patient involvement in drug development (especially as it relates to the healthcare productivity crisis discussed above) is notable and reaches far beyond the experience of those with rare diseases. A resource to improve rare disease communication and advocacy could translate to positive results for others in the healthcare system beyond rare disease actors, and the use of grassroots strategies and social networks could be more effective than simply touting the numbers affected. According to Pisani (2008), despite widespread knowledge of the rapidly skyrocketing numbers of people living with and affected by HIV during the beginning of the global epidemic in the 1980s, significant funding to understand and address the needs of patients and the nature of the disease only became available once the epidemic was framed in a way that demonstrated its influences on powerful elites responsible for funding decisions.

Theoretical Underpinnings

This study will rely on Uncertainty Management Theory and Weick's model of organizing for its theoretical foundation. Both provide a framework for understanding and evaluating the unique and complex processes that individuals encounter when confronted with a complex or uncertain situation. Weick's model of organizing, which is most commonly used in studies of organizational management, has been fruitfully applied to various settings because of its systematic identification and adept handling of a range of concepts that are crucial to human interactional social psychology (Gioia, 2007). In particular, Weick's model of organizing provides a background that aids in the understanding of the complexity of situations and the processes that actors engage in to adapt to these situations. UMT delves deeply into one facet of adaptation – the complicated role of uncertainty in complex health situations. The addition of UMT to Weick's model of organizing enables a focused understanding of the processes of information-seeking and information avoidance, which serve different functions for patients and can sometimes occur in parallel (Sairanen & Savolainen, 2010). Those who have encountered the equivocal situations associated with having a rare disease are best suited to accurately apply and interpret levels of complexity and equivocality and evaluate the potential of effective solutions. Therefore, these frameworks have a natural application to the underpinnings of a grassroots communication model.

Weick's model of organizing. Weick's model of organizing (Weick, 1969) is built upon three underlying theories, and is positioned in organizational behavior as a model for the study of complex organizations. This model states that organizations do not

actually exist but for a continuous cycle of interactions between actors through organized human activities, and identifies three phases of organizing: enactment, selection, and retention. Figure 2 is a flowchart, mapping the process of organizing as presented by Weick. This model of organizing builds upon Socio-Cultural Evolutionary theory; information theory; and systems theory (Kreps 2009). Socio-cultural Evolutionary theory states that people adapt to changes in their social and cultural environments through coordinated activities to survive. Systems theory is a study of complex organizational processes with different hierarchical levels of complexity – the system, the sub-system, and the supra-system. This theory explores how, within these hugely complex processes, the various systems operate autonomously but interconnectedly. Therefore, they all need to be functioning properly and effectively and achieve system goals. Information theory comes from the field of applied sciences, including electrical engineering and computer science and focuses on getting information from the source to the user efficiently by eliminating message obstruction. Information theory, though it is not part of the communication discipline, has been very influential in the development communication theories that address uncertainty and information acquisition.

Applied to public health settings, Weick's model of organizing states that individual actors require increasing help from others as situations become more difficult to interpret and respond to (Kreps, 2009). Weick refers to the complexity of an input and the difficulty of interpreting an input, as a high level of equivocality. In response to highly equivocal situations, humans engage in the process of organizing, which is a set of interconnected communication interactions whose primary input and output is

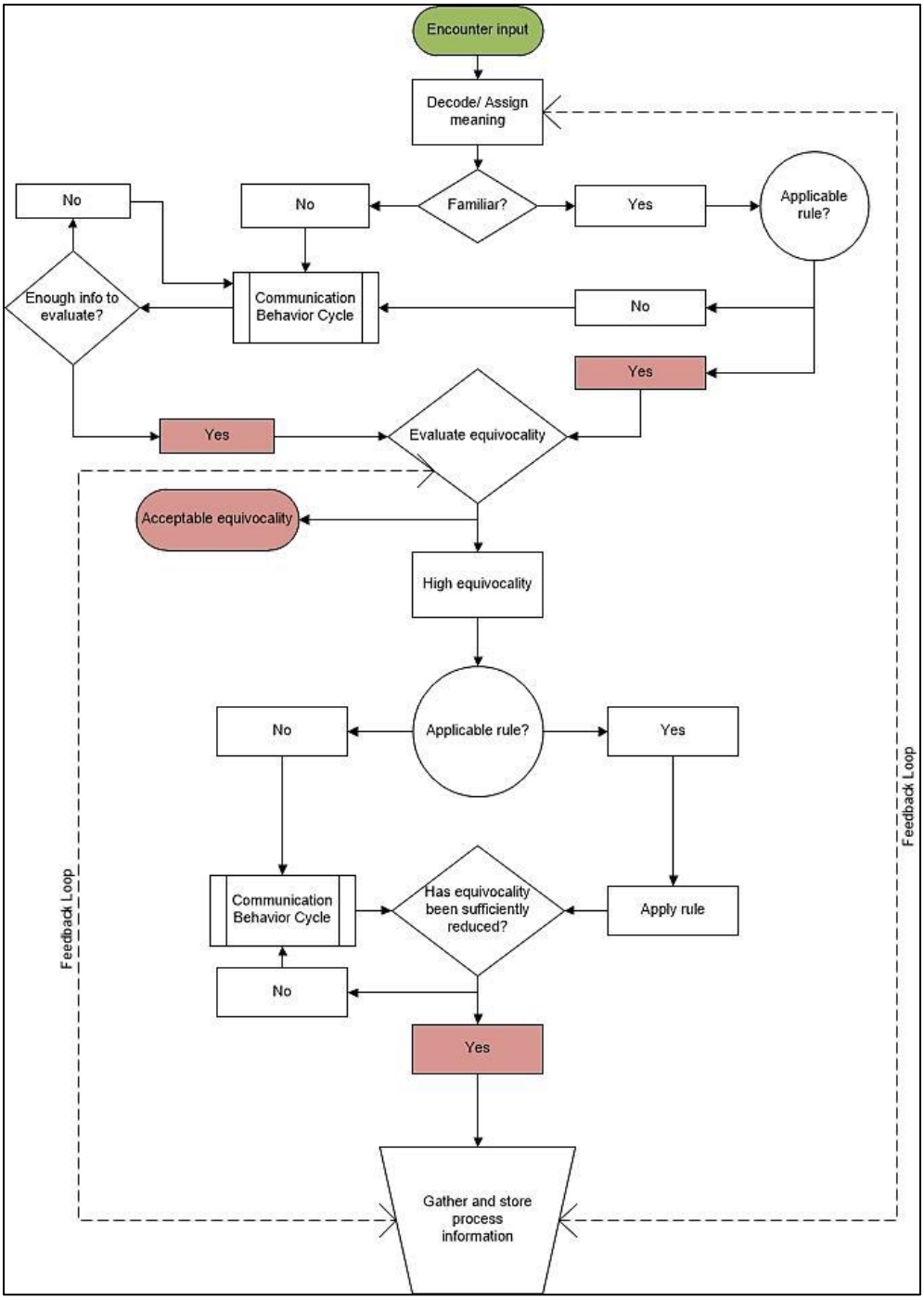


Figure 2 Overview of Weick's model of organizing

information (Kreps, 2009). These interactions reduce equivocality by promoting problem solving and adaptation to enable short-term and long-term survival. This model's foundation in studies of complex organizational systems is especially relevant to rare disease communication because of the frequency and variety of systems with which rare disease patients interact to survive.

Weick identifies three phases of organizing (Weick, 1969), which aid in understanding how people interact to resolve equivocality and are useful in understanding the ways that online communities could address the communal coping needs of rare disease patients. The three phases – enactment, selection, and retention – are punctuated by important process such as feedback loops, communication behavior cycles, rules, and interactivity.

Weick explains that the first step in coping with uncertain situations is to assess the level of situational equivocality through the process of enactment. Once an actor is presented with input that changes his or her environment, he or she will engage in interactions to actively decode, assign meaning, and assess the level of equivocality of the situation (Weick, 1969; Kreps, 2009). During this process, organization members utilize existing rules to guide enactment, or they engage in cycles of interaction to establish rules for ascertaining the equivocality of different situations. Previous applications of Weick's model of organizing have operationalized enactment as an initial consideration that a decision-maker would have when presented with a controversial issue (Griffin, 2005) and confusion leading to problems with adherence to prescription medication (Kreps, 2009). In the realm of rare diseases, the input and enactment phase

could involve making sense of symptoms and the process of diagnosing the rare disease. It is important to recognize that in the case of rare diseases, diagnosis is often a very equivocal process, and making sense of symptoms can demand a great deal interaction (Field & Boat, 2010). Other potentially equivocal inputs, especially in cases of chronic rare disease, could include the onset of new or intensified symptoms, information from physicians or informed others, introduction of new treatments, or interactions with members of the healthcare system such as physicians or insurance providers.

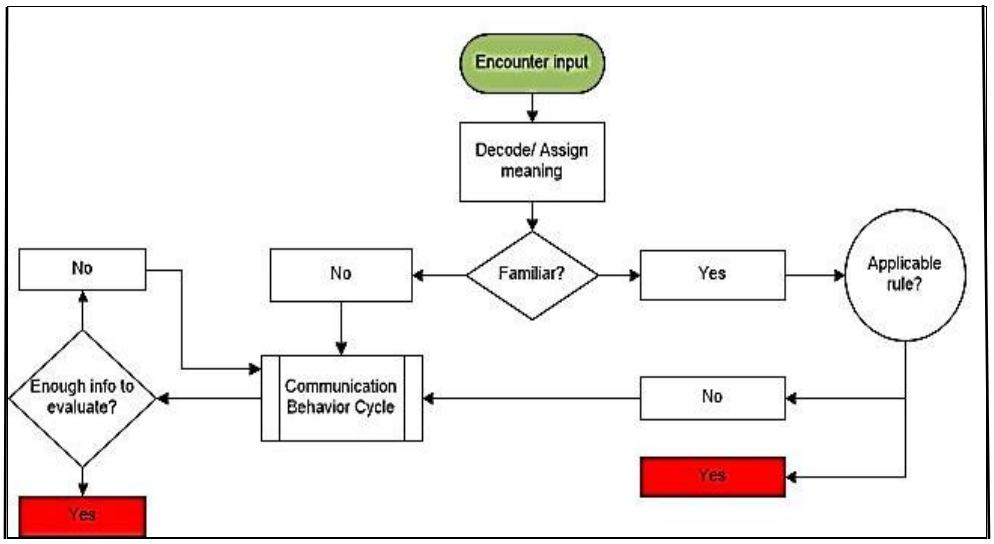


Figure 3 Enactment phase of Weick's model of organizing

Situations that are more equivocal are less likely to have existing, applicable rules that could guide enactment. In the absence of rules, an actor must engage in communication interactions to establish new rules to evaluate equivocality. This inverse relationship between equivocality and availability of rules is explained by the principle of requisite variety, which suggests that the level of equivocality of the reaction to an

input should reflect the level of equivocality of the input itself (Weick, 1969). The principle of requisite variety relies on three assumptions about the relationship between rules, cycles, and equivocality:

1. A direct relationship between equivocality and cycles means that high equivocality inputs require a large number of cycles to resolve;
2. An inverse relationship between equivocality and rules means that a highly equivocal situation is unlikely to have many rules that could guide it, and a less equivocal situation will have more rules;
3. An inverse relationship between rules and cycles leads to a simpler process for processing and responding to an input in situations of low equivocality, because the existence of rules eliminates or reduces the need to engage in cycles.

The principle of requisite variety, particularly the inverse relationship between complexity and use of rules, has been used in previous evaluations of Weick's model of organizing. In one example, ambiguous messages were delivered to subjects, and equivocality of the messages was assessed by counting the number of rules that were applied during their processing of the messages. In low equivocality situations, or when presented with clearer messages, subjects applied rules; no application of rules represented a high equivocality situation because of an obscure message (Griffin, 2005).

Once enactment is achieved and the level of equivocality of a situation is assessed, Weick explains that organization members either select an existing rule to reduce equivocality, or, in the absence of an appropriate rule, they engage in

communication behavior cycles. This process is the selection phase of organizing (Weick, 1969; Weick, 2003).

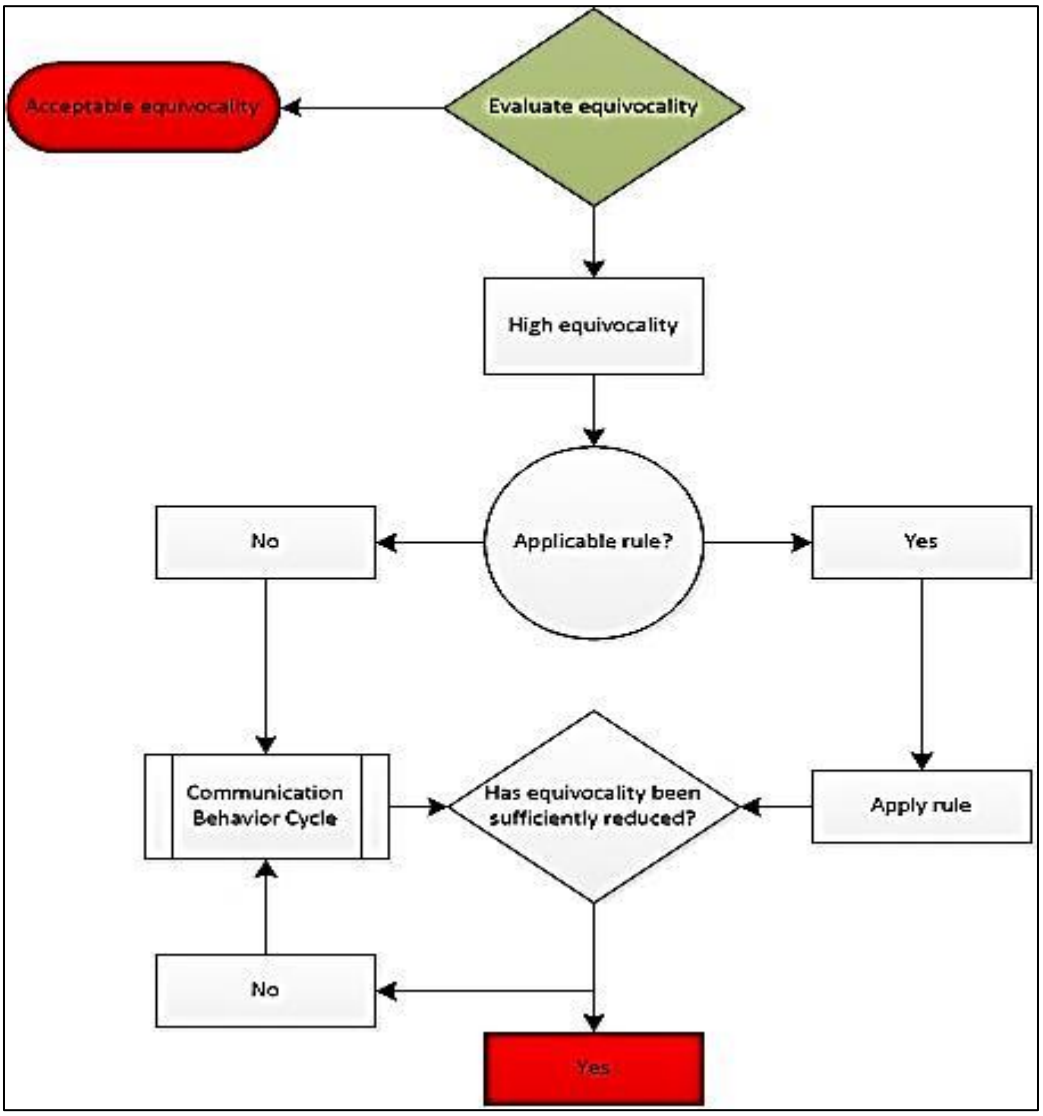


Figure 4 Selection phase of Weick's model of organizing

Similar to the enactment phase, the principle of requisite variety applies; fewer rules necessitate higher numbers of communication behavior cycles. These sub-processes of the selection phase are especially useful in operationalizing equivocality and evaluating

interactions as they apply to Weick's model of organizing. In one example, Griffin (2005) references a field test conducted by Kreps (1980) that found that the level of equivocality can be quantified by counting *double interacts* between group members.

Communication behavior cycles are interactions to reduce equivocality that are comprised of conditionally related messages between actors, or between one or more actor and the environment or input, undertaken to reduce equivocality (Kreps, 2009; Bietz, 2008). Weick's high-level assertion is that a cycle involves an action, receipt of a response, and then another action that includes an adjustment to account for the response (Weick, 1969). This cycle, called a *double interact*, is an important contribution to the understanding of information exchange, because unlike many models that evaluate human interactions, Weick gives due attention to the adjustment made by the initial actor as a result of an exchange (Griffin, 2005). Therefore, according to Weick's model, an *interact* is a contingent exchange between two actors (e.g. Person 1 acts, Person 2 responds) (Bietz, 2008, Weick, 1969). A *double interact* (shown in Figure 5) is a conditional three-part exchange that allows information to be gathered and feedback to be received (e.g. revisiting the example above, Person 1 responds to Person 2, completing the cycle).

A risk of the application of *double interacts* to evaluations in group settings is that an operationalization can oversimplify the "act, respond, adjust" messages to be more linear than Weick presented. This simplification fails to account for processional aspects of group communication, including message and member interdependence (Kreps, 1980).

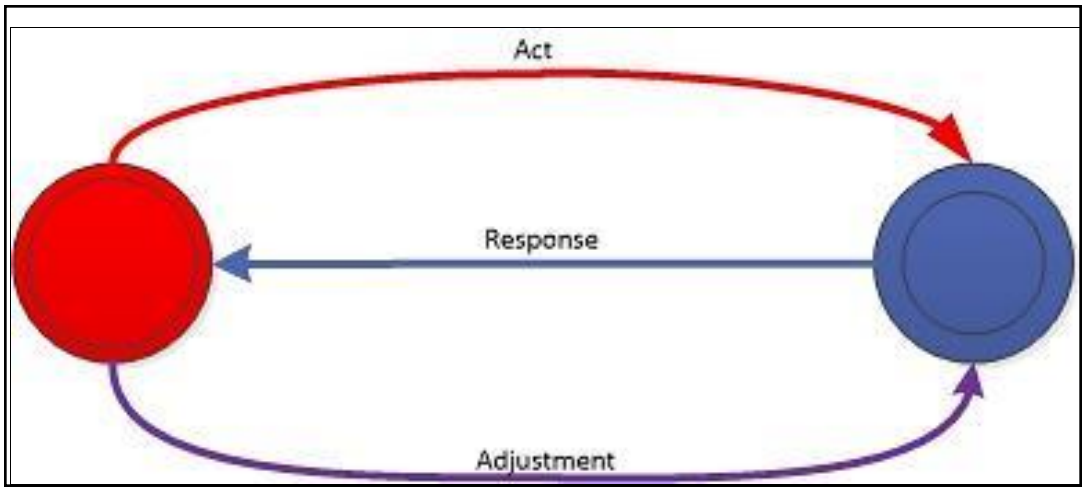


Figure 5 **Double Interact as described by Weick**

Kreps (1980) addressed this limitation by operationalizing *double interact* cycle messages as a series of three steps: 1) an act is any comment by a group member preceding any other two comments by group members; 2) a response is a comment that follows a comment by another group member and that is itself followed by a comment by a member; 3) an adjustment is any comment that follows two previous comments by group members. Kreps (1980) further states that if using this operationalization, the total count of completed *double interact* cycles should be the equivalent of the total number of comments minus two (n – 2). Each complete cycle reduces equivocality, but multiple cycles may be necessary depending on the level of equivocality of the situation (Kreps, 2009).

Rare diseases frequently lack easily available, well-established, and agreed upon treatment protocols for responding to the health care problems that patients are facing (e.g. Vesely et al, 2003). This means that patients and their providers often have to

engage in extensive interactions to develop the best treatment protocols to use. Furthermore, Weick's assertion that actors engage in a process of organizing to survive extends beyond a literal interpretation of survival as life and death; rather, an individual patient must determine effective personal strategies to reduce equivocality to effectively cope with his or her disease (Fox, 2011). In contrast to those with more common diseases, rare disease patients could have more difficulty finding others who have experienced similar situations from whom they could be exposed to potential rules.

The third phase of Weick's model of organizing is known as retention. In retention, the rules that have been established (knowledge that was gained from past enactment and selection processes) are stored for use in guiding response to future equivocal situations. Weick (1969) refers to this use of stored rules is referred as organizational intelligence. With access to organizational intelligence, actors are able to apply established rules to new situations to make sense of them (enactment) and decide how to respond to them (selection). The relationship between stored rules, cycles, and equivocality is very relevant to situations in which actors encounter complex inputs frequently, such as in cases of chronic rare disease. The application of the rule of requisite variety within the retention phase demonstrates how access to rules can help to reduce the equivocality of an input or situation, even if the input is very complex to those who do not have previous experience with similar inputs.

Health care consumers and providers who are trying to interpret new symptoms and determine the best ways to treat these health care problems would benefit from access to organizational intelligence. The development of effective communication

systems that could store and disseminate organizational intelligence about rare diseases quickly and efficiently could be a tremendously valuable resource with the potential to aid in decision-making and decrease stress for individuals confronting rare diseases. Previous studies have operationalized this preservation of organizational intelligence in groups that enabled strategies to be applied and rules disseminated to reduce equivocality (Kreps, 2009). Two feedback loops, which link retention to selection and retention to enactment, further aid in the process of determining effective strategies and retaining this knowledge to reduce future equivocality (Weick, 1979).

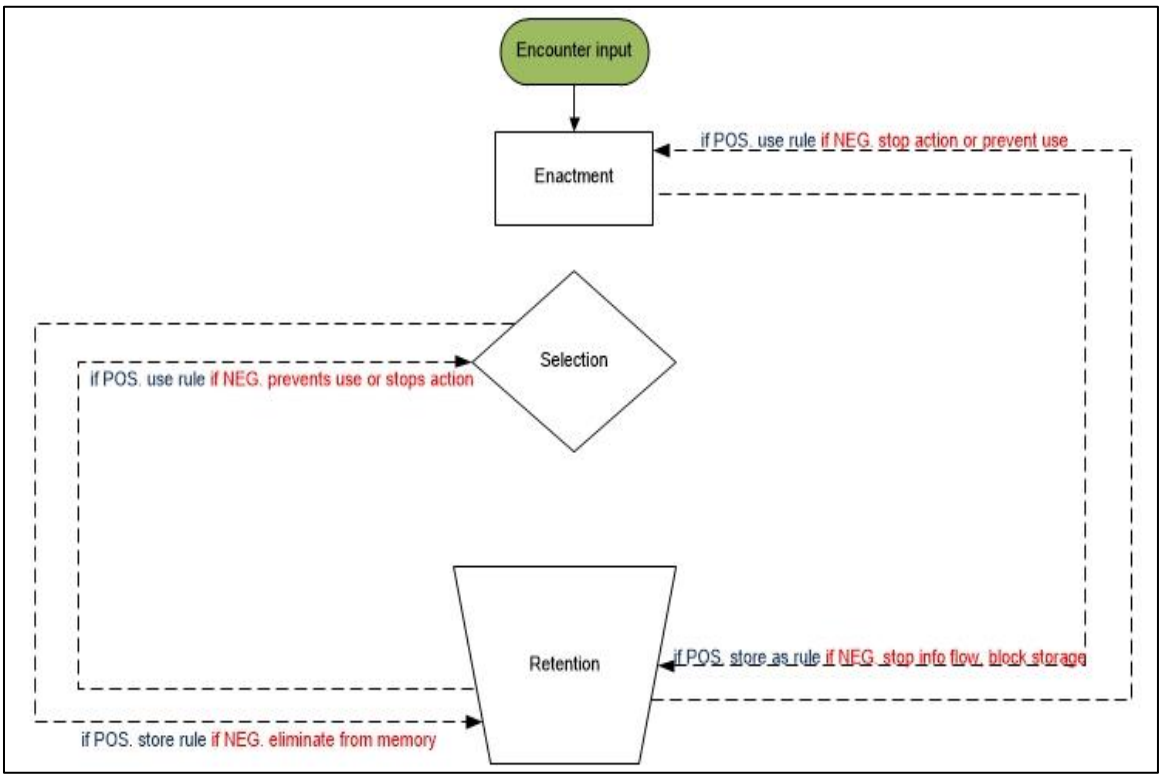


Figure 6 Feedback loops linking retention to enactment and selection

Uncertainty Management Theory. Uncertainty Management Theory (UMT) maps closely to the interconnected message exchange that occurs during communication behavior cycles, but gives specific attention actions taken to react to uncertainty. Unlike Weick's model of organizing, UMT is a communication theory within the field of communication that was developed by Dale Brashers, to address limitations of Berger's Uncertainty Reduction Theory (URT) (Brashers, 2000; Brashers et al, 2004). URT was among the first theories specifically developed in the field of interpersonal communication, as opposed to other theories that had been adopted from other disciplines and adapted for the newly emerging field of communication. URT explains how we communicate when we are unsure of what is happening to us or happening in our environment, and it was originally applied to the interaction between two people upon their first meeting (Berger and Calabrese, 1975). Over time, it was adapted to other settings, but the main premise underlying URT was that people dislike uncertainty, uncertainty produces anxiety, and thus people take steps to reduce uncertainty in their interactions with other people and their environments. In Brashers' application of URT to studies in health communication, particularly to people living with HIV/AIDS and other terminal illnesses, he found that uncertainty was not necessarily negative, but rather a very complex emotional consideration (Brashers, 2000; Brashers et al, 2004). For example, upon diagnosis with HIV/AIDS in the early years of the epidemic, a patient effectively was handed a death sentence. Over time, and with medical advances, patients' prognoses were less and less certain. Diagnosis was no longer conflated with an expectation of death within a few years, but still signaled many impending complications.

Here, uncertainty acted as a vehicle of hope. Brashers' identification of the complexity of uncertainty, as opposed to the interpretation of uncertainty as something that must be eliminated to the extent possible, led to the creation of Uncertainty Management Theory to address the role that uncertainty plays (Afifi & Matsunaga, 2008).

UMT begins with the premise that uncertainty is a complex experience, and the understanding that health communication processes must abandon the notion that uncertainty necessarily causes anxiety. Instead, UMT offers a framework for understanding the role that uncertainty plays in different scenarios, including the positive and negative influences that can be caused by the strategic use and perception of uncertainty (Sairanen & Savolainen, 2010). Three iterative and interconnected steps can be found in patients' experiences when confronted with uncertainty: 1. Experience; 2. Appraise; and 3. Respond (Brashers, 2006). When an actor experiences an uncertain situation, he or she will appraise the event or issue, along with their current state of confusion. His or her response will be based on an appraisal of the situation's meaning (Sairanen & Savolainen, 2010).

Brashers (2001) states that when an actor perceives uncertainty as dangerous or threatening, he or she has a negative appraisal, which initiates a response – he or she begins the process of information seeking. A positive appraisal, such as one in which an actor determines that the uncertainty will allow him or her to maintain hope or avoid confronting an unpleasant and potentially psychologically harmful reality, enacts a response of buffering strategies such as information avoidance or discrediting the source. Uncertainty may also be assessed as neutral, or a fact of life. For example, in cases of

terminal illness or chronic disease, which cause frequent encounters with uncertainty, patients may accept chronic uncertainty (Sairanen & Savolainen, 2010).

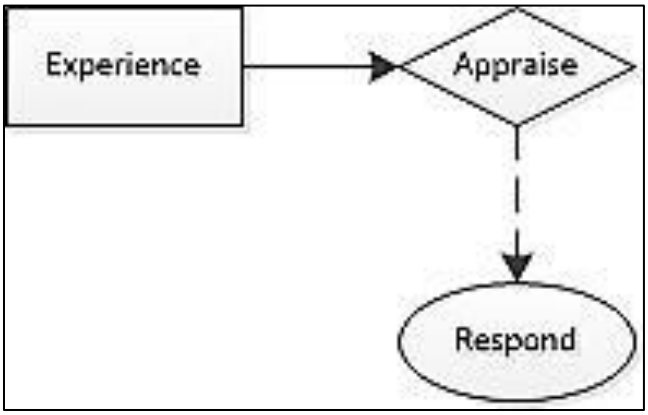


Figure 7 Process of reacting to uncertainty according to UMT

UMT also allows for the possibility that actors may simultaneously engage in information-seeking and avoidance, or may switch between the two (Brashers, 2001). Lambert et al (2009) operationalized information-related responses among cancer patients and found a range of behaviors: minimal information seeking (little to no effort in gaining information); guarded information seeking (selectively seeking information and avoiding negative information); complimentary information seeking (satisfied by finding information that is good enough and is in line with what is known); fortuitous information seeking (learning of discoveries from other patients or people in similar circumstances); intense information seeking (characterized by an interest in detailed information). Frequently, these responses correspond with seeking social support to assist

in information-seeking/avoidance behaviors and to provide a sense of stability and community (Brashers, 2004).

The three-step process outlined above is an instructive addition to Weick's model of organizing, and will serve as a useful complement. Importantly, this process maps closely with the communication behavior cycles that occur during enactment and selection. A detailed understanding of the role of uncertainty is crucial to understanding rare disease communication. When a patient is diagnosed with a rare disease, he or she faces a great deal of uncertainty beyond typical conceptualizations of equivocality, or equivocality experienced by patients with common terminal or chronic illnesses. Further, UMT serves as an important reminder that the rule developed and applied during the process of organizing could be avoidance or denial. Many rare disease patients have never heard of the disease with which they are being diagnosed, do not know where to look for information, and they are uncertain about how their lives will change. As patients begin a quest for information and seek understanding of the influences that this disease will have on their lives, they encounter even more uncertainty because of limited availability of information about truly rare diseases. These patients will go through many different phases in their search for information, and will at times be inundated with facts, and sometimes unable to find clear answers.

Applying these theories to the design of a study about rare disease communication leads to an examination of patients' interactions, participation, and processing highly equivocal situations, as well as an exploration of the role of equivocality and uncertainty over time. UMT will be used to help guide construction of data collection instruments

and will provide important contextual background information during coding and interpretation. Weick's model will factor into study design and analysis, especially when measured based on patient interaction in the face of equivocality, as well as in guiding coding in this study. The study will examine equivocality, as well as identify apparent needs during and applied to the various phases of organizing. By taking both of these theories/models into consideration while designing this study, it will be possible to reach a solid understanding of the patients' information needs throughout the course of their rare disease diagnosis and treatment.

CHAPTER THREE: STATEMENT OF THE METHOD

The research design in this exploratory study is extremely rigorous, and allows for a level of triangulation of findings that is difficult to achieve (Neuendorf, 2002) via a first order linkage between content analysis and other relevant data from surveys, interviews, focus groups, and external sources (Keyton, 2010). The study uses mixed methods, including a quantitative content analysis of the current RareConnect.org message boards and a case study that will be quantitatively and qualitatively evaluated and analyzed using SPSS Statistics 21 and Atlas.ti 7 software. Further, two of the variables analyzed in this study are considered universal in content analysis (uncertainty and complexity), demonstrating the strength of design and allowing for eventual comparison to other studies as part of future analysis (Neuendorf, 2002). Findings from this study will be particularly meaningful, since credibility was established by high participation, triangulation of results, and willingness of informants to be publicly identified in order to associate real people with a disease.

Six coders were recruited to assess inter-coder reliability for transcript and content analysis. Coders were only assigned to one portion of the study to avoid one sampling frame to pollute the other. For example, a coder who had listened to a TTP patient express their information needs may then apply this information to their interpretation posts on RareConnect.org. Coders were recruited via personal networks

and represent a heterogeneous group; this achieves the "common-ness" of interpretation that is necessary for valid and reliable content analysis (Krippendorf, 2004). In cases of interview or transcript coding, coders were only given the identifying information respondents wished to be affiliated with in the report; therefore, confidentiality was strictly maintained. To further protect sensitive information, each coder signed a confidentiality agreement to ensure that sensitive information would be handled in a manner that adhered to the protocol (see Appendix 1).

To capture group diversity, coders were asked to complete a confidential demographic survey (see Appendix 2 for instrument). This survey was administered online after all coding had been completed so as not to inject social desirability bias or researcher bias in coding. Questions used were predominately "fill in the blank" format to capture semantic differences in respondents' self-identification(s). .Exceptions to "fill in the blank" responses include cases where categories were defined (such as age), or when a continuous sliding scale was provided to indicate agreement with a certain statement. These scales were modified semantic differentials; unlike semantic differentials, they did not have paired opposites – only one word or statement that they would move closer to or further away from depending on their level of agreement. Additional questions were asked to determine how, if at all, personal experiences or beliefs influenced coding decisions. This helped to establish normative validity and, if necessary, could help to understand consistent differences between coders. Questions were included about characteristics, such as political interest and affiliation; religious identification; upbringing (e.g. biological or adoptive parents, educational attainment of parents and

immediate family); and plans for further education. Personal experiences or familiarity with mental healthcare, a chronic or serious illness or an atypical, dramatic life-changing event were also assessed, and finally, as well as personal internet use, and opinions on whether it is useful, weak, helpful, or brave when people talk about their problems. Notably, two of the six coders had experienced a chronic or serious illness; five of six reported a dramatic, life- or perspective-changing event. Internet usage was "constantly" for all coders younger than 50. Both coders over 50 reported daily use of the internet, and daily use of the internet for reasons other than email. One coder over 50 reported daily use of the internet for reasons other than work or school; the other answered "a few times a week". Indicators measuring religiosity and perception of prayer were included and assessed to understand whether people of faith evaluate strategies and information seeking or avoidance differently, since "prayer" was discussed frequently by respondents as a strategy or rule in certain scenarios. Perceived religiosity widely varied, ranging from 0 to 100 across categories, with means of 59.6 (self-assessment); 50.6 (from perspective of people who know you very well); 58.2 (from perspective of friends); 36.2 (from perspective of people who do not know you very well). Opinions on talking about your problems also varied but generally less than favorable, with 0 indicating the highest level of agreement with the word, and 100 indicating the most extreme disagreement with the word. It should be noted that these numbers were not visible on the instrument, only the slide, so participants were pulling the scale closer to the word if they agreed with it, and pushing it further away if they did not. This technique was employed in order to enable a continuous variable and to avoid confusion about the value of the number.

Further, discrete categories were eliminated to avoid desirability bias or the imposition of rhetorical categories that have different meanings across individuals' contexts (Reinharz, 1992). Answers were interpreted using a quintile overlay to categorize agreement. Specifically, coders reported that talking about your problems is: useful (range: 10 – 100, mean: 67.5 – slightly useful); weak (range: 0 – 87, 1 missing, mean: 31.6 - weak); helpful (range: 15 – 100, mean: 70.6 – slightly helpful); brave (range: 20 – 100, mean: 63 – slightly brave). Table 1 displays the diversity across basic demographic categories. These findings contextualize the many elements in which coders diverge, and represent the strength of inter-coder reliability scores reported below.

Age	Sex	Education (Completed)	Sexual Orientation	Race	Ethnicity
31 - 40	Male	Master's degree	straight	white	Spanish, Italian
51 - 60	Male	High school graduate	heterosexual	Caucasian	Irish, Scottish, German
26 - 30	Female	Some graduate school	bisexual	Other	Zambian-German
51 - 60	Female	Some college	heterosexual	white	Italian American
26 - 30	Male	Professional degree	straight	white	
21 - 25	Male	Bachelor's degree	gay	Mixed - black and white (both parents with one white grandparent)	Jamaican, American, Scottish, Irish, Grenadian

Table 1 Demographic characteristics of coders

The case study has three parts that serve complementary and distinct purposes, including a cross-sectional survey administered online, in-depth interviews (conducted via Skype or a similar technology), and online (also using Skype or a similar technology) focus group discussions with TTP patients and HSOs. Each component has sub-research questions that fall under the following three over-arching research questions:

RQ1: When and for what purpose are patients (and HSOs) most likely to use online communities focused on their specific rare disease?

RQ2: What are high equivocality situations for patients and HSOs engaged in rare disease communication?

RQ3: What do patients and HSOs report as their information needs regarding online communities?

These research questions illustrate that the purpose of this study is to understand what should be considered when designing online communities for people with a rare disease from the perspective of the consumer (who is identified primarily as the patient and secondarily as the HSO). Rare disease patients interact with the healthcare system more frequently than many other people, and they have unique and complicated experiences. As a result of their unusual encounters with the healthcare system, it is likely that their perception of which situations have high equivocality may be very different than the perception of a person with more limited or typical interactions. For example, my formative research suggests that issues that I would have interpreted as very mundane, such as difficulty obtaining an explanation of benefits from the insurance provider or challenges with a physician's receptionist or on-call practitioner, resulted in higher levels

of confusion and anxiety for some patients with rare diseases. Conversely, issues that I would understand as extremely complex, such as the appearance of strange symptoms that remained undiagnosed despite many rounds of tests, were met with acceptance and were less complex. To this end, I am interested in understanding situational equivocality from the perspective of the consumer. This is reflected in RQ2. Additionally, I hope to understand how these communities can serve the consumers throughout different stages of their diagnosis and treatment, as well as at different phases of community organization. Finally, the research sample will be drawn from people who have some level of interaction with the type of online communities in which I am interested, so I hope to learn from their experiences in addition to their desires.

Content Analysis

RQ1: What are the subjects or themes that commonly appear in online communities for people with rare diseases?

RQ2: What subjects or themes result in high levels of interaction in online communities for people with rare diseases?

RQ3: How are the three phases of organizing (enactment, selection, retention) represented among active participants in online communities for people with rare diseases?

The content analysis portion of this study will enable an examination of message content to understand the type of questions that patients and HSOs typically ask of colleagues in online communities for people with rare diseases, and the level of interaction that various questions elicit. This understanding will allow for an

extrapolation of how actors typically use these communities, and will lead toward an understanding of how actors are currently using these communities in the process of organizing. By examining the common themes, subjects, and levels of interaction, it may be possible to determine whether there are certain times or occurrences within the process of diagnosis and treatment in which actors are particularly active. Weick's model is a framework that is extremely useful in understanding this process, creating the research questions, and creating the coding questions. This model holds that people are more likely to require increased interaction in situations with higher equivocality, or complexity and uncertainty, and that they organize in three distinct phases: enactment, selection, and retention.

The population for this content analysis will be the RareConnect.org message boards managed by NORD and EURORDIS (available www.rareconnect.org). There are currently 32 message board communities for various rare diseases and disorders. Although there are other informal spaces where people with rare diseases form communities (e.g. Facebook, myspace), RareConnect.org unites the possibility of patient community building with a forum for self-advocacy because of the connections that NORD and EURORDIS have with their respective governmental institutions. Additionally, these communities may be seen as exemplar of the current trend in rare disease communication since the two institutions at the forefront of this initiative chair them. I do not plan to sample from the different message boards, but instead intend to conduct a census of all 32 boards. This will help me to be exhaustive, particularly since I am attempting to gain a sense of multiple types of diseases and how different actors

utilize these fora. Because of the nature of these communities, it is possible that new posts would be added by the time I received approval and began my study. Therefore, I captured each page using screen shots to maintain consistent coding and ensure all coders have the same material.

RareConnect.org hosts discussion boards that are unique to each rare disease community. The unit of analysis will be one conversation thread; the sampling frame is the approximately 900 threads currently present on RareConnect.org. Treating each thread as a unit of analysis will allow me to gather information about the messages provided by individual posters, and from that information I can extrapolate their likely goals, identities, and attitudes. Additionally, I will measure the amount of interaction elicited by the post and will observe the level of situational equivocality demonstrated by the post. Construct validity will be ensured by a review of similar applications of Weick's model which indicate that the scale used to evaluate equivocality must include measures that would allow for/anticipate the following occurrences (among others): changes in bureaucratic regulation, insurance, administration, medications, prescriptions (Kreps & Bonaguro, 2008), collective communication, interdependent communication, identification of appropriate responses (Kreps, 2009; Weick, 1969). Content validity will be ensured by consultation with other content analyses of similar fora. Examples include Evans et al (2011) content analysis of online post-partum depression discussion groups and Blank et al's (2010) study on breast cancer/prostate cancer support groups. The codebook is designed to measure manifest and latent content, which will improve validity. (See the sample codebook in the Appendices). The key variables coded for were

equivocality (defined as the complexity of the issues addressed in the messages posted and as measured by the actual variables of uncertainty, complexity, and urgency); interactions; role (e.g. patient, doctor, caregiver); purpose of posting (e.g. seeking information, venting/support) information sought (e.g. support, medical advice, referral).

Codebook development followed Compton et al's (2012 p. 42) outline: 1. Theoretical components and variables were considered and applied to this particular instance, and agreement between researchers familiar with the subject was reached (prior to advancement to candidacy); 2. Instantiation, or the representation of a theory in concrete terms, was conducted during coder training. I conducted a "first pass" of the sampling frame to conduct primary coding, using the initially constructed codebook that had been created deductively – beginning with theory and a review of the literature. To ensure my own familiarity with the data and meticulous coding, I ceased this initial pass of coding only once saturation was reached and no new goals, identities, or presentations emerged (Love et al, 2012). Questions were added to the codebook inductively as a result of this initial examination, using pattern-content (Potter & Levine-Donnerstein, 1999).

After sufficient familiarization with the sample, a representative sample of communities was selected via a simple random sample without replacement. Communities were chosen as a distribution frame, which was appropriate since the overall study was a census (Neuendorf, 2002), and to preserve ecological validity, since the communities on RareConnect.org represent a range of diseases and disorders. A pilot was conducted using the finalized codebook with one other coder, who was trained on the basic concepts and a rough cut of the training video that was later developed (discussed

below). Krippendorff's alpha for this sample ranged from 0.352 - 0.966, percent agreement ranged from 79.4% - 99.4%. Based on the results of this representative subsample, the codebook was revisited, looking specifically at key variables and variables with too many categories. Precision was addressed by analyzing the results and determining where it was appropriate to trade depth for reliability, and some categories were collapsed or removed, while others were added, to ensure that coders would be making decisions based on manifest data.

Four coders were assigned 10% - 30% of communities, depending on their time available. Coders were trained on key concepts using video that was created to demonstrate concepts necessary to understand the variables in the context of this study, but without divulging hypotheses or giving information that would create experimenter or expectancy bias (Rosenthal & Rosnow, 1984). For example, the video included clips from Argo to demonstrate equivocality and organizing, as measured by interactions between parties, despite drastically different levels of uncertainty or complexity. This enabled coders to move forward with the same operational definition of key concepts without biasing their decisions. Coders were also given a brief (approximately 5 minute) video, walking through the process of coding a thread. Coders were then trained an additional hour-long session, conducted via a Google Hangout. Finally, coders were given a comprehensive codebook with hints and tips to guide them in their decisions (see Appendix 6). Both the manner in which the coders were trained and the way that coding occurred were ideal for medium modality, enabling a similar interpretation since the sample frame was online (Neuendorf, 2002).

Lombard et al (2004) recommend continuously assessing reliability data with a small number of units, and refining/retraining as necessary. Krippendorf (2004) presents a debate within the methodological community, citing Potter & Levine-Donnerstein (1999) and Lombard (2002) regarding the best use of multiple coders. On one side, the more people coding the same group of data, the more meaningful the reliability will be. On the other hand, this is challenging to do with a large set of data. It is contended that even though this practice is common, paired analysis is only appropriate in situations where one member of the pair is an expert, which even then poses limitations. To address this, inter-coder reliability was assessed using both measures: a sample of 30-40% was drawn from each coder from the first three days that they coded, and again on the seventh day, based on an assumption that this would allow for the learning curve, if present, to be captured and addressed. Their decisions were compared against the researcher's for key variables: urgency, complexity, uncertainty, poster ID, purpose of original post, language, number of responses, and number of responses by a moderator. The percent agreement in all cases was 100%, with the exception of three instances in which multiple answer choices were possible. In each of these cases, the coders chose the same classification as the researcher, but also chose "other". Further, a representative sub-sample of threads was selected for all (coders and primary researcher) to code. The sub-sample is comprised of 10% of the "screens", that is, the visible portion of each webpage that was saved as a PDF. Each screen has approximately seven threads; however, in cases of exceptionally high interaction, "detail screens" are produced, which are comprised of only one thread. These screens were randomly selected using a naming convention that

was employed during coding, whereby Community ID (__ __) – Screen type (Detail = 1, Overview = 2) – Screen Number (__ __) – Thread Number (__ __). To generate the random selection, a 35 unit list was generated comprised of values 1 – 32, unsorted. Another set of 35 was generated comprised of unsorted, randomly generated values of 1 and 2. Finally, the third set was generated using 35 non-unique numbers between 1-8 to represent the screen number. Coders were given the complete screen so that they had some level of context, without limiting the sample to just a few communities. Intercoder reliability was assessed for key variables. Krippendorff's alpha was the primary formula used to measure inter-coder reliability; however, other measures are shown when Krippendorff's alpha posed limitations to effective reliability evaluation.

Variable	K α	Evaluation	% agreement	Evaluation	Fleiss' Kappa	Evaluation
Total number of posts	1.0	Perfect	1.00	Perfect	1.0	Perfect
Uncertainty	.61	< .667, generally accepted value	.93	Very high	.61	Good
Complexity	.8	Excellent	.96	Very high	.78	Excellent
Urgency	.7905 and 1.0†	Very good, Perfect	.98	Near perfect	.76	Excellent
Language of original post	.987	Excellent	.99	Near perfect	.98	Excellent/ Near perfect
Purpose of original post	.87	Excellent	.95	Very high	.93	Excellent/ Near perfect
Number of responses by a moderator	.81	Excellent	.92	Very high	.84	Excellent

†see discussion for an explanation of two variables

Table 2 Inter-coder reliability subsample

Overall, intercoder reliability was very strong. Neuendorf (2002) recommends choosing a very conservative measure for variables, as well as a more liberal measure. Krippendorff's alpha is generally accepted to be one of the most rigorous measures of intercoder reliability, and it allows for nominal, interval, ratio, and ordinal data interpretation (De Swert, 2012). Krippendorff states that there are no exact numbers that should guide interpretation of the score, but offers that an alpha of .667 is a good benchmark for evaluative studies, and >.8 is considered extremely reliable (2004). One limitation of Krippendorff's alpha is that where a particular value is very rare, (such as urgent), the score is heavily effected (Compton et al, 2012) Percent agreement can be valuable, and is the most frequently reported reliability coefficient. However, it is less rigorous and therefore a higher score should be used to determine acceptable reliability (Neuendorf, 2002). Finally, Fleiss' Kappa is especially useful in behavioral or interpretative analyses, correcting for the limitation presented above regarding Krippendorff's alpha. K values of .41 - .6 are moderately reliable, .61-.8 are good to very good, and .81 – 1 are very good to perfect (Babbie, 2007).

An acceptable to near-perfect α was found for each variable except urgent, however, there was very high percent agreement and a good K value. In this particular instance, there were very few cases that were coded urgent by one or more coders (n= 9, N = 101), which may explain the poor α. However, the K value is more than acceptable, as is percent agreement, so this is still viable for inclusion.

Because background data was collected about each coder, some interpretation of variance in coding is possible, representing "commonness" and demonstrating some

elements that are inherent to the coder that would be difficult to address with any amount of training. For example, the α for urgency was high, .79. However, there were several cases of missing data, and it happened that they disagreed with each other on urgency in many of these cases. Upon examination, the coder who assessed a situation as urgent was a parent, and the content of the message was about a child in pain. Additionally, of this same pair, the coder who evaluated as not urgent had previously experienced a chronic or serious condition. When eliminating these few occurrences where data were missing, α = 1.0. Since α accounts for missing data, this is solely reflective of those differences, and is not attributable to computation issues resulting from missing data.

Similarly, of the 10 cases where uncertainty was found by at least one coder, disagreement occurred in the following instances: all coders evaluated as uncertain with the exception of one coder, who was the only coder in the whole sample who had reported never experiencing an atypical or life-changing event (n = 2); all coders evaluated a case as uncertain, with the exception of one or both coders who had reported experiencing a severe or chronic illness (n = 7). This is notable, as it represents commonness, and did not have an impact that would require data to be re-examined. Additionally, as part of data collection, coders provided a narrative that justified their evaluation of uncertainty, complexity, or urgency, and this was applied to the interpretation of the entire sample to ensure consistency in interpretation of the codes.

Case Study

RQ1: How do rare disease actors utilize online communities for health information?

RQ2: What do actors report as useful in their use of online communities?

RQ3: What limitations do actors report in using current online resources?

The self-advocacy and community-building model that is currently applied by the leaders in the rare disease community (including NORD/EURORDIS) follows the same mass-communication model that is used for health communication about more common diseases. The literature review suggests that this model further alienates those suffering with truly rare diseases. To answer this, a case study was conducted of Thrombotic Thrombocytopenic Purpura (TTP) to achieve a nuanced and rich understanding of the information-seeking experiences of rare disease actors. This case study applied Weick's model of organizing and Uncertainty Management Theory to communication surrounding rare diseases. (For a detailed explanation of TTP, see Ch. 1). The information gathered from this case study will only be directly applicable to TTP actors; however, many other rare disease patients will likely share the experiences of TTP patients. TTP patients experience challenges that are faced by many rare diseases patients, including difficulty achieving diagnosis, limited clear treatment options, variable and dramatic prognoses, and a possibility for recurrence. Like TTP, many rare diseases are autoimmune, which results in a certain kind of complexity and rhetoric since one's body is attacking itself.

This case study was comprised of three phases of data collection: 1. an online, cross-sectional survey with multiple-choice answers and an unlimited character text box next to each question; 2. in-depth interviews conducted using Skype or a similar technology; 3. online focus group discussions using Skype, Google+, or a similar technology.

Recruitment. Currently, there is no RareConnect.org community for TTP. I have found the online presence for this disease is limited to one unmoderated message board that has had extremely limited activity since 2010 and lacks organizational or medical affiliations. There are three fairly active Facebook groups that are unmoderated, and have substantial membership overlap. The groups have somewhat high activity.

After obtaining ethical approval from George Mason University's IRB, recruitment occurred concurrently with stage one of data collection, which was a cross-sectional survey administered online. Participants were recruited from the Facebook TTP groups with a posting that included a brief solicitation, study background a link to the online survey. At the end of the survey, participants were asked whether they were willing to participate in an online in-depth interview and/or an online focus group discussion with other TTP actors. Participants were also given this option at the beginning of the survey, in case they wished to participate but do not desire to fill out an online survey. However, this was not encouraged because a goal of the survey was to gather background information to inform the in-depth interview.

The primary goal of this case study was to gain the consumers' perspective on the needs and gaps in seeking health information about TTP. This case study was conducted to achieve "verstehen", or an understanding of shared meaning based on the context of those affected who have experienced that which I am studying (Glass, 2005). This is reflected in the recruitment process, which did not have a specific sample target, but continued until saturation was reached. Because the recruitment process was layered, saturation was determined using in-depth interviews as the benchmark. These interviews

explored individuals' experiences, opinions, and motivations, and active recruitment ceased when saturation was reached, according to the seminal definition offered by Glaser and Strauss (1967), being the point at which "no additional data are being found whereby (one) can develop properties of the category". Despite the cessation of active recruitment once saturation had been achieved, interviews continued for an additional fifteen days to enable participation from all who were interested and enable the members of this community who wished to speak to have a voice (Reinharz, 1992). This decision was made as a result of feedback received from respondents, including one respondent posting on my behalf on one of the facebook pages, urging people to participate and have their voices heard. The surveys were meant to provide background information and allow for data aggregation, and focus group discussions were conducted with a goal of enabling reflection on themes extracted from in-depth interviews and providing actors with an opportunity to generate and discuss ideas for next steps. According to Griffin and Hauser's (1993) discussion of the law of diminishing returns, a sample of 30 participants for in-depth interviews typically gives insight to all but the most minute of differences. Mason (2010) found that qualitative researchers recruit a mean of 31 participants for in-depth interviews. Therefore, I anticipated that I would require a maximum of 30 participants for in-depth interviews. I oversampled, suspecting that more participants would be willing to complete the online surveys than participate in interviews, and it was anticipated that fewer still would agree to participate in focus groups.

In the event that not enough interest was generated via the Facebook TTP group, I other options for recruitment included a somewhat less active Yahoo group and other

TTP-specific interest groups that are available online but are less active than the Facebook group. This was not necessary. Recruiting via Facebook will self-select people who have sought information and community building online; I am comfortable with this, because these are also the people who will be first-level users of the proposed intervention. Additionally, I suspect that there are people who lurk on the Facebook group and do not post, and it is possible that they will come forward to participate once I disclose the purpose of the study. Finally, due to interest in the research that was generated by the Facebook communities, three participants (two HSO and one patient) were interviewed who are not members of these Facebook groups.

Data collection. Surveys, interviews, and focus group discussions were rolled out in a staggered fashion – interviews were not begun until the survey was available for a period of two weeks to allow enough time to gain trend understanding that could inform the interviews. Focus group discussions did not commence until interviews had taken place for at least two weeks and enough participants agreed to participate in focus group discussions. The survey, interview questions, and focus group topics inquired about experiences trying to get information, address issues of equivocality, as well as gain an understanding of the person's unique experience as a contextual unit. (See the survey instrument, sample interview questions, and the focus group guide in the Appendices).

Cross-sectional surveys. A link to the survey was included in the recruitment solicitation. The survey was administered online using SurveyGizmo, which gave participants the option of saving their survey and returning to it later. The survey is primarily close-ended, utilizing a multiple-choice format that is intended to be brief, but

participants also had the option to include open-ended responses to provide illustrative examples or give feedback in an unlimited character text box next to these questions.

During formative research, I found that participants often have complicated backstories, which include various medical episodes and relapses. This posed a challenge, since it be difficult to have an effective in-depth interview without access to this medical background information if the participant is interested in sharing it; however, sharing this background information can exhaust participants before they are able to speak to their information needs and their experiences seeking information online. An online survey format enabled the participants to share background information that they felt relevant and helped to avoid spending time on this during the in-depth interview – because some background information had already been shared, rapport-building was easier despite the personal nature of the questions. Information from the survey was used to inform the in-depth interview, especially probes. Participants were given the option to remain pseudonymous, to allow for their privacy while enabling information from survey, interview, and focus group discussions to be tied to one individual. Participants were also given this option to receive credit for their contribution, which participants granted, citing a range of reasons, including the desire to help other patients and to lend credibility to the study from one patient to another.

In addition to informing subsequent stages of data collection, information from the survey was analyzed qualitatively and quantitatively. Data from the multiple-choice portion of the survey has been aggregated and analyzed using SPSS Statistics 21. Open-ended answers will be coded for themes using constant comparative analysis, using

Atlas.ti 7 for management and organization. Emergent themes were aggregated and frequencies were generated in relation to statistical analysis of survey data.

In-depth interviews. The interviews followed a low-to-moderate level interview schedule. Probes were drawn from survey data, when available. This will allowed for flexibility to adapt to the interaction while still providing ease of transcription and ease of coding. Interviews were conducted using Skype, which will grant the highest level of interpersonal reaction in addition to the greatest level of consistency across interviews. Interviews will provide an opportunity to achieve more depth than the surveys and will enable directed questions toward specific experiences, identified needs and gaps, and personal reflection. Interviews also allowed for follow-up questions and confirmation of information reported in the surveys.

Because of the rareness of the disease, it is probable that the participants will be geographically diverse and sparse. I also note that because of the online nature of the anticipated intervention, there is a layer of protection to individuals who would be communicating with me electronically, as opposed to sitting in a room with a stranger telling them very personal medical information. While this could be a detriment in some scenarios, I think this is a positive consideration in this study. Interviews were audio-recorded and transcribed, and coding was done with audio and text files paired to allow for the impact of inflection and tone. Themes were extracted using grounded theory and constant comparative analysis. Two coders were given a list of codes and a sample of transcripts to ensure some level of inter-coder reliability. Coders found themes consistent with my findings, including cases thematic overlap. Quotations of key themes will are

included to demonstrate saturation, and themes will be statistically analyzed to demonstrate applicability across the sample population.

Focus group discussions. Focus group discussions took place online using Skype teleconferences. For privacy considerations, participants were surveyed about whether they preferred to participate using audio technology (e.g. Skype voice only), audio and visual (e.g. Google+ Hangout), or to remain more anonymous (e.g. online chat room). All groups took place using a Skype teleconference. Each focus group consisted of approximately 5 participants, based on participant availability. Focus group discussions were moderated toward identifying next steps toward an intervention and will build upon data collected during the first two phases of the case study. Analysis of these data was largely qualitative and quotations will be used to illustrate key themes.

Limitations

While this study is likely to offer compelling insights into the needs of a particular community of patients with a rare disease, there are some limitations that should be considered. My partner is a TTP survivor who has undergone extensive treatment, is in remission, but who still has complications related to this disease. This personal experience with TTP will be beneficial because it may allow me to achieve in-group status with study participants, but may also bias my interpretation of data. I will address this potential for bias by ensuring inter-coder reliability for the content analysis data; attempts will be made toward inter-researcher reliability for the case study, including in-depth interview data, open-ended survey data, and focus group discussion data. Instead, they will be given a list of codes and sample transcripts. Text from interview and focus

group discussion transcripts, message boards, and open-ended survey questions will be entered into the Atlas.ti 7 tool to further reduce potential for bias.

Online data collection is the most appropriate method for this study, but it presents some challenges, especially because of the sensitive subject matter. I will not be able to conduct member checks. While online sampling will avoid regional bias, I will be limiting my sample to people who are already either actively or passively participating in online communities. This could exclude valuable insights from people who cannot or choose not to interact online to find health information. I will not have a random sample, but will instead recruit until the targets are met.

This study will not be generalizable across rare diseases. Instead, it will suggest what communication interventions are needed as they apply specifically to TTP, and the findings can be contextualized and applied to other disease communities. By learning from the experiences of those confronting rare diseases, and comparing these findings with the current activities of established online communities, I will be able to effectively conclude what considerations must be made when designing successful grassroots strategies to improve access to information for patients with rare diseases.

CHAPTER FOUR: ANALYSIS, RESULTS, AND DISCUSSION OF EXEMPLAR ONLINE COMMUNITY FOR PEOPLE WITH RARE DISEASES

Summary

Under the overarching research questions, this content analysis was undertaken to explicitly answer three sub-questions:

RQ1: What are the subjects or themes that commonly appear in online communities for people with rare diseases?

RQ2: What subjects or themes result in high levels of interaction in online communities for people with rare diseases?

RQ3: How are the three phases of organizing (enactment, selection, retention) represented among active participants in online communities for people with rare diseases?

Analysis

The review of the literature showed that advocacy organizations for people with rare diseases tend to follow the same model of health communication that has been shown to be effective for mainstream diseases and health issues. In cases of mass communication or mass outreach, this typically means that a top-down model is followed, as opposed to a model that is more patient-centered. Scholars critical of the top-down approach advocate instead for a grassroots strategy, noting that by including the target

population in all stages of design, their needs would be properly understood and more likely to be met (Hoffman, 2003; Obregón & Waisbord, 2010). In the case of rare diseases, a patient-centered model would be representative and inclusive of many of the principles advocated for by proponents of grassroots communication, and would comport with the social and feminist models of medicine described in Chapter 2. In order to validate the claims that 1) major advocacy organizations follow a top-down model and 2) that this restricts their ability to meet the needs of individual patients or even individual rare disease communities, an exemplar rare disease community was selected and content were analyzed. The selected community, RareConnect.org, is a collaborative effort from two pre-eminent rare disease advocacy organizations from the United States (NORD) and Europe (EURORDIS).

RareConnect.org has 32 individual online communities for specific rare diseases. Recognizing that the communities may be very diverse, the a census quantitative analysis of all communities was conducted. The unit of analysis was a discussion thread. Across the 32 communities, there was a total of 852 discussion threads. Because RareConnect.org is a collaboration between American NORD and European EURORDIS, 188 of the 852 threads were not originally posted in English. Although RareConnect.org provides third party translation, quality could not be verified; in some cases, human translation was conducted, while in others, an electronic translation service appeared to be employed. To ensure accurate understanding of nuance and purpose, threads for which the *original post* was not in English were excluded from analysis, reducing the sample size to 664 threads.

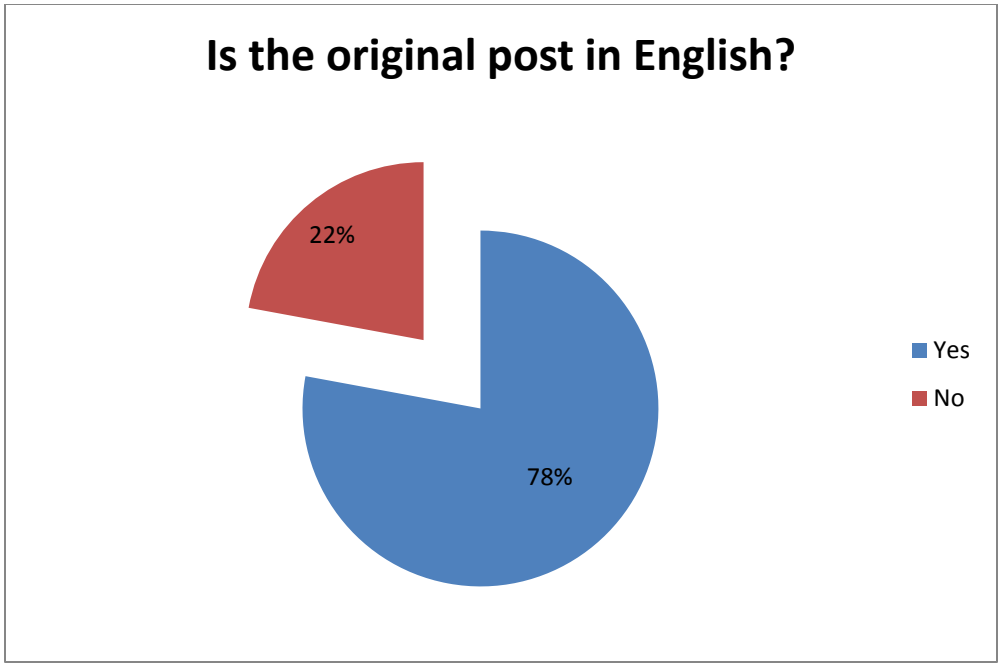
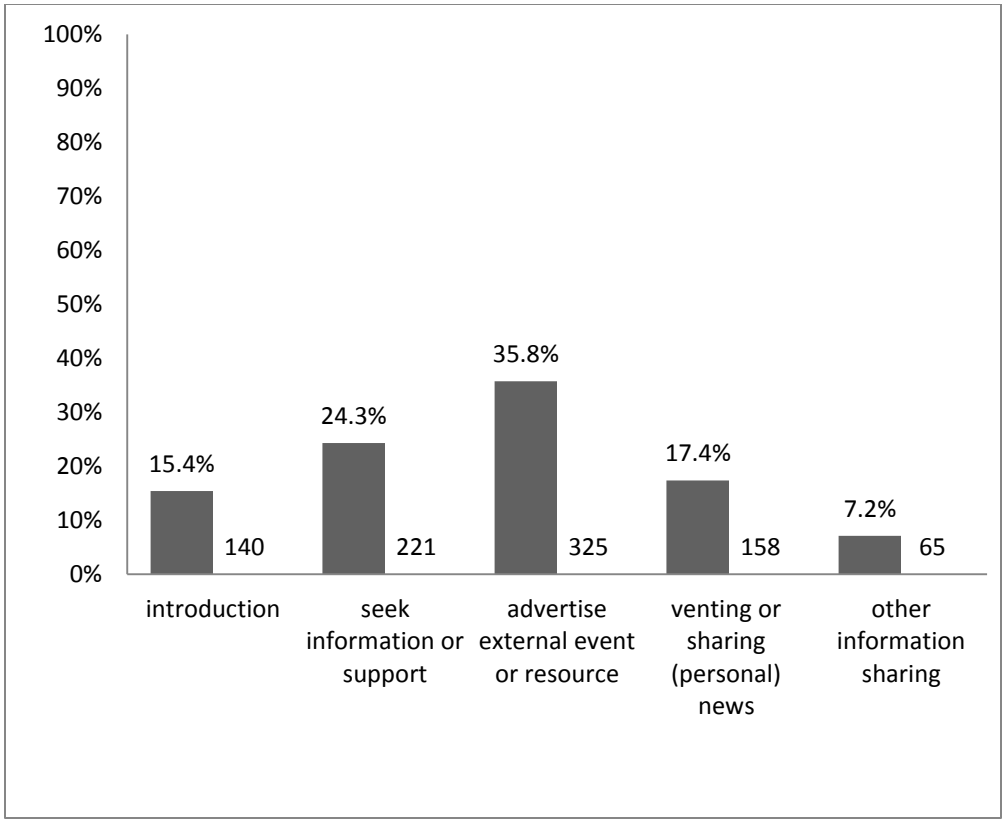


Figure 8 Language of original post

The primary focus for analysis was on the original post. The key variables coded for were equivocality (defined as the complexity of the issues addressed in the messages posted and as measured by the actual variables of uncertainty, complexity, and urgency); interactions; role (e.g. patient, doctor, caregiver); purpose of posting (e.g. seeking information, venting/support) information sought (e.g. support, medical advice, referral). Please see Appendix 3 for the codebook.

Content Analysis Results

As Figure 9 illustrates, the most common theme among all posts as measured by the purpose of original post was to advertise an external event or organization. This observation may be explained by an examination of who is using these communities.



Note: Some posts had more than one purpose.

Figure 9 Purpose of original post

Demonstrated in Figure 10, of the cases in which the identity of the poster could be determined (n = 579), nearly two thirds of threads were initiated by a moderator or someone affiliated with an advocacy organization, while about one third were started by patients or HSOs. These figures should be kept in mind while interpreting the remaining findings from the analysis of RareConnect.org communities, and will be discussed in greater detail in the discussion section of this chapter.

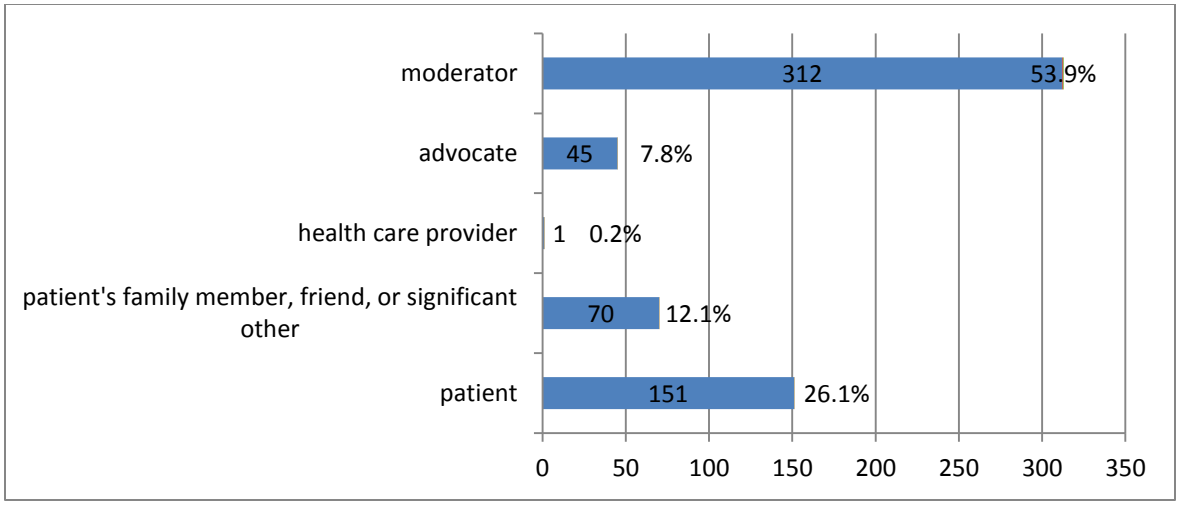


Figure 10 Identity of original poster

A great majority of original posts received zero or one response; with original posts receiving a mean of 1.81 responses. However, this mean is influenced by a few outliers where higher response rates were seen; the median and mode are both 0 responses (see Figure 11). Further to the level of activity by moderators, of those posts that received one or more response, 51.2% received responses from moderators, and 45.1% had one or more responses from the original poster. Said differently, most users interacted solely with a moderator, if anyone at all.

It is interesting to note, however, that despite the low levels of interaction, posts by patients and advocates typically generated more responses than posts by others (see Figure 12 for a cross-section of responses by identity of original poster). This is especially noteworthy considering the relative infrequency of posts by patients.

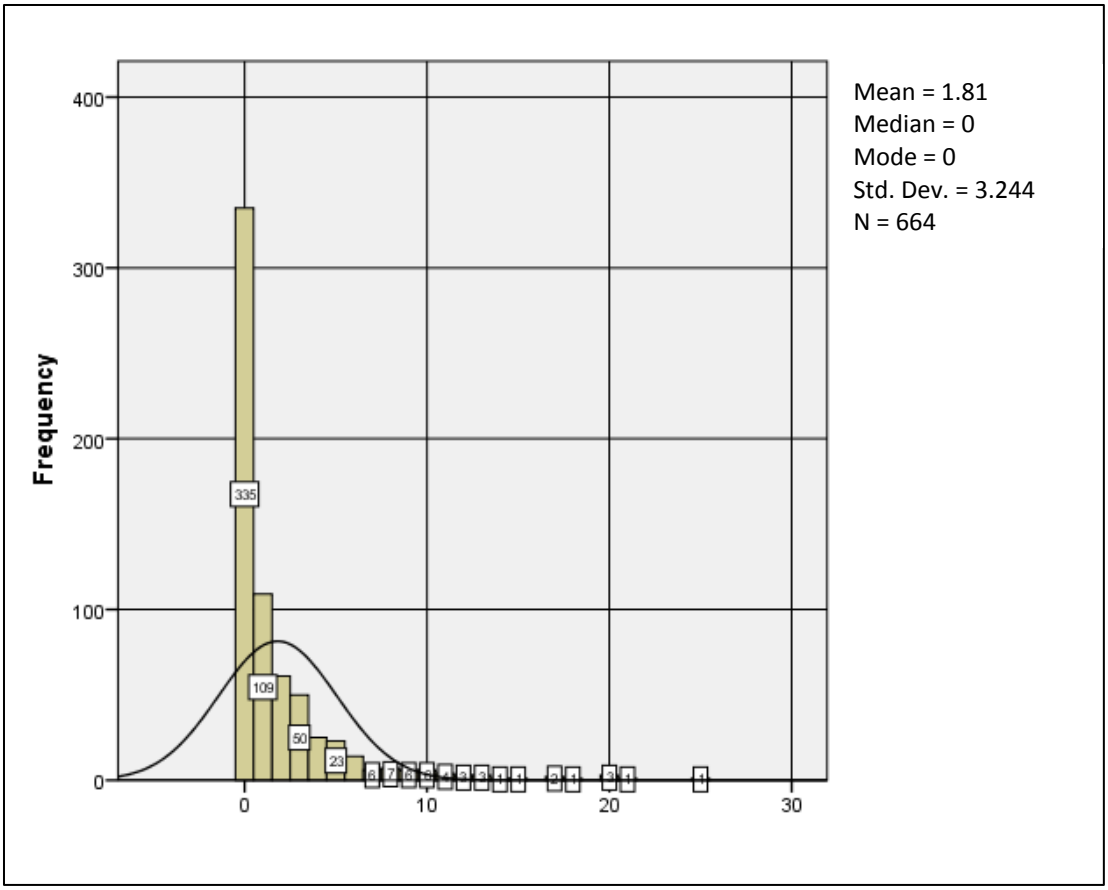


Figure 11 Number of responses to original post

Activity in all communities was consistently relatively low, especially on the part of patients and HSOs. However, among those posts that were urgent (5.6%), complex (4.7%), and uncertain (7.0%), recurrent themes emerged. Because of the highly subjective nature of "uncertainty", "complexity", and "urgency", coders were not randomly assigned threads, but rather, randomly assigned communities to improve ecological and normative validity so that they may achieve a better understanding of what may be equivocal to those particular patients. Inter-coder reliability on these three variables was a key focus of training, and acceptable levels were reached. Coders ranked

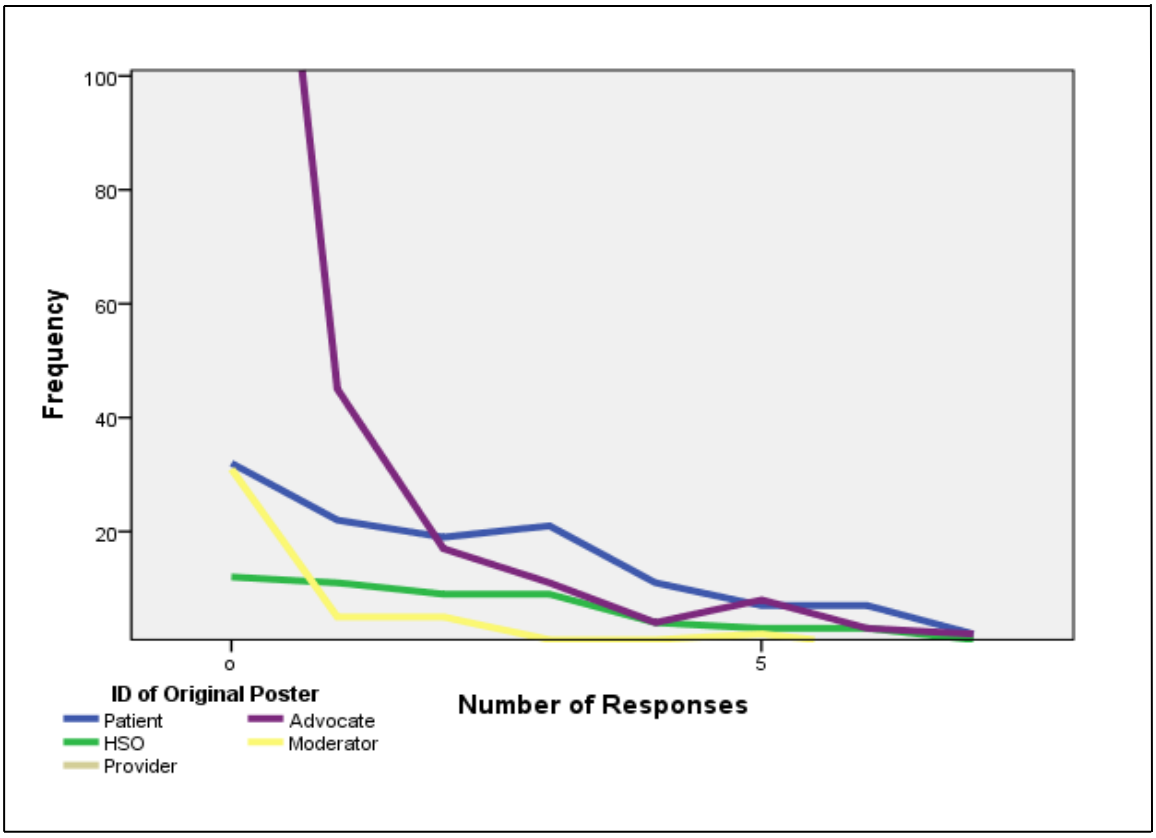


Figure 12 Frequency of number of responses by Poster ID

uncertainty, complexity, and urgency on a 5 point Likert-style scale. These themes were collapsed into dichotomous scales, with uncertain and very uncertain representing "uncertain", complex and very complex representing "complex" and urgent and very urgent representing "urgent". Themes from these categories were recorded to explain what about these posts contributed to their equivocality. Recurrent themes from this subset were recorded and are identified below, demonstrating common themes and answering RQ2.

Complex (n = 32 threads; n=79 mentions of selected themes)	
Theme	Number of mentions†
Additional problems unexplained by diagnosis	11
Treatment not working	10
Different diagnoses from different doctors	10
No one can explain this/offer advice	8
Finances	8
Unable to get diagnosis	8
Trying to prevent additional damage (e.g. lost ability to use my fingers, my good eye will be affected)	6
Doctors report not being able to help or inexperienced doctors	6
Discrimination, isolation	6
Lawsuits	3
Searching for local patient groups	2

†multiple themes may be mentioned in one thread

Table 3 Complex Themes

Uncertain (n = 46 threads; n = 66 mentions of selected themes)	
Theme	Number of mentions†
Unable to find specific information, even from doctors	14
Conflicting information from doctors	11
Seeking strategies for coping and managing	9
Symptoms are getting worse despite treatment	6
Trying to prevent additional damage	6
Cannot get diagnosis	5
Unsure if treatment will work	3
Finances	3
Medication may have been part of a bad batch	3
Not knowing if symptoms are related to disease	3
Inability to plan for future	3

†multiple themes may be mentioned in one thread

Table 4 Uncertain Themes

Urgent (n = 37 threads; n = 68 mentions of selected themes)	
Theme	Number of Mentions†
Help! (e.g. can anyone help me, please help asap, can someone help please, I need help immediately)	16
Isolation	13
Doctors unfamiliar with condition/cannot help	10
Tips/strategies sought	9
Extreme pain	8
Fear	5
Rapid deterioration of condition	5
Do not know who to turn to	2

†multiple themes may be mentioned in one thread

Table 5 Urgent Themes

It is notable that certain themes appeared across categories, such as finances, difficulty getting a diagnosis, feeling that doctors are not knowledgeable, and feelings of isolation. These categories are consistent with the literature review and case study findings. The prevalence of these themes indicates an agreement with Weick's model, and that many patients who are on RareConnect.org are seeking tips, strategies, and methods to cope. RareConnect.org embraces the concept that patients want access to information, but ignores the importance of a development of a norm of reciprocity, shared identity, or individual reputation building. Likely due to the low activity, there was no notable trend in response level according to level of urgency, complexity, or uncertainty.

Discussion of Content Analysis

An analysis of the ways that the active patients and HSOs utilize RareConnect.org indicates an agreement with Weick's model – that people seek increasing help in times of high equivocality – however because of the lack of activity in these communities, participants are simply unable to organize, despite their intention or purpose for posting. To put the somewhat inflated mean of 1.81 responds per post in context with what one might expect from such an online community, Malik & Coulson (2010) conducted an analysis of online infertility support groups, and the 864 discussion threads contained 17,686 messages, for mean of 20.4 responses per thread.

To make sense of the low activity level on RareConnect.org, it is useful to consult Brandtzaeg & Heim's (2008) analysis of user loyalty and online communities. In this study, the authors outline 9 main factors that affect user participation over time:

1. Lack of interesting people/friends attending,
2. Low quality content
3. Low usability
4. Harassment and bullying
5. Time consuming/isolating
6. Low trust
7. Over-commercialized
8. Dissatisfaction with moderators
9. Unspecified boring (p. 1)

Based on my analysis of RareConnect.org, I suggest that they fall short on a number of these factors. The relatively high presence of moderators and other authority figures undermines many of the benefits of online communities, such as peer-to-peer networking and the organic development of a collective identity, which may influence the activity level (Putnam, Phillips, & Chapman, 1999). For example, the overwhelming presence of moderators negatively influences 1, 3, and 8 in the list above. Further, one third of posts are advertising something external to the site, rendering item number 2 problematic. RareConnect.org's attempt to have high usability and be accessible to a global population ultimately backfires; the languages are fragmented and translations are piecemeal, few rare disease communities (< .005) are represented, and unless one is looking for information on rare diseases writ large, it is not well-optimized for online searchability. Fox (2011) quotes an HSO, speaking about the utility of online communities, who says that "patients and caregivers are there for each other and no question remains unanswered." Clearly, this is not the case on RareConnect.org, where just over half of the posts received zero responses. Therefore, it is both time-consuming (insofar as time invested vs. return) and isolating, which is devastating to an already isolated community. Finally, while there are some moderators who have some experience with a rare disease, the omni-presence of the same handful of moderators across all communities renders the site inauthentic and does not add trust or credibility. One person can certainly not know enough about each disease to have meaningful contributions, yet moderators make up a huge proportion of the content generation, and the same

moderators appear across communities, frequently attempting to generate discussion by asking general questions.

While there is general information sharing, the relationships developed do not seem particularly supportive and sociable. The prevalence of moderators is a detriment to a shared identity (Brandtzaeg & Heim, 2008) which is important to motivate people to share personal and meaningful information, which is a necessary element that contributes to the establishment of truer relationships.

RareConnect.org embraces the concept that patients want access to information, but ignores the importance of a development other elements that are important to patients. Instead, the "communities" essentially become clusters of links to outside studies with limited interactions, impeding the establishment of a norm of reciprocity, shared identity, or individual reputation building. This can be seen particularly clearly by examining the low patient/HSO activity, combined with the fact that most of the activity was between a single user and a moderator. Patients are simply overwhelmed by moderator presence or de facto moderators who present as disease experts but are on the board to promote their fundraising organization. Here again, the low barriers and accessibility/usability have a negative effect; the ideal scenario is for people to become friends and develop a sense of community to reduce alienation while learning. The lack of a norm of reciprocity is a concern across online communities (Kanuka & Anderson, 1998); unless a shared identity and sense of community are developed, participants are unlikely to engage in communication cycles which enable a "negotiation of meaning resulting in new knowledge construction" (Kanuka & Anderson, 1998, p. 10). This is particularly

problematic, since it contrasts directly with Fox's (2008) finding that a particular strength of online communities is the development of a collective wisdom between members. From the perspective of Weick's model of organizing, RareConnect.org is ineffective platform for organization. Many posts seemed to be from patients in the enactment or selection stages, but because of the low activity levels and the fact that their questions were not answered, they could not develop or access a repository of knowledge developed during the retention phase of organizing.

NORD's strength is its affiliation and reach. Rare disease patients would benefit from a cheerleading squad and connections that can be leveraged, which NORD and other advocacy organizations do. The limited reach of the RareConnect.org boards is troubling because it represents the effort of NORD, a pre-eliminate organization for advocacy for patients with rare diseases in the United States. It is worth mentioning that of the 188 threads that were not analyzed because they were not originally posted in English, 23% were from detail screens, which indicates that they had four or more responses. In contrast, approximately 15% of the posts that originated in English were detail screens. This is notable, because it may mean that EURORDIS is more effectively promoting RareConnect.org than NORD, and as a result, there is not as much active engagement from the NORD side. This is particularly problematic for patients in the U.S., as NORD is one of the primary places that they are referred to upon diagnosis with a rare disease (Genetics Home Reference, 2008; Office of Rare Diseases Research, 2013). This demonstrates that despite NORD's great efforts at advocacy, they do not have their attention correctly focused on this important, but ignored, component of

patient advocacy and patient needs. This also demonstrates the problematic nature of a top-down approach (e.g. foundations and advocacy organizations) as outlined above (Hoffman, 2003; Obregón & Waisbord, 2010), in that they often do not address issues of the affected population, and in this case, we see many patients stranded, despite attempts for support and information on their part.

CHAPTER FIVE: CONTEXTUALIZING THE EXEMPLAR COMMUNITY

In light of the growing body of research and advocacy for rare diseases in recent years, additional Rare Disease advocacy organizations' online content were analyzed qualitatively in order to ensure that RareConnect.org was still representative of other advocacy communities. This enabled an understanding of what might be considered the current gold standard that rare disease advocacy organizations follow. These non-randomly selected websites were collected by conducting a search until it appeared that saturation had been reached using Google and Bing. All content, including sub-pages, but excluding videos, was analyzed using Atlas.ti 7. Key themes were noted. This step was not part of the original study design, but was included to identify whether RareConnect.org was still relevant as an exemplar online community. Findings from this mini-analysis indicate that RareConnect.org remains a good representation of rare disease advocacy organizations and their approach to communication. In fact, several of the advocacy organizations sampled follow the dominant, top-down model of health communication even more obviously than NORD/RareConnect.org. The point of saturation was reached when sources began linking back to each other, concluding with official reports issued by US Governmental agencies and their associated offices, and when no new results could be queried.

As mentioned above, a primary theme identified by the review of the literature was that current rare disease interventions employ similar strategies to mainstream health communication interventions, which can marginalize rare disease patients. Interestingly, by following these top-down health communication "best practices", these organizations are not doing good health communication, which includes substantial formative research in order to determine the proper scope, assess the needs of the population, and ensure purposeful placement to reach and ultimately resonate with the target community (Fishbein et al, 2002). The previous chapter demonstrated that this was a problem with NORD, and subsequent explorations of rare disease advocacy organizations confirmed that NORD was not alone in this practice.

The Global Genes Project

A number of organizations, including non-profit and governmental, focus rare disease research on genetic issues. The Global Genes Project is one such organization, and a qualitative analysis of the resources offered on this website demonstrates a reliance on tactics used by health communicators working with prevalent diseases, including the use of ribbons that are so prevalent across diseases. The Global Genes website is very image heavy, and Figure 12 encapsulates many of the messages that appear across the website. Also seen in this image is the reliance on the total number of people affected, with no differentiation between the diverse set of health problems encountered by the 7,000+ diseases they mention. This is particularly striking because their focus is on *genetic* rare diseases, yet they still rely on the aggregate number.

Figure 13 Social media graphic from the Global Genes Project (source: www.globalgenes.org)

The focus on genetics adds an interesting rhetorical dimension for a number of reasons. Field and Boat (2010) speak to the ethical considerations surrounding genetics – for example, what should one do with the information that they may be genetically predisposed to a rare condition? However, in contrast to idiopathic diseases, diseases that have confirmed genetic determinates provide researchers with an increased ability to identify preventative measures, instead of focusing solely on treatments. To add a bit of auto-ethnography to this exploration, I first became interested in this research when I learned of reactions that my partner received in his quest for information about his own idiopathic TTP, during which he was told that his disease was not an area of interest for researchers or organizations because it could not be prevented and it could not be cured,

so it lacked a human interest element. This feedback came from one of the advocacy organizations discussed in this dissertation.

In the context of genetic predisposition to rare diseases, there are a few stigmatizing items of note. “Faulty genes” (mentioned in Figure 12) implies blame, weakness, or brokenness. EURORDIS (2005) produced a white paper on the importance of rare diseases as a public health priority, and noted that while up to 80% of rare diseases have identified genetic origins, the genetic or chromosomal abnormalities can either “be inherited or derived from *de novo* gene mutation or from a chromosomal abnormality” (p. 4). Still, in this same report, a parent discusses the severe impacts the genetic revelation has had on her – she feels responsible for being a “carrier”. Blaming parents for passing along “faulty” genes is fairly common. In fact, this even appears in popular culture. For example, see below the exchange between the main character and her parents regarding obsessive compulsive disorder, excerpted from an episode of *Girls*.

> Hannah: It hurts me more than it hurts you. I’m the one who has to experience it, not you. I’m the one who has to experience it.
>
> Mother: You think we didn’t experience it? You think we didn’t suffer, wondering whether you’d have a normal life? We don’t know why you have OCD! We don’t know why. We’re still married, we never raised a hand to you – it’s not our fault.
>
> Hannah: Well it’s genetic, which is sort of the ultimate your fault, so…
>
> Father: Oh, come on.

(Dunham, Rubinshteyn, & Schoeneman, 2013)

Global Genes includes content that provides some context about rare diseases. Interestingly, the final point on their "rare facts" page is that approximately 50% of rare diseases do not have a disease specific foundation supporting or researching the same (globalgenes.org, 2013). The fact sheet itself is primarily concerned with demonstrating the reach of rare diseases, which is consistent with the literature review findings. Other resources provided include a list of rare diseases (not limited to those that with genetic origins) that were compiled primarily from NIH resources. They request that one does not reproduce the list, since it is updated frequently, but rather to link to the site. In order to provide context for how sites like this may be overwhelming to patients, increase their sense of isolation, or make them feel insignificant or hopeless, Figure 13 is a portion of the list as of March 6, 2013. It is intentionally reduced so that disease names are not visible. The complete list, which is currently 99 printed pages, may be accessed at http://globalgenes.org/rarelist.

To direct my search in this quest for "verstehen", I searched for TTP, which was listed in both its acquired and congenital forms. This is a major improvement over other sites that are not frequently updated and are not comprehensive, which increases a sense of isolation. However, the presentation in a 99 page list, where it appears directly above five thumb deformities, may not be the most sensitive way to give patients hope, which is part of Global Genes' mission.

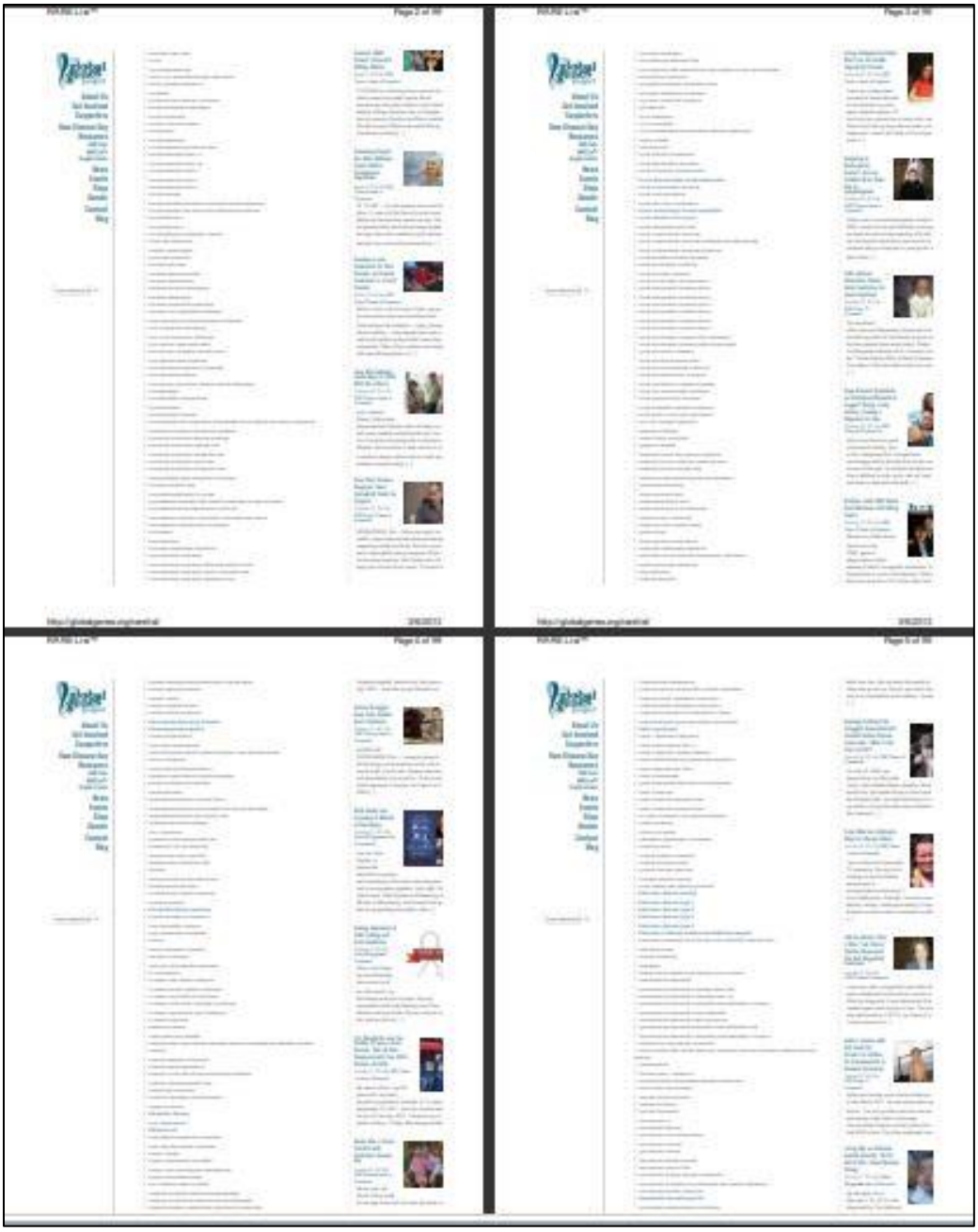


Figure 14 Four (of 99) pages of the Rare List accessible at globalgenes.org/rarelist

Additional observations strengthen the case that patients utilizing these resources may ultimately leave feeling more marginalized than when they began. For example, one

can imagine patients may feel fairly insignificant while searching for their disease and finding the following error:

- *Thiopurine S methyltranferase deficiency*
- *This list supplied by the RARE Project – Feb 2012*
- *Thomas Jewett Raines syndrome*
- *Thomas syndrome*
- *Thompson Baraitser syndrome*
- *Thoracic celosomia*
- *Thoracic dysplasia hydrocephalus syndrome*
- *Thoracic outlet syndrome*
- *Thoraco abdominal enteric duplication*
- *Thoraco limb dysplasia Rivera type*
- *Thoracolaryngopelvic dysplasia*
- *Thoracomelic dysplasia*
- *Thoracopelvic dysostosis*
- *Thost-Unna palmoplantar keratoderma*
- *Three M syndrome*
- *Thrombasthenia*
- *Thrombocytopathy asplenia miosis*
- *Thrombocytopenia 2*
- *Thrombocytopenia cerebellar hypoplasia short stature*
- *Thrombocytopenia essential*
- *Thrombocytopenia Robin sequence*
- *Thrombocytopenia with elevated serum IgA and renal disease*
- *Thrombocytopenia acquired amegakaryocytic*
- *Thrombocytopenia x-linked*
- *Thrombomodulin anomalies familial*
- *Thrombotic thrombocytopenic purpura acquired*
- *Thrombotic thrombocytopenic purpura congenital*

Figure15 Subsection of Rare List

While editing errors are inevitable, this type of mistake has the potential for very negative emotional impacts on patients and to further increase their sense of isolation. They may infer that their disease, if listed, is a blip, it doesn't matter, or that it matters so little to this organization that they could overlook an alphabetical sorting error. If this seems an over dramatization, it is not. It is incredibly challenging to find rare disease resources online as it stands, and it is mistakes like these that make patients have difficulty trusting the information they find online. Furthermore, during the interviews that will be presented in the next chapter, a few patients told stories about how they looked at lists online for the name of their disease because they could not remember the exact name, which would explain why someone may have an incentive to search through all 99 pages instead of doing a Crtl+F-type search. Patients who only vaguely recall the name of the disease would typically look for it in context. This will be discussed in greater detail in the next chapter.

Finally, a large portion of Global Genes is dedicated to thanking corporate sponsors (largely pharmaceutical companies and insurance providers) and disseminating social networking graphics (including ribbons!). From this, we may infer that these stakeholders understand the importance of connecting with rare disease patients, but lack a grasp of the significance of engaging with this population in a way that is meaningful to the individuals affected.

TTP Resources

Turning to a search for TTP, information was much more difficult to find and what was available was extremely inconsistent. Further, thanks to an extensive

consultation with the scientific and medical literature, I noted that much of the information was factually inaccurate. Health Grades Inc. (available: rightdiagnosis.com/thrombotic_thrombocytopenic_purpura_acquired/doctors.htm) suggest, in this order, specialists for TTP: generalists, allergy and immune diseases, dermatologists, and finally, "blood health specialists (hematology)". This will be important to consider during the discussion of hematologists that will take place in the following chapter. This website also gives confusing and inaccurate information about the prevalence and incidence of TTP, failing to distinguish between acquired or congenital forms.

Failure to distinguish between types of TTP was fairly common. Further, several sites conflate TTP with other diseases that are similar, yet pathologically distinct, such as ITP, Microangiopathic Hemolytic Anemia (a symptom of TTP), sickle cell anemia, and numerous others (see: NORD: Thrombotic Thrombocytopenic Purpura; rightdiagnosis.com). For example, clicking on a link for "Other Names for TTP" on the NHLBI's page for TTP information actually directs the user to a list that entitled "Other Names for Hemolytic Anemia" (NHLBI, 2012). This may simply be a result of careless web design or unclear communication but one only will have the ability to identify this as an error if they are very knowledgeable about TTP. It is unlikely that the target audience for a factsheet called "What is Thrombocytopenia?" possesses this level of knowledge, and thus confusion mounts. Similar inconsistencies were present in sections devoted to describing and identifying TTP symptoms (see NIH, NIH:NHLBI, NORD, WebMD).

This is especially problematic because many of these websites link to each other. Further discussion of these findings will be provided in the following chapter.

Governmental Initiatives

A return to the literature review will remind one of what the U.S. Government is currently doing for rare diseases, as well as the linkage between patient involvement and reducing negative consequences of the R&D Productivity crisis outlined above. The *Institute of Medicine (US) Committee on Accelerating Rare Diseases Research and Orphan Product Development* reports on the current state of affairs as far as treatment development and research for rare diseases, including an assessment of policies that influence rare disease and orphan products (Field & Boat, 2010). Many of the mechanisms to propel knowledge about rare diseases that are included in this report are outlined in Chapter 2. Visiting the OOPD website, I viewed the application that is required for a grant or to get orphan status for a drug or medical device. Under the FAQ, I was interested to note the following question:

> What if the sponsor has difficulty finding data on prevalence? What if data is not available? What are the best prevalence estimate resources? What should a sponsor do if the best resource they can find is 10-20 years old (or from other countries only)?

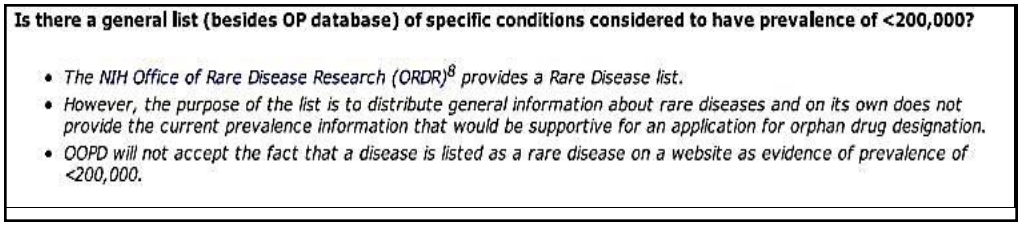
I had recently encountered this challenge during a search for TTP prevalence data when trying to calculate the power of my case study sample. To my great frustration, this was impossible, and rendered calculating prevalence (and sample power) virtually impossible. Incidence data, not prevalence data, were available, but were extremely

varied: 1 – 5 / 10,000 (Orphanet, 2012), 4.5/million/person year (Peyvandi, Palla, & Lotta, 2010), 1.7-11/million/year (Genetics Home Reference, 2008), and 4.46 per million (combined TTP and HUS) (Terrell, et al., 2005). There are a few presentations from rare disease working groups that are available online that discuss these implications and potential solutions (Lilford, 2012). An application of obstacles created by the requirement for precision in clinical trials is identified by Lilford (2012): and is attributed to the reliance on the Frequentist Paradigm for sample size calculations, since the number of participants needed to achieve adequate power increases substantially as disease prevalence decreases. Lilford makes several suggestions for reconceptualizing the design of clinical trials for rare diseases, ranging from massive overhauls to study design, questioning the ethics of an underpowered sample (concluding that subjectivity is inevitable in any research endeavor), and the somewhat controversial but relatively simple solution of using Bayesian methods in place of frequentist interpretations (2012). Another presentation on study design and rare diseases identifies the issues discussed above and offers some alternate study designs toward a solution (Hull, 2010). Interestingly, this presentation is FDA branded and was given by FDA staff. It begins with a disclaimer – these views do not necessarily reflect those of the FDA – and moves to the benefits and advantages offered by the Orphan Drug Act no mention that the Orphan Drug Act does not take these limitations into account. The rest of the presentation is devoted to alternative designs, but offers little by way of an application of these designs that would be acceptable according to the OOPD grant requirements.

This is only one area where TTP's uncommon characteristics, extreme rareness, and not-quite-accurate/inconsistent clinical definition have an actual consequence. OOPD's answer to this question is that incidence data is only acceptable if the disease is an acute condition. Unfortunately for those interested in TTP, this policy only adds more complexity – according to some classifications, some forms of TTP are acute; many surviving patients have only one manifestation. However, TTP is often chronic or relapsing, and side effects after clinical TTP last beyond the year after which the symptoms in the acute clinical pentad have been restored. While there is some scientific progress that might help to identify predictors of a relapse, (outlined in Chapter 1) it is impossible to say whether a particular case will be recurrent or acute. Certainly, some researchers will be convincing in their applications, but this does seem to present an additional barrier to research diseases that are especially rare, for which reliable data for incidence, prevalence, and morbidity are not readily available. This leads to intra-marginalization of the very rare diseases within the rare disease classification, because there is little incentive for researchers to go through the substantial additional work to make their case and receive financial support for their research. This fact is not lost on rare disease patients, and it was raised by several case study participants as an element that adds to their sense of isolation; further discussion will occur in the next chapter.

Among initiatives that have been established with the intention of clearing the path for research on rare diseases, it is interesting to note that the considerations are primarily financial. There remains a reliance on practices that are standard for mainstream diseases but practically impossible for diseases that are very rare. The

prevalence example described above is one facet of this. Further exploration seems to indicate that this limitation will not be addressed:

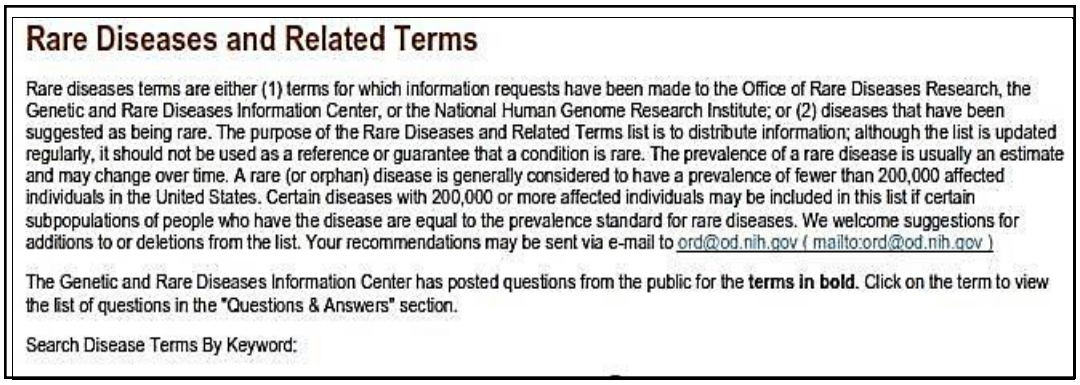


Is there a general list (besides OP database) of specific conditions considered to have prevalence of <200,000?

- *The NIH Office of Rare Disease Research (ORDR)[8] provides a Rare Disease list.*
- *However, the purpose of the list is to distribute general information about rare diseases and on its own does not provide the current prevalence information that would be supportive for an application for orphan drug designation.*
- *OOPD will not accept the fact that a disease is listed as a rare disease on a website as evidence of prevalence of <200,000.*

Figure 16 Selection from OOPD FAQ

The list to which they refer, excerpted in Figure 16, is from what many might consider the most credible and definitive resource on rare diseases: the Office of Rare Disease Research at the National Institutes of Health.



Rare Diseases and Related Terms

Rare diseases terms are either (1) terms for which information requests have been made to the Office of Rare Diseases Research, the Genetic and Rare Diseases Information Center, or the National Human Genome Research Institute; or (2) diseases that have been suggested as being rare. The purpose of the Rare Diseases and Related Terms list is to distribute information; although the list is updated regularly, it should not be used as a reference or guarantee that a condition is rare. The prevalence of a rare disease is usually an estimate and may change over time. A rare (or orphan) disease is generally considered to have a prevalence of fewer than 200,000 affected individuals in the United States. Certain diseases with 200,000 or more affected individuals may be included in this list if certain subpopulations of people who have the disease are equal to the prevalence standard for rare diseases. We welcome suggestions for additions to or deletions from the list. Your recommendations may be sent via e-mail to ord@od.nih.gov (mailto:ord@od.nih.gov)

The Genetic and Rare Diseases Information Center has posted questions from the public for the **terms in bold**. Click on the term to view the list of questions in the "Questions & Answers" section.

Search Disease Terms By Keyword:

Figure 17 Selection from ORDR List

Note that even here, definitive information is not available. This will be discussed further in Chapters 6 and 7; however, this is a particularly strong example of the unique difficulties that were reported in Chapter 2 (Brown, 2011) that rare disease patients encounter as they seek information. Basic information that may be taken for granted by

those experiencing a common illness is unavailable or incomplete for rare disease patients. The inability to develop a basic framework to understand their condition hinders patients' abilities to interpret equivocal inputs and develop strategies to aid in the resolution of equivocality. The presentation of the same uncertainty by trusted and well-funded experts increases equivocality and undermines patients' assessment of the credibility of information (Dutta-Bergman, 2004).

CHAPTER SIX: ANALYSIS, RESULTS, AND DISCUSSION OF CASE STUDY

Analysis

Fifty seven individuals completed surveys; a subset of 24 participated in one-on-one interviews. An elderly patient who does not own a computer "or any of those gadgets" was informed about the study by her sister, who was also a participant, and after informed consent procedures were followed, she was interviewed over the phone. Finally, one patient and two HSOs learned of the study via the facebook posting and wished to participate in interviews and focus groups, but did not complete surveys. Therefore, 28 interviews were conducted. Finally, four focus groups were held with three or four people participating in each group. Three of the groups were comprised of patients, and one of the groups was comprised of two couples (wife – patient; husband – HSO).

Recognizing the tendency of researchers to treat rare diseases as a single entity, the case study was conducted to gain a thorough understanding of specific issues that patients encounter when navigating life with a rare disease. Because of the diversity of problems patients with rare diseases may encounter, results would be superficial unless a focused analysis of on specific condition was conducted. Although specific findings are not generalizable, a replication of a portion of this case study could easily be conducted as a needs assessment for the development of a community for a different disease. Additionally, as described in Chapter 1, some findings are generalizable or could be

adapted across diseases since many of the equivocal inputs encountered by TTP patients are common across diseases, including difficulty achieving diagnosis, limited clear treatment options, lack of accessible and consistent information, variable and dramatic prognoses, and a possibility for recurrence.

Results

Under the overarching research questions, this portion of the study answers three discrete questions applied to acquired and/or idiopathic Thrombotic Thrombocytopenic Purpura:

RQ1: How do rare disease actors utilize online communities for health information?

RQ2: What do actors report as useful in their use of online communities?

RQ3: What limitations do actors report in using current online resources?

TTP patients and HSOs reported difficulties that are consistent with the issues raised in the literature review and seen in the content analysis of the exemplar rare disease online community. Generally, patients lack access to clear information, find information to be inconsistent, and encounter physical, psychological, and socio-economic effects for which they lack support. These results will be presented first by an identification of material obstacles to diagnosis, treatment, and coping with TTP. Following the discussion of these barriers, strategies that patients have developed to cope with their disease will be presented and applied to Weick's model of organizing and UMT. Finally, patients' and HSOs assessments of online communities and TTP resources that are currently available will be presented and discussed.

Obstacles in the diagnosis and treatment process. Individual TTP patients and HSOs confirmed that due to the rareness of this disease, there is not a clear identification of *what* their disease actually is or what its side effects may be. This lack of clear identification results in psychosocial, health, and interpersonal consequences. In one example, a respondent spoke to her difficulty obtaining disability due to the fact that she was in clinical remission. However, clinical remission was defined solely by her platelet count, and did not adequately capture her actual health or physical abilities. She was experiencing incapacitating side effects that were not officially linked to TTP, but that occurred as a result of the disease or treatment. Until the side effects could be linked to a concrete diagnosis, since they were outside of the clinical scope of TTP as it is currently understood, she was unable to access necessary social support:

> …The residual effects of TTP should be included (in the definition of TTP) …if it gets so far as to where you can't work and all that other stuff and you need to try and get disability… Because (I was) in remission, they wouldn't give me the disability for the TTP itself, it was the polyneuropathy and the fibromyalgia is what helped me get my disability and stuff. So yeah, they denied me when I first tried for just, for the TTP. Because like, when I was on the steroids, I didn't realize the nerve damage until after I was being weaned off and then that's when all the pain started kicking in after the steroids were gone.

(Lisa Monteria, Personal Interview, January 11, 2013)

Similarly, another respondent is not well enough to work, and has a cluster of side effects, including memory loss, anxiety, depression, ADHD, chronic pain, and lack of energy, but is having serious difficulty navigating the bureaucratic systems to get disability and other necessary support services that she would easily achieve if her symptoms were officially acknowledged as being side effects of TTP:

> I haven't relapsed except for one time in the hospital during my stay, but it's such an unknown—even with Social Security disability, I've been fighting it for three years now. I mean, I don't know what more they want from me, except come into my home and follow me around and see how my mind cannot focus on anything for any length of time.

(Mary Jo Reynolds, Focus Group Discussion, January 14, 2013)

In another case, a respondent recalls that in order to receive benefits, she was instructed to work part-time despite her on-going in-patient treatment and confinement to the hospital. This is particularly shocking because it is not an instance in which the patient had symptom improvement that had been sustained for any length of time, but instead occurred on the day that a normal platelet count was achieved as a result of aggressive, on-going treatment:

> Just when I was sick, you had some idiot at the disability office looking at the number 150 because 150 is (a) totally normal (platelet count) so one day, I was still in the hospital, my count went up to 150, this nutcase is telling me I can go back to work part time. I'm still with tubes inside of me and everything in a

> hospital and he's telling me I can go back to work because—they don't have a clue.

(Ginny Chambers, Focus Group Discussion, February 20, 2013)

These bureaucratic and insurance obstacles represent some of the major material challenges that patients with TTP reported experiencing due to the lack of a clear and accepted definition of the disease and its side effects. This lack of consensus understanding also extends to health professionals and can also have health impacts, as reported by the following respondent:

> I still go (to get my blood tested) every week and I imagine I will for a while. My hematologist is being very, very cautious throughout this whole thing. I think I'm her first TTP patient… I understand what you were saying …about having to ask about what your platelet counts are all the time because I did get sick a couple weeks back and I had a bruise on my leg and so of course when I got my blood drawn, I wanted to know the counts were. I said, "Can you let me know right away?" and they said, "Well, we're only going to call you like if they get down in the teens." This was the nurse telling me that and I was kind of—that made me really nervous because I thought, "Well, maybe that's how you deal with the cancer patients but if mine go down into the teens, I'm going to be very, very sick." So that's part about being your own advocate and finding out your counts and knowing what they are.

(Sarah Taylor, Focus Group Discussion, February 20, 2013)

Due to providers' lack of familiarity with the pathology of TTP, participants report that they are frequently treated as though they have cancer or more common diseases, so the unique warning signs that could signal an impending relapse are frequently ignored by healthcare providers unless patients (or their HSOs) become vocal, educated advocates. However, this too presents a particular challenge for rare disease patients. Beyond the limitations associated with others' lack of knowledge, there is an element of patient identity and naming that renders patients' attempts to gain information about their disease especially challenging. Of the 57 survey respondents answering the question, 55 had never heard of TTP prior to their diagnosis. Those who had heard of TTP learned of it through a previous misdiagnosis with ITP, and through work as a medical technician (see Figure 18).

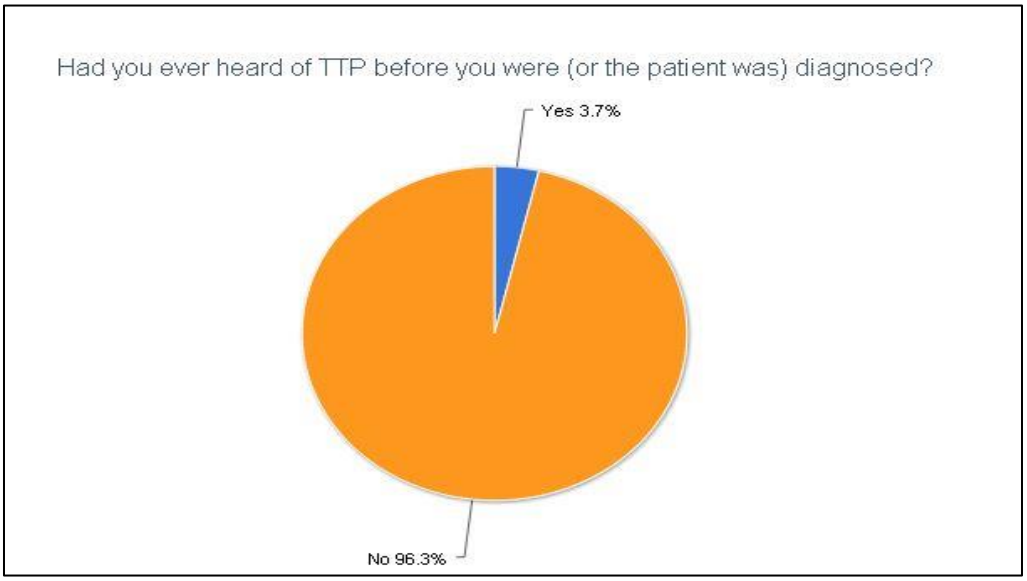


Figure 18 Familiarity with TTP prior to diagnosis

An additional complication reported by more than 80% of respondents is that they were in a coma or literally have no memory of their initial hospitalization and diagnosis.

Therefore, learning of TTP, frequently from family members after one has been in the hospital for weeks, could be considered a highly equivocal input, and seeking information about something with which you have no familiarity and have previously had zero exposure is especially challenging.

> The doctors, the first time they explain it to you, they use such big words. I told one doctor I said, "You know what? Whatever that word was, can you like chop that in about five pieces because I can't even digest the whole word, let alone I don't even know if I can digest in five pieces?" I said, "I'm in construction" and I said, "That's just not something I'm used to. You're talking in medical terms."

(Ron Elmore, Personal Interview, February 13, 2013)

Collins suggests (in a guest post on e-patients.net, 2012) that part of this difficulty has to do with the conventions that are used to name diseases. She offers two reasons that patients may have difficulty making sense of diseases, such as Thrombotic Thrombocytopenic Purpura, whose names are descriptive: 1) The names are difficult for the average person to spell or pronounce, posing complications when searching for or communicating with others about the disease; 2) The diseases are named when they are first discovered, but subsequent research often results in the identification of additional variables that had been missing from the initial characterization. This can lead to multiple names for the same disease, or similar yet distinct diseases being lumped together due to lack of understanding of the differences, as was demonstrated in Chapter 5.See, for example, this excerpt from a focus group held with three TTP patients, during which they

attempt to make sense of conflicting information regarding the relationship between ADAMTS13 and their condition, different names for TTP, and distinct illnesses:

Jennifer And that's not true for me for the ADAMTS13. I know what you're talking about, but because they—I was reading online where they called it Von Willebrand, they called it all of these different names and it's not. It's just TTP or it's ITP and actually they've pretty much combined ITP and TTP together.

Mary Jo Well, that's bull crap because ITP is not as severe as TTP.

J.A.D. Right.

Jennifer I know, that's what I said too.

Mary Jo That's bull crap and Jennifer, listen, I want to remember to say this because I want to respond to something you said about not responding to the plasmapheresis. I go to a conference in Columbus, Ohio twice a year, they do research there and what they discovered is people that have been diagnosed with TTP might have HUS. Now, have you ever heard of HUS?

Jennifer Yes, I've heard of HUS, okay.

Mary Jo Okay, now, most TTPers do not go into kidney failure. Now, I was in kidney failure.

Jennifer I was too.

Mary Jo You were too? Okay, now. I'm more convinced the more I read and the more education I get from Columbus that I actually had HUS, which does not respond as quick to plasmapheresis and they have a new drug out and I

	can't—I don't remember the name or how—I think it's… I'm trying to. But actually, it's a whole different treatment for HUS versus TTP remember and that's why you didn't respond the third relapse I think you said.
Jennifer	Right, the third relapse. The first two I responded quick.
Mary Jo	Yeah, now, because when I go to these conferences in Columbus and people—or if I read it on Facebook and people say, "Oh yeah, I was in and out of the hospital a week." I'm thinking, "Oh my gosh, well, how come they responded so quickly?" So I'm more apt to believe that and to write HUS in my medical chart now versus TTP.
Jennifer	It doesn't matter, either way, the doctors and the nurses still haven't heard of it. They still skip over that chapter.
Mary Jo	Yeah, yeah.

Note: Refer to clinical description of TTP in Chapter 1, "Clinical Information about TTP and Communication Implications" for context in interpreting this conversation

(Jennifer Butz, J.A.D., and Mary Jo Reynolds, Focus Group Discussion, January 14, 2013)

This very rich excerpt has been examined for its multiple themes. First, the attempts for making sense of treatment and continued health revolve tremendously around the identification of what the actual disease is. This problem is consistent across rare diseases, and is discussed in Field and Boat's (2010) analysis of the state of rare diseases and orphan products as an impediment to research since clinical definitions vary. Presented in Chapter 5, my own search led to numerous websites that direct visitors to

"other names for TTP", and include conditions that share similar characteristics, but are distinct diseases with unique treatment needs.

Turning to the discussion of TTP and HUS leads to an examination of agenda setting in the rare disease community. Interestingly, renal (or kidney) failure is one of the five items in the pentad that characterizes TTP. But Mary Jo is not alone in the assertion that renal failure is indicative of HUS, not TTP; in fact, she's in good company. When immersed in TTP communities, one hears of Dr. George very frequently. This seemingly larger than life specialist is regarded among TTPers (as some call themselves) as *the* expert on TTP. He, or his center in Oklahoma, were referenced eight times in the cross-sectional survey and in 84% of the interviews and focus groups. Dr. George refers to the disease as Thrombotic Thrombocytopenic Purpura-Hemolytic Uremic Syndrome (TTP-HUS). During a focus group discussion, two participants gasped audibly when another mentioned that she had met Dr. George at a conference. Similarly, Dr. Scully in the UK is highly regarded as knowledgeable about TTP during pregnancy. The presence of these physicians as somewhat mythical is an interesting observation that will be explored more fully below. Many patients reported that their own hematologists have consulted with Dr. George to confirm a treatment protocol. For some context on how i Dr. George's opinion factors into patients' treatments, refer to Figure 18 is a semantic overview generated from selected interviews, including two inductively identified codes (expert, celebrity/"best-known") and one *a priori* code (strategy).

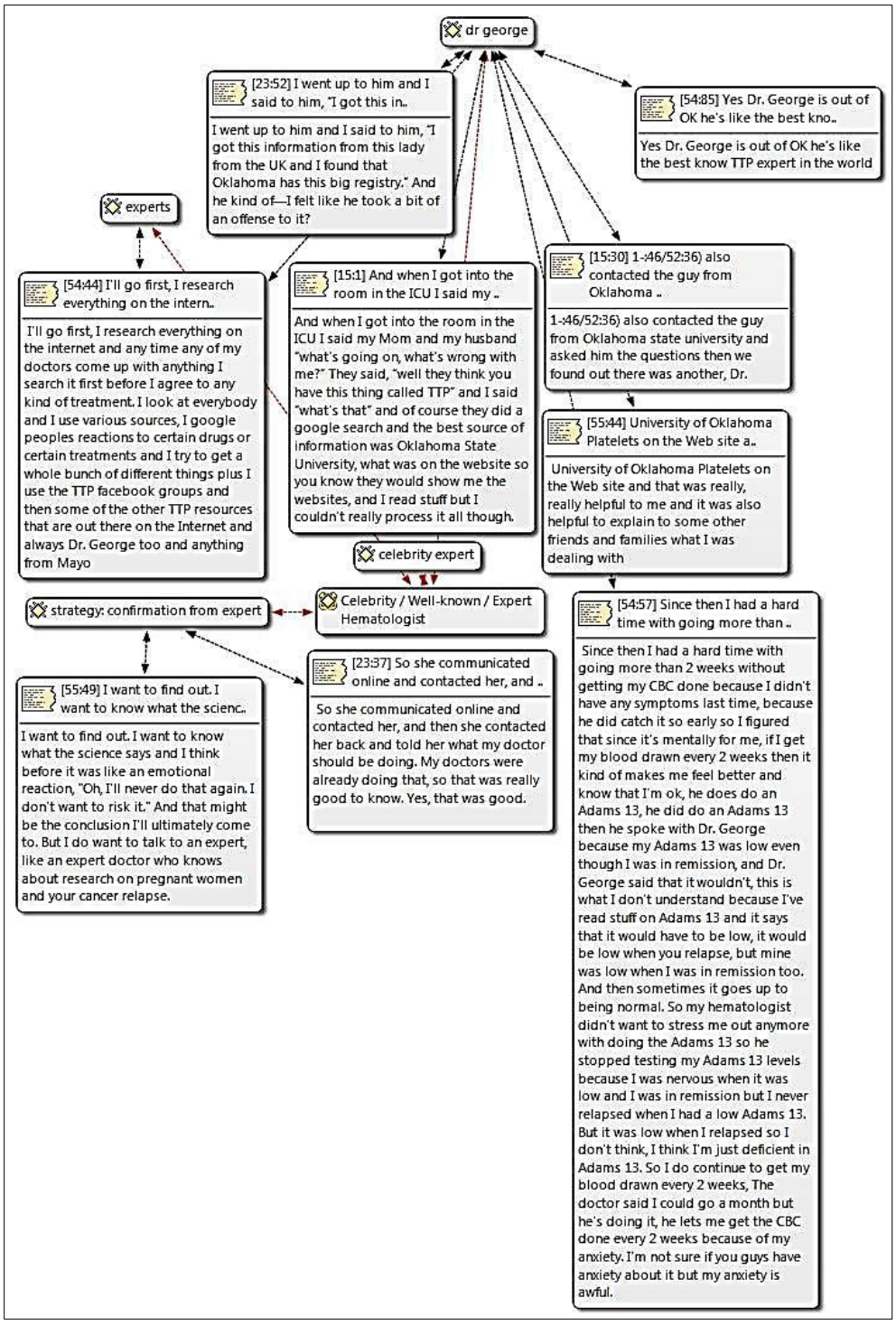


Figure 19 Semantic overview of "Celebrity Hematologist"

Survey results suggest that patients may be particularly eager to have a figurehead because of their relative lack of confidence in their own physicians. In addition to inconsistent information available online, respondents reported hearing very different information from different physicians. Rare disease patients are particularly apt to experience this challenge because of the range of physicians and specialists they have to see. It is not surprising that patients desire confirmation from an authority figure. More than a third of patients report that they are not confident that their doctor knows much about TTP (see Figure 20).

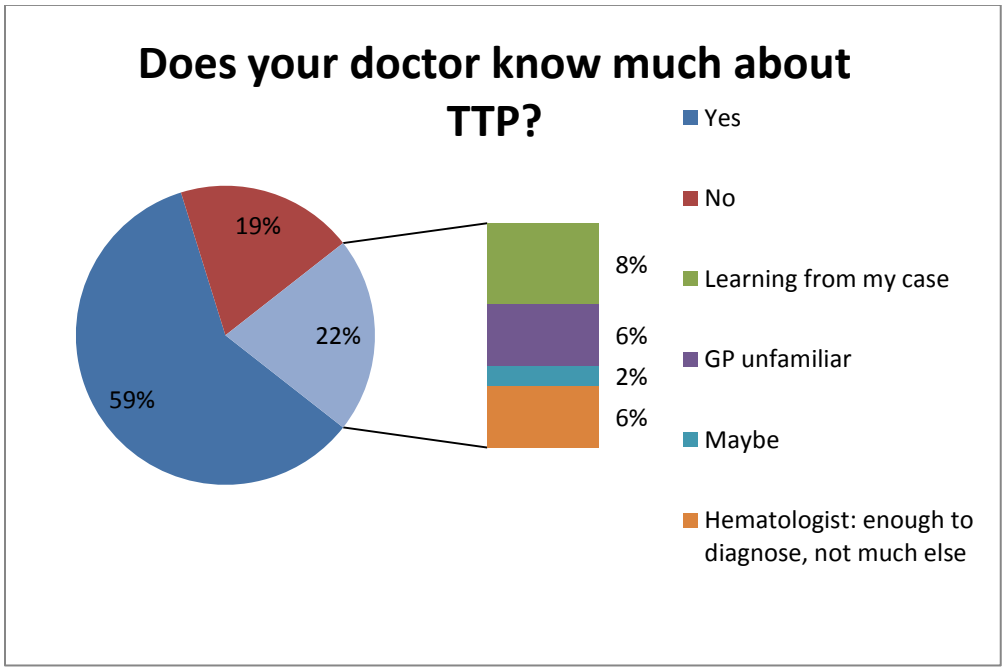


Figure 20 Patients' reported confidence in their doctors

The interconnectedness and ability for patients to learn from an expert and to disseminate this information to other patients as well as to their own doctors is demonstrative of the power of movements that are based in grassroots strategies. Recall from the review of the literature that the strength of grassroots communication is the use and reach of informal networks (Riano, 1994), which is especially true among communities who are disenfranchised in some way such that they are not easily accessible to one another. Notably, grassroots communication and technology can allow anyone to be a conversation leader, and eliminates the need for a centralized conversation held by a few empowered opinion leaders (Ruh, 2010).

While it is immensely encouraging that information is now available and can be shared, this is somewhat problematic in the context of scientific inquiry, where debate is central to the creation of knowledge. However, this debate is fundamentally at odds with patients' need to clear information and answers to provide a sense of certainty to help them make sense of their health. For mainstream diseases, a great deal of information is often available so scientific debates are further removed from patients' view. In contrast, there is so little information available concerning a given rare disease, patients conducting a search are likely to be inundated with conflicting information, which negatively impacts their assessment of its credibility. Therefore, the existence and accessibility of a figurehead who provides concrete information is attractive; respondents reported that the ability to reach out to *the* expert reduced their anxiety and guided the negotiation of treatment protocols. Through the grassroots strategy that is enabled through informal, peer-to-peer social networks, patients have access to an authority figure

who has an extremely deep repository of knowledge, which is a particularly strong and compelling example of the importance and utility of the retention state of Weick's model of organizing. However, the reliance on *one* authority figure based on popularity is also somewhat concerning in the context of the advancement of medical research, since consensus on the TTP/HUS issue has not yet been reached (Hosler, Cusumano, & Hutchins, 2003). Findings will constantly evolve toward more effective treatment and better understanding of the disease, provided the debate and inquiry continue.

Strategies. Many people with rare diseases and disorders report facing serious adversity when it comes to dealing with their health, and as a result, what is equivocal to them may be completely outside of the realm of possibility for a healthy person. According to Weick's model of organizing, these patients would develop strategies and rules to survive these high equivocality situations, and that is certainly something that emerges in conversations with TTP patients. Further to Weick's argument, patients develop these strategies over time, after they have had the opportunity to encounter similar challenges and to determine effective strategies for coping. One respondent reported that she had full faith in doctors' decisions, until she slipped into a coma after being given five times the recommended dose of a sedative upon being admitted to the hospital. She reports that at that point, her family began to seriously question the doctor's recommendations, began to educate themselves, and learned to advocate on her behalf.

> …that's when I went into a coma and I guess my, they had a knock-down, drag out on the floor of the thing. So like my husband said (laughs) my husband said if the

> window would have been open I would have thrown him out the window because he basically told them, hey, you put my wife in this coma, and he, the doctor came in, slammed the door, started yelling at my husband, and eventually the doctor got in major big trouble over it. (Interviewer: Oh, he did?) Yeah, he did, and the nurses came out with a total different attitude, anything, then, from that point on, before they did anything to me, they asked my dad and my husband... they should do that anyway, yeah, but you know, the only experience we had with the hospital was having, I had 2 kids at the hospital, that was it.

(Sondra Childs-Smith, Personal Interview, January 3, 2013)

Respondents report a fear being perceived as a hypochondriac, and patients are often treated as if they are overly fearful. Sondra's comment that her only other experiences at the hospital had been when she was having children is rhetorically meaningful. Childbirth represents something that is life-changing, painful, and highly equivocal to the individual; however, it is routine for the hospital staff; even in the general population it is not uncommon to poke fun at parents who act as though they are the first to ever give birth, downplaying the situational equivocality they are experiencing. If, as discussed in the review of the literature, the traditional biomedical model of medicine creates a division between physician as expert and patient as subject (Low & Schuiling, 2005), the situation for the rare disease patient is incredibly complicated. In these cases, hospitals and doctors are not necessarily repositories of knowledge, and the condition is not something that they see every day. The norm of physician/expert and patient/subject is interrupted, which could add additional

complexity and equivocality to doctor-patient communication; they are not only navigating symptom reporting, diagnosis, and negotiation of a treatment protocol, but are also stepping outside of established boundaries and creating new roles and norms. As Sondra points out, her previous experiences at the hospital had been ordinary, so she and her family understood that their role would be to rely on the doctor. However, the quick adaptation of her HSOs is consistent with Weick's contention that people learn from their interactions with equivocal inputs and store useful information to develop strategies that will be applied to future encounters in the future.

Another factor that leads to patients' reported fear of being labeled a hypochondriac may also be attributed to the biomedical model's lack of acknowledgement of the patient's role in their treatment, including the possibility that a patient may possess a more in-depth knowledge of their disease than the healthcare provider. One patient discusses how the fear of this label impacted her experience over time, including developing strategies to overcome this fear as she learned to advocate for herself over the six years following her diagnosis:

> It's like I want to know (my test results) now. I don't want know four to five days from now. And it each time it was, like, okay, you kind of look like a hypochondriac but I had to (have them immediately). (As a result of feeling judged) I wouldn't go (get the routine blood tests). But I just had to get through a (perception) thing – I'm not a hypochondriac. Sometimes I just need to know (my results) because I don't know how (the TTP) started. So when I ask, don't think I'm crazy. People in the office, they get all ugly with you and stuff because they

> think I’m just (overreacting). “Oh, boy, she’s just coming and telling she’s – there’s something wrong with her.” Whatever, and they don’t understand.

(Ginny Chambers, Focus Group Discussion, February 10, 2013

The experience mentioned above was not uncommon among the sample. Patients reported having to advocate to a great extent to even be allowed to speak with a doctor if they felt in danger of relapse. Even in cases where patients are able to discuss test results that are directly related to their TTP with a knowledgeable, trusted doctor, they frequently reported not being taken seriously or having their concerns dismissed:

> I rely on the complete blood count (CBC) checks that I get with the hematologist and I go every three to four months at this point. But unfortunately, I think my normal platelet count is on the low end of normal like I have always, since the remission, it's been always—the highest probably like a 100-190.
>
> And I went in last in December and I hadn't been in like almost five months because I'd been feeling really good and I went in and my count was like 158 and it sent me down to like paranoia basically. And I didn't even get to talk to the hematologist because I just went in for labs and when everything's in the normal range, they don't have a need to talk to you, but I called them and they called me back and said, "Yeah, there's nothing to worry about it. It's the normal range."
>
> And I explained, "Well I looked at all the other labs and this is 30 points lower than it's been and we know this (is a risk for me)," but yeah he said, "Nothing to

> worry about. Come back in three to four months." So I just had to sort of get over it...

(J.A.D., Focus Group Discussion, February 14, 2013)

The use of concrete numbers and statistics as a strategy was common among those interviewed. This presented both in the form of analyzing their blood counts and by presenting statistics and findings to their doctors. In fact, many respondents reported a sense of responsibility as a rare disease patient, because they could not expect even their hematologist to be very familiar with the disease. Several patients reported bringing findings to their doctors, some of whom embraced a more patient-centered approach and would then conduct research on their own to augment the work done by the patient. One patient reports merely viewing her doctor as a source of reassurance:

> My GP did not know, had never heard of TTP when I got it, she'd never heard of it. So she can't answer, she researched it but she doesn't, I can give her more information than she can give me. So, I'm not getting any information from her as to what I should be doing. So a lot of it I get from the support groups. She's reassuring more than anything, because I went recently because I was blowing blood out of my nose, so it's that reassurance that no, it's not coming back, you've just got a mild infection. Normally, before I was ill I wouldn't have bothered about blowing blood out of my nose in the mornings, but since I've been ill, you sort of think ah, that's not good, get it checked.

(Ann Holland, Personal Interview, January 3, 2013)

Due to treatment side effects, which will be presented in greater detail below, many patients reported having a compromised immune system. Therefore, the scenario discussed by Ann above was common among participants. A majority of respondents had at least one anecdote about becoming more vigilant about what would otherwise be minor illnesses and becoming more reliant on their doctors to assure them that any ache, pain, or fever was not the first sign of a relapse. While patients report developing this strategy of confirmation as a way to reduce anxiety, some patients note that when health providers do not share their sense of urgency, anxiety can increase:

> I do freak out often if I am sick and I can't get into the doctor relatively quickly. Again, it's sort of what I need to know and I want to know right now, again because I guess with most people, (TTP) kind of sneaks up on you and there's no real reason why it originally started.
>
> I think it's just the peace of mind. I want to rule out anything going funky other than me just having a cold and so that's sort of the way I've managed anxiety other than getting into idiosyncrasies of other anxiety-producing events. That's sort of how I manage the healthcare and the medical care of it related to the anxiety.

(Raphael Mazzone, Focus Group Discussion, February 10, 2013)

In addition to formal, empirically-grounded strategies, many respondents reported other strategies that they have developed in order to monitor their health and assess their risk of a relapse. Patients routinely reported checking for the symptoms that they now recognize were apparent during the time leading up to their diagnosis. For example, one

respondent whose TTP caused her to have a great deal of blood in her urine when it first presented estimates that she has checked her urine color almost 10,000 times in the five years since her diagnosis. Since bruising is often an indication of TTP, nearly 100% of respondents reported paying very close attention to bruises. Included in these strategies are rules – when a bruise reaches a certain size, or urine a specific color, these patients reported automatically going to the doctor to have their blood screened.

On the other hand, it is also important to recognize that some patients have developed strategies to reduce equivocality by taking a more avoidant approach. This is especially true of patients who are particularly troubled by anxiety, do not have a scientific background, or who cannot find clear, consistent information. One respondent who does not have access to the internet relies on her family and friends for information, but as a group, they report having largely disengaged from active searching because the information they found was so contradictory. The patient's sister and HSO reports that during the quest for information:

> I had to rely on the internet a lot and then when she did get out of the hospital and did see specialists, I felt like we were being treated like children, like we weren't being given full information all the time and like I just felt kind of patronized. But my worry is also maybe that they didn't have a lot of experience themselves with TTP. That was my concern and certainly with my sister's GP, who's a wonderful doctor, but I just don't think some doctors have enough knowledge. Because I sat in many appointments with her where he reassures her there was no—people

didn't go into remission with TTP and I found that very disturbing because I've heard people do.

So that was my experience but as far as getting information, it's really tough I find and I know you shouldn't rely on the internet all the time because information isn't always totally accurate. But there isn't really—you can't really go walk into a (bookstore) and find books on TTP. I mean, you can find lots about cancer and heart disease and that but it is hard to get information for a layman on TTP… I would find articles that have been written I guess by hospitals or medical journals, I did find those but I don't trust them because it's just—I don't trust—it's not those but I don't trust everything I see on the internet because you don't know who's written it and how valid it is. I mean, that's just the way I've always thought about the internet: you take everything with a grain of salt. Because people post things on the internet, right? So they might not always be totally accurate.

The internet cannot replace a professional to me, a medical professional. I think that's why I like what I found or heard about you (referring to this study). There is a Facebook support group so I looked there also because just by reading people's posts, I could kind of say, "Oh, yeah, that's right. That's what happened in here." So I could compare. 'Cause sometimes people post about what's happening to them. You can relate to better.

(Joan Arias, sister/HSO of Marian Sottenz, Focus Group Discussion, February 10, 2013)

Clearly, patients and HSOs engage in a multitude of strategies to reduce equivocality, which are complicated by limited information availability, inconsistent information, and, as demonstrated by Joan, conflicting values about whom to trust. The examples outlined above are particularly illustrative of the themes that emerged when participants discussed their strategies to gain information and reduce equivocality.

Patients recognize the multiple roles that information can play. In addition to active information seeking, there are a number of strategies that may be developed to manage uncertainty toward a preservation of health and sense of self. This is consistent with the underpinnings of UMT, which state that individuals encountering uncertainty take action that may "reduce, maintain, or increase uncertainty" (Hogan & Brashers, 2009, p.48).

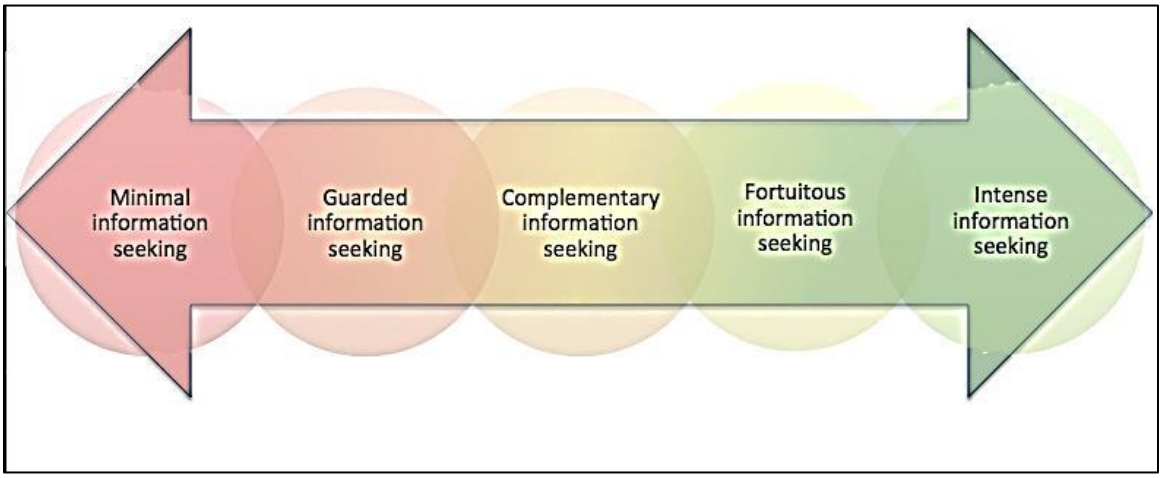


Figure 21 Information seeking behaviors characterized by Sairanen & Savolainen (2010) in the context of UMT

As in the example below, information avoidance, or selective information seeking, can be a very healthy decision provided one is not ignoring information that will help them to

make better health decisions. Further, individuals must weigh their ability to process information with regard to their mental health and psychological well-being when considering overall health.

> Right before I was about to have my spleen removed and I found where it said like eight out of ten people never have a relapse. That was encouraging to me, but at the same time, I also saw on Facebook where there were people that talked about they had their spleen removed, five or six years later, because they have another relapse and like she said, I don't want to read that anymore. It's like, "You know what, never mind." Never mind… I am not relying on somebody to tell me that they relapsed.

(Jennifer Butz, Focus Group Discussion, February 10, 2013)

In addition to the seeking and avoidance strategies illustrated throughout this section, certain behaviors were commonly reported by respondents that also fall under Weick's definition of rules and strategies that are established to maintain an acceptable level of equivocality to enable survival. These behaviors are representative of the full spectrum of information seeking illustrated in Figure 21. The breadth of reported behaviors illustrates the importance of understanding the complex and sometimes useful role of uncertainty, underscoring the value of the addition of UMT to an application of Weick's model of organizing to health communication for rare diseases. Seen in Table 6, strategies employed by participants encompass the full spectrum, and can range from scientific to idiosyncratic.

Strategy	Behavior
Carry paperwork when traveling to avoid the need to negotiate with ER staff	Intense information seeking and preparation
Learn scientific jargon to be taken seriously by physicians	Information seeking/preparation
Seek confirmation by expert (including contacting a leader in the field such as Dr. George or Dr. Scully)	Information seeking/ in some cases, active, in others fortuitous.
Draw circles around bruises to monitor their size and shape	Information seeking/ passive or routine
Draw circles around bruises to monitor their size and shape	Information seeking/ passive or routine
Check urine color routinely	Information seeking/ passive or routine
Check feet and extremities daily for bruising	Information seeking/ passive or routine
Pick scabs and monitor time until clotting	Passive information seeking/ fortuitous information seeking
Validating/confirm information with knowledgeable other (e.g. peer rare disease patient, doctor)	Fortuitous or complementary information seeking
Accept explanation offered that supports your goals	Complementary information seeking
Require doctors/providers to prove necessity/applicability of treatment before proceeding	Guarded information seeking
Avoid or block access to websites with negative stories if anxious	Information avoidance

Table 6 Reported actions and associated strategies and behaviors to manage uncertainty

Information gaps identified by patients. When questioned about their information needs, patients and HSOs reported that they needed access to clear, consistent information, but they especially appreciate hearing things from people who have had a similar experience. The utility of communities of peers is two-fold: participants may gain information from other patients, and experience a reduction in their feelings of isolation that result from the rareness of their disease. Further, as discussed in Chapter 2, community membership helps patients to identify and make sense of conflicting information, since consensus-building may occur and collective wisdom generates more knowledge and understanding than any single doctor (Fox, 2011).

> I would like to find more people who are aware of this, because as I've mentioned to you before the last interview that when the nurses-the nurses pretty much told me that they basically skipped over that chapter in the book because it's such a rare condition. But there's four people right here that have had it because you talked about your partner who has it and everybody else has it right here. It's not as rare as what they're saying it is. What I want to know is what is so common about it? What is the common factor that's in this so that we can figure out when people go for a physical what they need to be screened for beside just your platelet count is below 150,000? There's got to be more to it than that.
>
> I mean, they tried to say ADAMT12 (sic) that it was all of this other stuff. It's not necessarily the case for everybody, because apparently it sounds like that everybody was diagnosed TTP for different things, pretty much collectively the same symptoms, but not necessarily what happened before that.

> So I think it's not only online resources of more patients being out there advocating what TTP is or learning about TTP, I think it's also the doctors and the nurses also need to step up too so that they can at least talk about it and not say, "Oh, that's a rare condition. Don't even worry about that. You're not at a risk for that." We don't know who's at risk for it.

(Jennifer Butz, Focus Group Discussion, January 14, 2013)

Jennifer articulates something that many participants echoed, which is a feeling of insignificance or abandonment due to the low prevalence and associated interest in TTP. Several participants expressed that even though the disease was rare, they were still human beings deserving resources and research that would help to save or improve their lives. Many patients reported that they felt their treatment was largely guesswork. Survey responses validate those feelings. Therefore, one major limitation that patients identified was a lack of access to information about their illness, proposed and available treatments, and, importantly, side effects. The uncertainty brought on by the experimental feel of treatment, coupled with the need for quick action due TTP's high mortality rate, has the potential to create a highly equivocal situation. In Chapter 2, the somewhat standardized roll-out of treatments is discussed, which generally includes some combination of plasma exchange, corticosteroid treatment, chemotherapy, transfusions (red cell and platelet), and splenectomy (Furlan, et al, 1998). However, the survey respondents who answered this question (n=51) reported 37 unique treatments.

Participant Response (as entered into survey) (n=51)	Unique Treatment Codes (n=37)*
29 (plasma exchanges) Plasmapherisis 4 rounds of Rituximaub	Plasmapheresis
I had 7 treatments of plasma replacement.	Rituxin/Rituximab
I had several blood transfusions, plasmapheresis, and Rituxan	Blood transfusion
Plasma Apherisis, Rituxan and a Splenectomy.	Splenectomy
Plasma Exchange.	Plasma Exchange (less frequent than plasmapheresis, plasma is replaced as opposed to cleaned)
Plasma Transfusion	Dialysis
Plasma everyday for 2 weeks, blood transfusions, dyalisis 10 times.	Prednisone/steroids
Plasma exchanges, prednisone, blood	Vinchristine (less frequently used, for use in various chemotherapy regimens)
Plasmapheresis and rituximab, my doctors imformed of the necessary treatments.	Solumedrol/steroids
Plasmapheresis Rituxin Steroids My doctor told me about the treatments	Venofer Infusion (Iron treatment)
Plasmapheresis as well as rituximab and also vincristine	Whole blood transfusion
Plasmapheresis, steroids, Rituximab	WinRho (treatment for ITP)
Plasmapheresis...Solu-Medrol...Prednisone	Intravenous immunoglobulin
Plasmapheris and Rituxian	fresh frozen plasma
Plasmapherises Chemotherapy Dialysis Venofer Infusion	Cyclosporine (immunosuppressent drug)
Steriods and plasmaphoresis	Octaplas (pooled plasma blood product)
Whole blood. Plasma transfers daily Steroids (Prednasone) Rituxan (4 doses)	Cyclophosphamide (used to treat certain types of cancer)
WinRho, IVIG, Plasma Exchanges, Predinsone. All were learned from my hemo doc.	Aspirin
ffp cyclosporine octaplas Rituximab Cyclophosphamide asprin Heparin Nifedipine Metformin	Heparin (prevents clotting)
i only have a plasma exchange that all my doc told me	Nifedipine (calcium channel blocker used to treat high blood pressure)

i was given vinchistine, had plasma frezzazas then had mine spleen removed	Metformin (Type 2 diabetes treatment)
kidney dialysis, Fresh frozen plasma, 40 plasmapheresis treatments, blood transfusions,	None
None	Folic acid
plasma exchange, rituxin,steroids	Clexane injections (prevents clotting)
plasma pheresis, blood transfusions, 8 doses of rituxan.	mycophenalate motefil (immunosuppressant)
plasmapheresis, blood transfusions, spleenectomy, chemo just to name a few	ferrous gluconate (iron, to treat anemia)
plex, steroids, rituxin, dialysis Started while in coma	Benadryl
Plasma exchange, high dose steroids, folic acid, aspirin, clexane injections, mycophenalate motefil, ferrous gluconate, rituxamab, fittings of Hickman, femoral and jugular lines for administering treatment.	bendrofluazide (for treatment of hypertension)
Before diagnosis was on high dose 90 mg of prednisone daily to raise platelet count. I recieved donor platets prior to the emergency C-Section and continued prednisone post pregnancy and through plasmapheresis. My TTP episode was a total of 6 weeks and in that time i recieved 21 plasmapheresis treatments. I learned about treatments from Dr. George of the University of Oklahoma web page. Family members also did research and we learned of the use of Rituxan and spleenectomies as alternative adjunct therapies. While in remission i have done significant research on TTP by reading journal articles from blood, etc. I have also reasearched potential clinical trials and corresponded with an author and researcher at a Washington University hospital.	lisinopril (hypertension treatment)
My first occurance with TTP in 2008 was treated with steroids and blood tranfusions because they didn't know what it was. I was in and out of	propranolol (beta-blocker for hypertension, anxiety, and panic)

consciousness and barely survived (there was no plasma exchange). All of my other hospitalizations where treated with plasma exchange, I was hooked up with a CVC within 12 hours of being admitted and then the exchange starts no matter what time. They have nurses on call that do the exchanges. At the same time I was given steroids. Currently I'm taking another immunosuppressant called cyclosporin modified (Neoral).	
I had huge doses of prednisone, 200 mg daily. Also plasmaphaeresis which I wasnt familiar with. Kidney dialysis.	topiromate (anti-seizure)
I was in a coma when I arrived to the emergency room and had lost over 50% of my blood volume, every organ in my body was hemorrhaging (except for my brain!). I received a good number of blood transfusions. After my coma, they started me on plasma pheresis treatments through a central pic line surgically places into my jugular vein. I continued the plasma pheresis for about a month after that. While in telementry, I remember having to take liquid Benadryl in my iv due to a severe allergic reaction to morphine and I remember having to take prednisone for quite a while also.	amyltriptolene (anti-depressant)
Plasmapheresis was the only treatment specifically for the TTP. I also was on various oral medications as well, mainly steroids.	sodium valporate (treatment for epilepsy and a range of psychiatric conditions)
Blood transfusion when they thought I had ITP and I was started on a high dose of prednisone. When I was re-diagnosed with TTP, I had a catheter inserted into my groin and began plasmapheresis treatments. After a few days, my platelets were not going up as expected so I had my groin catheter pulled and received a chest catheter that was placed into my jugular. The first treatment was	Chemotherapy (un-named)

unsuccessful and I had to have it replaced the next day. After each treatment, heparin was placed into my catheter to keep it open.	
While as a patient in hospital for 3 months , everyday i was given 24 bags of plasma , and then i was given 12 bags of rituximab ,	Pregnancy termination
Plasma exchanges via sub-clavian line Dialysis Intravenous steriods and anti-biotics Due to the extreme nature of this condition I was made aware of the treatments as I was having them.	Iron tablets
plasma exchange, blood transfusion, steroids. Had 16 bags of plasma each day for 4 days and 4 units of blood. on steroids for 2 months. I trusted my doctor knew what was because. they had to give me the treatment aggressively to save my life.	Ecluzimab
plasma exchange: at the facility of ruby memorial hospital at wvu morgantown west virginia. 9 days of treatment 3-4 hrs a day.	
Plasmapheresis - 6 treatments before I started producing my own platelets. I also learned of other treatment off of the internet but the plasmapheresis is the treatment I've received.	
Revived 231 bags of plasma On was on up 28 med Plus got a blood clot in right lung from line change so had to self give blood thinner injection for 4 months	
I had over 100 plasma exchanges, sometimes double exchanges, blood transfusions, pregnancy termination, cyclosporin(neoral), Steroids, iron tablets, folic acid,heparin injections, Had a Double Hickman line inserted and removed, central line inserted and removed, Bendaflurozide, Lisonipril, for blood pressure, propanolol for blood pressure, antihistamine for reactions to	

plasma and various medication . Amyltriptolene, Topiromate, Sodium Valporate for Migraine control. Beta blockers for blood pressure	
Prednisone - familiar with preds from previous injuries. Rituxamab - Was told it was a relatively mild chemotherapy option and I have numerous rounds from my original month long stay in the hospital until later in 2009 as an outpatient at my hematologists offices. Vincristine - This was delivered in summer as the combo of Rituxan/Pred/Plasma was not managing the continued loss of platelets. This drug caused extreme fatigue and caused massive weight gain (upwards of 40lbs). Splenectomy - Performed in winter 2010. Plasmapheresis - Originally was mandated by my hospital physicians, starting at twice daily, expanding to three times a day, but eventually falling down on a graduated scale.	
I was immediately put on high dose predisilone steroids and was started on plasma exchanges after femeral line fitted whilst waitig for theatre space to have a permanent chest line (hickman Line) fitted. Had the plasma exchanges daily for the first 3 weeks along with blood transfusions. Also had bone marrow taken.	
plasama pheresis, plateletes transfusions, blood transfusions, and rutuxin- thankfully had a oncologist on my case who had treated others for TTP	
I had 5 days of plasmaperesis which worked for me. I had my platelets tested every day for about a week after that and then once every few months. I forgot to mention this earlier: As a child, when I as given asprin, I would frequently have nose bleeds. In 1997 I was at the Toronto	

General Hospital having surgery to remove a plexiform neuroma from my cranial nerves. I was given heparin. I had an allergic reaction to the heparin. I was told it was mobilization of the platelets.	
began with prednisone and plasmapheresis. then just plasmapheresis. I had that 59 times before finally it was put into remission with rituxan	
First treatments started with fresh frozen plasma, then on to Cryo-poor. After that stopped working after 5 months, my doctor did a splenectomy that put me in remission, the first time. The second and third remissions were treated with cryo-poor and Rituxan, which put me in remission much faster, 3 months.	
I have had MULTIPLE plasmapheresis treatments; when that didn't work, they used Rituxan on me when I relapsed in 2008. I was diagnosed in 2006 (in hospital for 10 days), relapsed in 2007 (in hospital for 8 days), relapsed in 2008 (in hospital for 38 days); about 5 months after I relapsed in 2008, I had my spleen removed and no more relapses since then.	
Plasma apheresis Blood transfusion Dialysis Rituximab Soliris (eculizumab) Plus more I don't remember names	
plama exchange (total of 148) and steroids...plus all the supplements (calcium, iron, folic acid, vitamin D)	
plasmapheresis, was the one of the treatments while hospitalized. Cyclosporine, prednisone. and Rituxim, chemotherapy. I learned from the doctors and nursed at the hospital.	

***Patient reports are taken directly from the survey in order to show the disparity of familiarity and range of treatments. Attempts have been made to identify duplicates, but it is possible that patients are using incorrect terms, for example, Fresh Frozen Plasma could be plasmapheresis, but because the distinction was made, the categories were retained.**

Table 7. Patient-reported treatments

As is evident from this list, treatment is largely catered to the symptoms of the patient and the interpretation of the physician. It should be noted that although several treatments have received Orphan Drug classification for TTP in recent years (Field & Boat, 2010) none were reflected in the reported treatments. A frequency analysis shows that while there are some treatments that are used with some consistency across cases (e.g. plasmapheresis and corticosteroids), an overwhelming 62% of the treatments identified were only reported to have been administered to one patient. When taken into consideration with other results, this important finding provides context to patients' feelings of isolation and inability to access consistent information. This may also contribute to patients' reported lack of confidence in their healthcare providers. Figure 21 below illustrates the frequency of each treatment identified by patients as reported in the cross-sectional surveys.

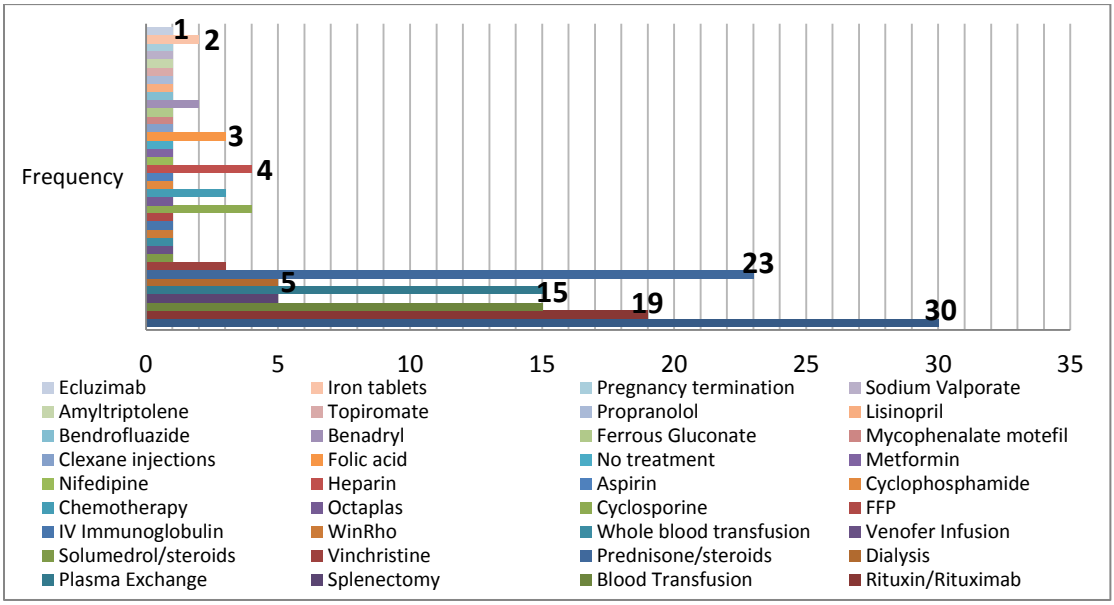


Figure 22 Distribution of treatments across survey sample (n = 51)

Patients also reported that insurance, cost, and convenience influenced the treatments that they were offered. For a particularly stark contrast, observe the role of splenectomy as understand by two patients during their interviews:

W:. My disease was raging, it was just, they could not arrest it, so they talked to me about the splenectomy. At this point of course, whatever they thought was best, I was going to do. I had the splenectomy, it didn't work and so they upped the steroids and upped the number of plasmapheresis treatments that I had and that began to help. That began to help and then they were really reluctant to try Rituximab because it's so expensive, but Rituxan is what got me to remission and that was the last thing that they tried, was the Rituxan. Interviewer: It's really interesting that they did the splenectomy before they did the chemo and the reason they did was the cost of the Rituxan? W: Yeah it was expensive and I can't remember if, I did have insurance, yes I did, because I've been treated without insurance too. But I did have insurance at that time, but it was so expensive and it was just like a last ditch effort, they really wanted to see if I could get along or get it under control without Rituxan and that just never happened.	R: The only time it (splenectomy) was ever, the only time that was ever brought up was when he first was telling me what I had and kind of the course of treatment they go through he mentioned the plasmapheresis and the Rituxan and then he said in absolute worst case scenario, you know he's treated I think 10 cases of TTP, and he said in the 10 cases he's only had to remove 1 individual spleen. That's basically the absolute last resort. That's the only time it was ever brought up for me, I still have mine. L: Okay. He actually did say that's the last resort? R: Yeah, he basically said if nothing, if absolutely nothing else works, then we'll have to look into doing that. That was the only time it was ever mentioned.
Wendy Stubblefield, Interview, February 2013	Rhiannon Stanfield , Focus Group Discussion, January 5, 2013

Table 8. Splenectomy Rhetoric

The current utility of online communities. My research did not expose any advocacy group or foundation specifically engaged with TTP. However, since recruitment was conducted via three unmoderated facebook groups for people with TTP, almost every participant in the case study was participating in some level of informal organizing around TTP. While it was not a goal of this study to attain an understanding of effective informal organization via online social networks, respondents were able to provide information about the way that they currently engage online that will be tremendously valuable in the development of a formal, official resource for people with TTP. Discussed above, through organizing, patients have been able to gain access to experts and peers, enabling a reduction of uncertainty, improved negotiation of treatment protocols, and access to similar stories. However, the greatest benefit to participation in the facebook communities consistently reported by participants was a feeling of validation, specifically with regard to side effects and complications. Notably, 22 of the 25 TTP patients interviewed reported significant mental health side effects, including feelings of isolation, alienation, and overwhelmingly, anxiety. Patients spoke about random panic attacks, feelings of panic and fear of reoccurrence or relapse, loss of interest in things they used to enjoy, memory loss, fatigue, and insomnia. All respondents who were receiving treatment for anxiety or depression got the medication from their GP or hematologist with the exception of one, who already had an established relationship with a psychiatrist. Patients were fairly divided on the rhetoric of mental health. Some initially bristled at the suggestion of psychological side effects, but would eventually disclose taking Xanax or Zoloft to calm their nerves. Frequently, these patients observed that the social element of

facebook enabled them to reduce their feelings of isolation and to feel less alone, crazy, or weird, which in turn had positive mental health outcomes.

Interestingly, when speaking of the benefits of the facebook group, a number of respondents contrasted TTP with cancer to express their frustration with the lack of awareness of their disease and the lack of resources available to explain it to others, in addition to a sense of wistfulness for the feeling of certainty that they associate with having a more ubiquitous disease. For example, respondents consistently spoke about encountering difficulty when trying to explain TTP to others, in contrast to more prevalent diseases for which many people already have a conceptual schema to provide at least basic understanding:

> See, what concerns me is I want to wear a T-shirt that says, "I Have TTP Brain, What is Your Problem?" I made a little picture up and put it on our Facebook page once, but see, how many people are really going to stop and say, "Oh, what's TTP?" Now, if people see cancer, brain aneurysm, diabetes, they all understand all that, but I don't know really how to get the information out there to take up the people's time to explain, I don't—and the more I would talk to people, the less I would say and get it more in a nutshell.

(Mary Jo Reynolds, Focus Group, February 10, 2013)

> It’s not like cancer, where ok we are going to start chemo and radiation and you know it’s not the same, I don’t think it is, anyway.

(Rhiannon Stanfield, Personal Interview, December 31, 2012)

The fact that TTP patients lack a framework to understand or explain their disease may be further complicated by some of the other side effects of TTP. In addition to the psychological side effects that are discussed above, certain neurological side effects are attributed to TTP in some scientific literature (Hosler, Cusumano, & Hutchins, 2003). To that end, 100% of patients interviewed spoke about memory problems and fuzziness following their TTP. Many describe something similar to anomic aphasia (Rohrer, et al., 2008), where they can see a word but cannot articulate it. Of those who have discussed these issues with their doctor, zero reported receiving an explanation. One respondent reported such neurological difficulty that he sought a referral for a full neurological evaluation, and because it was not "required", his out of pocket expense was over $1500, even with insurance. Another person reported that when they mentioned memory and speech issues, their hematologist laughed and said it was out of their league, but made no referral to an appropriate specialist and offered no suggestion about what possible steps to take. One respondent noted that their doctor had been concerned that there would be brain damage brought on by the strokes that accompanied TTP, but most reported that their doctors adamantly asserted that memory issues were unrelated to the TTP:

> But I mean, all of the (members of the TTP facebook group), (it's the) same thing with the memory and all that but none of the doctors told me that. You tell them that (you have memory issues related to your TTP), they pooh-poohed and said that was not, you know, that's not true but every single one of the (facebook group members) had that and they had that same frustration trying to explain to

> their doctors about this memory issue or this feeling, disconnected, things like that.

(Ginny Chambers, Personal Interview, February 10, 2013)

The confirmation of "TTP Brain", albeit informal, was reported as one major quality of life and self-efficacy improvement as a result of membership in an informal online social network. This particular side effect is not one that many patients had been warned of, and because their physicians have not been helpful, they report it as being particularly jarring and alienating. The overwhelming consensus was that facebook enabled access to others with similar experiences.

Peer support should not be viewed as the only outcome of an online community for people with a specific rare disease, but it is a very important component. J.A.D. offers a particularly eloquent description of her relationship with the facebook TTP groups throughout different stages of her diagnosis, treatment, and recovery:

> I didn't stumble on the facebook site until I was in remission, unfortunately. It would have been really helpful at the time when I got my diagnosis to be able to talk with somebody who had been through the same experience, so I think I really needed that. I had a really good family support system, but still, initially I didn't understand what was going on and what was happening and really understanding what the disease is about. I don't know that I still fully understand, but I didn't stumble across it probably till I'd been in remission for three months and I wish I had come across it sooner. But there were other sources of information I used. My

> husband and my mom, of course the first thing they did when I got to the ICU, I said, "Well, what is TTP?" and they said, "Oh, well, we were going to talk to you about that. We Googled it and we found some resources."

(J.A.D., Focus Group Discussion, January 10, 2013)

This example represents the way that a patient would use organization to make sense of the situation and to identify what, if any, rules or cycles exist to respond to the input. This is characteristic of the *enactment* phase of organizing, which is characterized by Kreps (2009) as the stage in which organization members assign meaning to information via a decoding process. In the case of a rare disease where even medical specialists are at a loss, the collective wisdom of an organized group of peers is extremely beneficial toward assessing the level of equivocality of the various information changes they are encountering.

However, as patients move through the phases of organizing and into *selection*, their information needs may change. Continuing with the example of J.A.D. above, she ultimately determined that her best strategy for navigating equivocality was by using empirical findings. As such, the utility of facebook is limited for J.A.D. during selection. She goes on to say:

> But now as (my daughter) gets older and you kind of have your experiences past and I haven't had a relapse, now like I'm kind of more inclined-I want to find out. I want to know what the science says (about the risks of TTP and pregnancy, since the initial TTP occurred during pregnancy) and I think before it was like an

emotional reaction, "Oh, I'll never do that again. I don't want to risk it." And that might be the conclusion I'll ultimately come to. But I do want to talk to an expert, like an expert doctor who knows about research on pregnant women and your relapse. I don't really look to facebook I think for that type of answers. I'm always curious when I see people posting stories that are similar to mine what their experience has been, but I also remind myself and I think we all should remind ourselves on facebook, it's not a clinical study, it's not scientific and I think my guess is that sometimes people who are on the site and posting, may have more experiences perhaps with relapse than perhaps been in remission longer.

(J.A.D., Focus Group Discussion, January 10, 2013)

Ultimately, high activity groups like those on facebook lead to the development of collective wisdom which is stored during *retention,* which reduces equivocality, even if subsequent situations are more complex or urgent than the initial episode. This is evident in this exchange between Mary Jo and J.A.D. during a focus group:

Mary Jo But you know with me, what I want to say to J.A.D. is, J.A.D., you're going to be your best advocate the next time around because you've been educated with this. So if you decide to have a child, you know what to expect and you will go to a specialist, you will go to someone that will have your back.

J.A.D. Yeah, I know this if it so happened again, pregnancy or not, I would be onerous to all the questions asked and I wouldn't put up with any bullshit from the doctors this time around.

(J.A.D., Mary Jo Reynolds, Focus Group Discussion, January 14, 2013)

Organizing, whether via formal or informal networks, has the potential to improve health outcomes by creating a common scale of equivocality. Kreps (2009) notes that for organizations to survive, members must process equivocality at a level that is consistent with the actual risk of the input being handled, or they risk fatal errors. This scale can translate to more efficient assessment during the enactment phase, the development and retention of personal strategies to assess one's health, and may reduce the likelihood that one will avoid information simply because it is inconsistent with their desire or perception. For example, when Ann was first diagnosed with TTP, she refused to acknowledge the gravity of her illness. She told her kidney specialist that this was "just a blip" and she'd be back on her feet in no time. It was important for Ann to take things seriously, since lifestyle changes such as quitting smoking, improving her diet, and taking a sabbatical from her job teaching young children to protect her compromised immune function, were necessitated; failure to act on these needs could have had adverse consequences. Eventually, after engaging with literature that had been prepared by other TTP survivors and joining online support groups, she has developed a set of indicators about which she remains vigilant, such as the size of bruises and the color of urine, which can be signs of relapse. Through the process of organizing, she has successfully made sense of inputs in the context of the disease, building on the experiences of others and applying the lessons to her own routine.

> I'm of the opinion if it does come back, if I'm that unfortunate that it does come back, at least now I'd know what to look out for and I will be in hospital 3 days sooner than I was last time, so hopefully I won't have the amount of damage that

> it did to my body, yeah, believe me I don't want it back, definitely planning on it not coming back

(Ann Holland, Focus Group Discussion, January 5, 2013)

An additional outcome of organizing, especially online, is the ability for a rich repository of knowledge to be developed and stored. This is what occurs during the *retention* phase of organizing, but it also happens quite literally in online communities. One of the most common themes that arose during interviews was that patients wished they understood *why*. Because information is not available about what causes idiopathic TTP, through organizing, patients share experiences and over time, patterns began to emerge. This process was described above with regard to the acknowledgement of psychological and neurological side effects, but participants in these communities identified other patterns, too. Almost all respondents reported experiencing an elevated level of stress leading up to their initial TTP episode. Some patients reportedly have developed subsequent strategies in an effort to moderate their anxiety regarding a relapse so that the stress will not actually cause a relapse. Unlike the genetic stigma discussed in chapter five, there is another type of stigma associated with TTP that is *acquired*. It is notable that all participants had acquired TTP, which has much more uncertain rhetoric and treatment protocols, has more auto-immune implications, and more variation in symptoms than congenital TTP. Many of these patients have no idea why they acquired TTP, whereas genetic predisposition at least offers a reason, and results in less uncertainty and fear about what else may inexplicably go wrong. A few patients reported fear of other diseases, or being interrogated about their sexual or drug use habits,

suggesting that they did something to acquire this disease. Peyvandi, Palla, & Lotta (2010) distinguish between acquired and idiopathic TTP, stating that acquired TTP is brought on by drug use, HIV, or other medical issues. However, they go on to say that they will use the terms interchangeably in their article; similarly, these terms are used inconsistently and interchangeably throughout the literature. Fortunately, most of this stigma is restricted to rhetoric within medical literature, but this is not always the case.

> I need people with a very good bedside manner that ask me questions that do not belittle me, you know, don't make me feel like this was my fault, don't make me feel like it's hopeless, you know, things like that. Even if you may think it's hopeless, to me, as a doctor, caretaker, medical provider – you're supposed to make your patients feel very comfortable and secure... for example, there is one doctor, actually she was a gynecologist – I'm single, I'm 35, I'm black, you know, but I'm not married so you know I was pregnant and she was asking all these questions that, I'm like wait a minute. They thought I had miscarried and she asked me did I want a tubal ligation. I don't have children. Why would you ask me that, you know, like questions like that. Just very condescending questions. She stereotyped me.

(CJ, Personal Interview, January 5, 2013)

Beyond this very specific stereotyping, the rhetoric surrounding the role of stress in TTP and other auto-immune diseases does implicate the patient to an extent. Some researchers call for compulsory inclusion of stress management as part of treatment, citing that

relapse may be caused by neuroendocrine hormones leading to immune dysregulation (Stojanovich & Marisavljevich, 2002).

> Our thoughts and feelings have a direct impact on our immune system. Loneliness is now recognized as the number one predictor of disease due to its immune suppressing action. Laughter and feelings of happiness, on the other hand, increase and enhance the actions of our immune cells. (Evenbetterhealth, 2013).

These characterizations seem to imply that patients possess an impractical aptitude to exert an extraordinary level of control over chemical reactions occurring within their bodies. Poor immune function is likened to not being able to protect oneself against rape (Edelson, 2003), evoking Sontag's arguments about metaphors of war, as well as the implication that patients may be responsible for their own demise in the event that they do not maintain a positive outlook (1989).

Despite this problematic rhetoric, arguments for managing stress as part of a multidimensional approach to treating auto-immune conditions are appropriate (McCray & Agarwal, 2011), especially considering the collective understanding that patients have negotiated as a result of their shared experiences. Furthermore, when participants discussed their anecdotal findings tying stress to relapse, this was frequently done with a sense of relief, perhaps stemming from increased self-efficacy due to the belief that they may be able to have some control over their bodies after all. Interestingly, Lazarus' application of transactional theory to the appraisal of stress and emotion is strikingly similar to Weick's model of organizing. Lazarus and Folkman (1984) state that individuals appraise an event in two stages: primary and secondary appraisal. In primary

appraisal, they determine whether the situation is stressful, or poses a potential for harm. (Matthieu & Ivanoff, 2006), which maps very closely to Weick's enactment, as well as the act portion of a double interact. Secondary appraisal involves the individual making a decision about whether they have the resources to cope with the situation, which is similar to Weick's selection, as well as the response portion of the double interact. Finally, if the situation is deemed stressful, an emotion will be generated and a person will (successfully or unsuccessfully) attempt to cope (Matthieu & Ivanoff, 2006). This corresponds with the adjustment part of Weick's double interact, whereby a strategy is created or selected. It is remarkable that this group, through informal, unmoderated organizing, has identified a pattern, leading to the development of a strategy to reduce stress and, potentially, improve health outcomes. It is particularly noteworthy that the process of developing a strategy to cope with stress on an individual level, mirrors so closely the interpersonal process of organizing in order to adapt, cope, and survive.

Informal social networking has obviously improved many aspects that affect the quality of life for most of the participants. However, results were limited to social support and information sharing. It is clear that advocacy and organizing on a larger scale will be required to enable more tangible improvements, such as improved diagnostics, increased research, and a more coordinated effort to understand this disease.

CHAPTER SEVEN: THEORY, CONTEXT, AND DISCUSSION OF PRACTICAL WAYS FORWARD

Summary

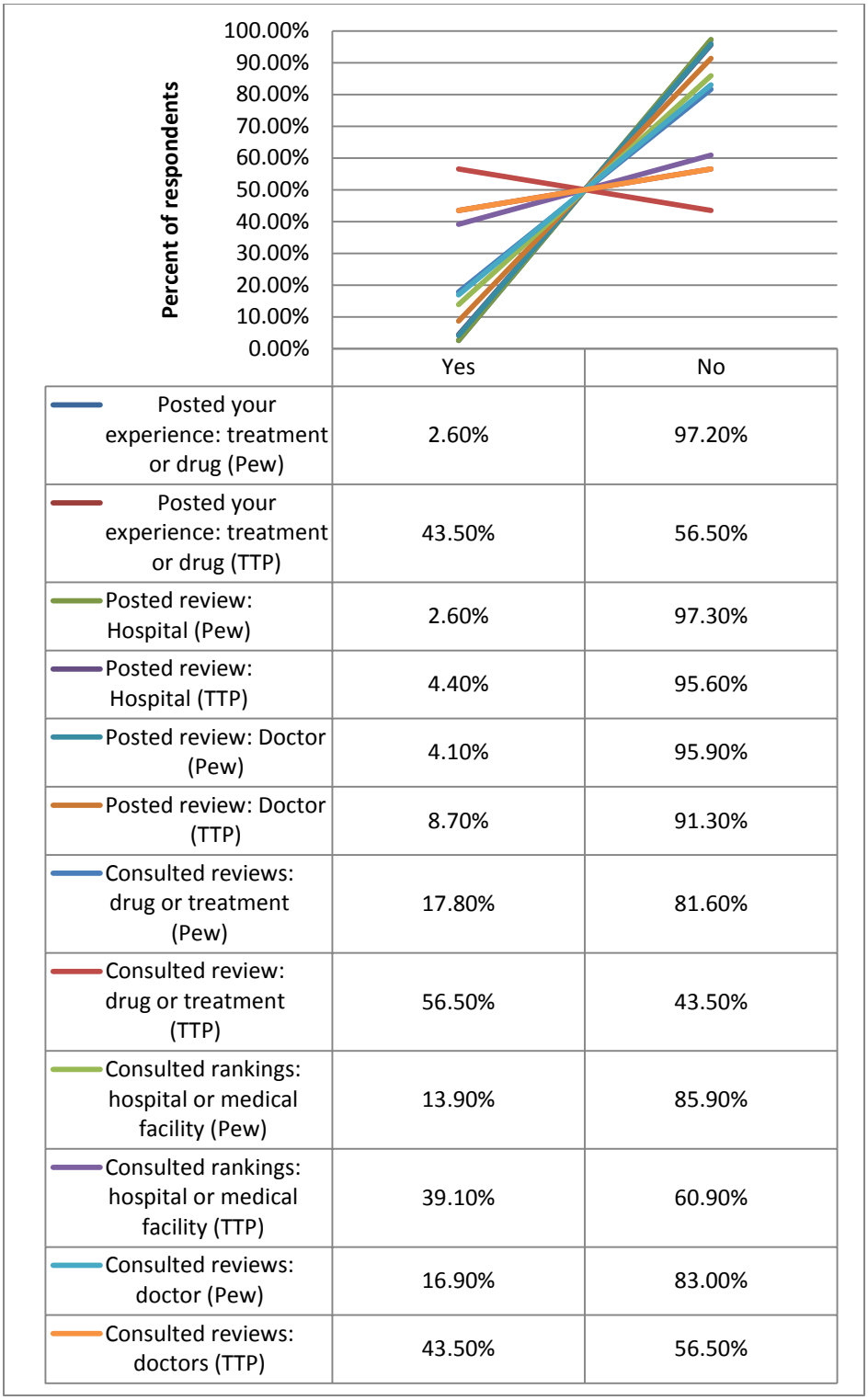
This study set out to explore rare disease communication, using Weick's model of organizing, supplemented by Uncertainty Management Theory, as a guiding framework. Through this analysis, valuable information was gained over and above the initial research questions. Due to the reach of mobile technology, rare disease patients have an opportunity to reach each other, to learn from one another, and to organize together. The two sub-sets of this study both have very promising elements, but neither is reaching its full potential. This discussion section will address overarching research questions, and then explore possibilities to leverage current resources toward a meaningful and useful solution.

In contrast to the low activity of the RareConnect.org boards, the activity on facebook was quite high. During the period of data collection (December 15 – March 30), the three groups had 74 posts with 281 responses (mean 3.7 responds), 75 posts and 559 responses (mean 7.5 responds), and 75 posts with 413 responses (mean 5.5 responds). Further, respondents reported that they frequently take conversations off of the public message board and into direct messages, so further interactions that cannot be seen are occurring. Contrast this with RareConnect.org's mean of 1.81 responds per post (which

was heavily influenced by a few outliers, whereas the distribution on facebook appeared to be more consistent).

As presented in the review of the literature, Fox (2011) found that rare disease patients are particularly active users of the internet for health information – more than half of rare disease patients turned to family and friends, as well as others with the same health condition online, compared to 13% and 5% of overall ePatients. A selection of questions in the online cross-sectional survey were drawn from the same survey Fox used in her sample of rare disease patients (sampling frame: NORD members) in 2011, and while her sample is substantially larger (n=2156 vs. n=57), the comparison offers some interesting insights. This comparison is presented in Figure 23.

When evaluating how rare disease patients use online information, it is worth noting that a norm of reciprocity is not strictly maintained, and people typically consume more than they provide; however, online interactions begin to look more like typical interpersonal interactions as a sense of community is built. It is also interesting to see that while Rare Disease patients are extremely active in their use of the internet for health information (Fox, 2011), the respondents from the TTP case study were much more active, by all accounts. Perhaps because of the extreme complexity of treatment for TTP, an exceptionally high proportion of TTP patients posted information about treatment compared to the Pew/NORD sample. These numbers are too low to be generalizable, however both samples are self-selected participants who have already engaged online, so they are more likely than the general population to participate in online activities. (Fox, 2011).



	Yes	No
Posted your experience: treatment or drug (Pew)	2.60%	97.20%
Posted your experience: treatment or drug (TTP)	43.50%	56.50%
Posted review: Hospital (Pew)	2.60%	97.30%
Posted review: Hospital (TTP)	4.40%	95.60%
Posted review: Doctor (Pew)	4.10%	95.90%
Posted review: Doctor (TTP)	8.70%	91.30%
Consulted reviews: drug or treatment (Pew)	17.80%	81.60%
Consulted review: drug or treatment (TTP)	56.50%	43.50%
Consulted rankings: hospital or medical facility (Pew)	13.90%	85.90%
Consulted rankings: hospital or medical facility (TTP)	39.10%	60.90%
Consulted reviews: doctor (Pew)	16.90%	83.00%
Consulted reviews: doctors (TTP)	43.50%	56.50%

Figure 23TTP Case Study Findings Compared with NORD/Pew Findings

Using online communities to reduce equivocality

When asked what they would like to see out of an online community, or what would really benefit them compared to what is available now, patients and HSOs offered several suggestions. One theme that arose consistently throughout the interviews, focus groups, and surveys was that many patients felt very lucky that a hematologist happened to be on duty to diagnose them. Patients report a strong sense that no one is familiar with their condition, and many said that they would have died if the doctor hadn't walked by when they did, or if they had gone to a different hospital. Therefore, several patients and HSOs suggested that any intervention also include a component that would sensitize medical professionals to the symptoms of TTP, and the potential severity. Patients reported their symptoms not being taken seriously, being sent home from urgent care, waiting for nearly 10 hours in the emergency room, and essentially treated as though they had the flu. Therefore, sensitization of the medical community must occur to increase the likelihood of fast and accurate diagnosis, and reduce the feelings of luck. While somewhat counterintuitive, at least 4 patients reported that because they were at a teaching hospital, their physician was more recently out of school and remembered TTP from their studies.

> I believe that if I would've gone to St. Lukes, I could've gone undiagnosed because there are very well-known doctors there on call and I just don't believe that I would had a brand spanking new doctor in her residency. And that was my saving grace.

(Terry Elmore, Focus Group, February 15, 2013)

This points to a definite need for physician and medical professional sensitization, which could be accomplished fairly easily using traditional health communication channels, such as flyers or posters in breakrooms.

Patients appreciate the social support component that is offered by facebook, but they overwhelmingly report taking what they read with a grain of salt, or approaching the information cautiously, because it is anecdotal and not tied to any scientific community. When asked what makes a website trustworthy, one HSO said that she looks at the web address and feels more confident if it is a .org or a .gov as opposed to a .com, since this affiliation adds credibility. Another mentioned that he would trust a website if it had some sort of endorsement by someone who was willing to put their name on it and to say, upfront, "I am telling the truth, this is where I am getting this information." This observation, in combination with the credibility findings cited in Chapter 6, are important considerations moving forward. This is consistent with findings reported by Dutta-Bergman (2004), specifically patients' desire for completeness of information and accessible language.

Because so many patients referenced Dr. George's website, "Platelets on the Web" (available: http://www.ouhsc.edu/platelets/ttp.html), a qualitative content analysis was conducted for themes and trends. This analysis was also consistent with the needs patients reported and Dutta-Bergman's findings. It is not difficult to see why patients are so drawn to writing. He clinically and scientifically describes TTP and other related disorders, has personal stories of patients', and maintains a registry in Oklahoma of all patients receiving plasma exchange for suspected TTP or HUS (Terrell, et al., 2005).

Clearly, one can gain substantial traction with patients by speaking to them about complex issues clearly, concretely, and in terms that are easily understood but avoid a condescending tone. Dr. George confidently asserts his findings and offers an explanation as discussed above, whereas much scientific literature uses a language of hypothesis testing, potential implications, and, often, presents alternate viewpoints. While the latter is representative of good scholarship, many respondents reported that it gave them a sense that no one knew what they were talking about.

Respondents mentioned that a key challenge is explaining their illness to friends and family, because unlike more well-known diseases, friends and family do not have a frame of reference for TTP. They hoped that an online resource could have dedicated sections for patients, HSOs, and friends and family, where higher-level information would be available, as well as more detailed, scientific information for interested parties. It was reported that what is currently lacking is something of a grey area – current offerings are limited to information that is either extremely complex and scientific, or inconsistent and unprofessional. While patients report very positive experiences on facebook, many said that they would prefer a dedicated TTP website, for both privacy reasons, and to have more comprehensive and trustworthy component.

Patients, and particularly HSOs, wish to gather as much information as possible so that they may educate themselves to better respond to a similar situation, should it arise in the future. The desire to organize is evident, particularly because of the constant fear of relapse and the constant questioning of *why* they *acquired* TTP. Many were very

grateful for the research that was being conducted. A particularly effusive and complimentary HSO noted:

> We as spouses, I just want to know peace of mind is that then okay, if it was E. coli bacteria and I can live with that and we can move on and we just have to be careful where we eat and how we handle food and that kind of stuff. But if they're a virus, that's a whole different thing. We all can contract it from just about anywhere and there's no way to avoid that other than take good care of our body. And we know cancer is kind of the same thing. If you have a weak area in your body, you can contract cancer.
>
> And so I think it all boils down to this, this knowledge is how do we take better care of ourselves and if something were to happen, which similarly we're all going to get sick from something, but where can we go to as patients to help ourselves out and the knowledge rather than being in the dark about stuff?
>
> And I think where Lindsay is going to me, is I think is a great avenue because I look forward for other people like going through what we've gone through and we may still go through this again we don't know because there's always a chance of relapse, the information available to us is invaluable when we're taking care of people that have gone through this disease. There's just a place of information to help I think in our quest of knowledge, and I think that's—I guess, my ultimate goal.

(Ron Elmore, Focus Group, February 15, 2013)

Toward a Practical Solution

During a review of the literature, several issues were identified that render the application of mainstream health communication to rare disease communication problematic, including intramarginalization, alienation, and the conflation of many different diseases into a composite entity. This study has confirmed that those are indeed major problems created by the approach that is embraced by rare disease advocacy organizations. Additionally, however, I suggest that a very simple fact is being overlooked by these organizations – the motivation of the users. As Ron noted above, he wants to know everything he possibly can about TTP to make sure it doesn't come back, or so he can be ready for it in the event that his wife does relapse. Patients' greatest concern was that they did not know what caused the TTP. Instead of relying on numbers to attract attention, a focus on the fact that this devastating disease could sneak up on anyone would be a powerful motivator, similarly to the strategy discussed by Pisani (2008) in which HIV finally received funding when the rhetoric shifted to entire, innocent populations who were at risk.

When asked how they learned about TTP, respondents reported searching primarily on the internet, beginning with search engines like Google or Bing, and less frequently, WebMD. Patients type in TTP, or the name of the disease to the best of their recollection. Not a single patient reported going online and searching for "rare diseases", but rather, they searched for their specific issue and navigated until they could make sense of the articles. Patients with a research background or a higher level of education

typically reported tackling scientific journal articles, whereas others were satisfied with taking information from the facebook group to their doctor.

When patients described what an ideal online resource would be, they mentioned: searchability – nearly everyone said that as soon as they could, they had a laptop at the hospital and started with Google. Effective rare disease communities should enable discussion that could be taken offline to a health professional, as facebook does, but also provide more concrete and sound information. Further, this would enable transactional flow of communication, whereby patients' collective knowledge would reach the experts, who may begin to act on these symptoms, instead of dismissing them, which is the current trend, and could enable **more** experts to take part in the conversation, instead of a handful of active figureheads. Finally, respondents mentioned that this type of community would help to mitigate some of the misinformation that is currently being circulated via facebook.

More than half of TTP patients surveyed reported that more than anything else, they went online to consult with others with their condition the last time they had a health issue – offline consultation with a health professional was a close second. This is important. Patients and HSOs are eager to organize, and this community has a great deal to learn from each other. Currently, they are limited by their platform and lack of visibility, in addition to the limited input from experts. Rare disease patients and HSOs turn to online communities to gain information and support from people with similar experiences. They desire to feel as if they are part of a community, and they lament feelings of alienation and isolation offline – from the medical community, from family,

friends, and others who do not understand their experiences, which include chronic pain, serious psychological side effects, and physical side effects. Many of the TTP patients interviewed reported that their anxiety increased substantially when they officially entered remission, both because of the constant fear of relapse and because they were no longer "patients". Many had been diagnosed with PTSD. This is something that is difficult for others to understand; respondents reported feelings of judgment friends and family who feel that they should be relieved and feel lucky to be alive. Some do! But these patients and former patients have dealt with substantial physical and emotional turmoil, and they are not uniformly relieved – many are fearful, and quite a few are very tired.

Fox (2011) cites a 2007 study of the Association of Cancer Online Resources, which found that the primary driver for community members was not social support, but rather, information. My findings disagree with that statement, if only because the distinction is impossible. Considering the feelings of alienation and the lack of available information, these categories are not mutually exclusive. The emotional support comes in the form of information exchange, since one of the biggest emotional problems cited by patients is a feeling of isolation. While some patients did rely on the facebook groups for information, many did not. However, emotional support via knowledge exchange was consistent across cases where patients relied on facebook for actionable information and to assist in a decision, as well as cases where participants primarily visited facebook to hear other stories, but not necessarily to learn from them.

Even more than other Rare Disease patients, TTP patients use the internet and rely on peers for health information. In the case study, there was a high representation of patients who were early in their diagnosis (and in the beginning processes of organizing), and patients who had already developed strategies for coping with TTP. This seemed to contradict Weick's premise of requisite variety, since those who were most comfortable with their disease and who possessed the most strategies were also among the most active. This also leads to an answer of a sub-question – who is not going online? Many respondents reported going online initially, and then turning away – they reported returning later, when they could better handle the information or were overwhelmed by isolation. Even the respondents who were furthest along in the process of organizing and possessed a repository of strategies and rules mentioned isolation. This, in addition to the reports mentioned above regarding an intensification of anxiety after being released from treatment, suggests that isolation is extremely prominent in the evaluation of equivocality. I suggest that it can be inferred that the isolation itself is one of the highest creators of equivocality among patients with a rare disease; Lazarus' appraisal theory helps to explain this, by suggesting that the interactions are actually a coping strategy, even if they are not interacting about an equivocal situation per se. Isolation is so equivocal and universal that it cannot be eliminated by a rule, but only managed by participating. As seen in Figure 24, more than half of TTP patients got support from other TTP patients, slightly outranking the amount that consulted a physician or other health professional.

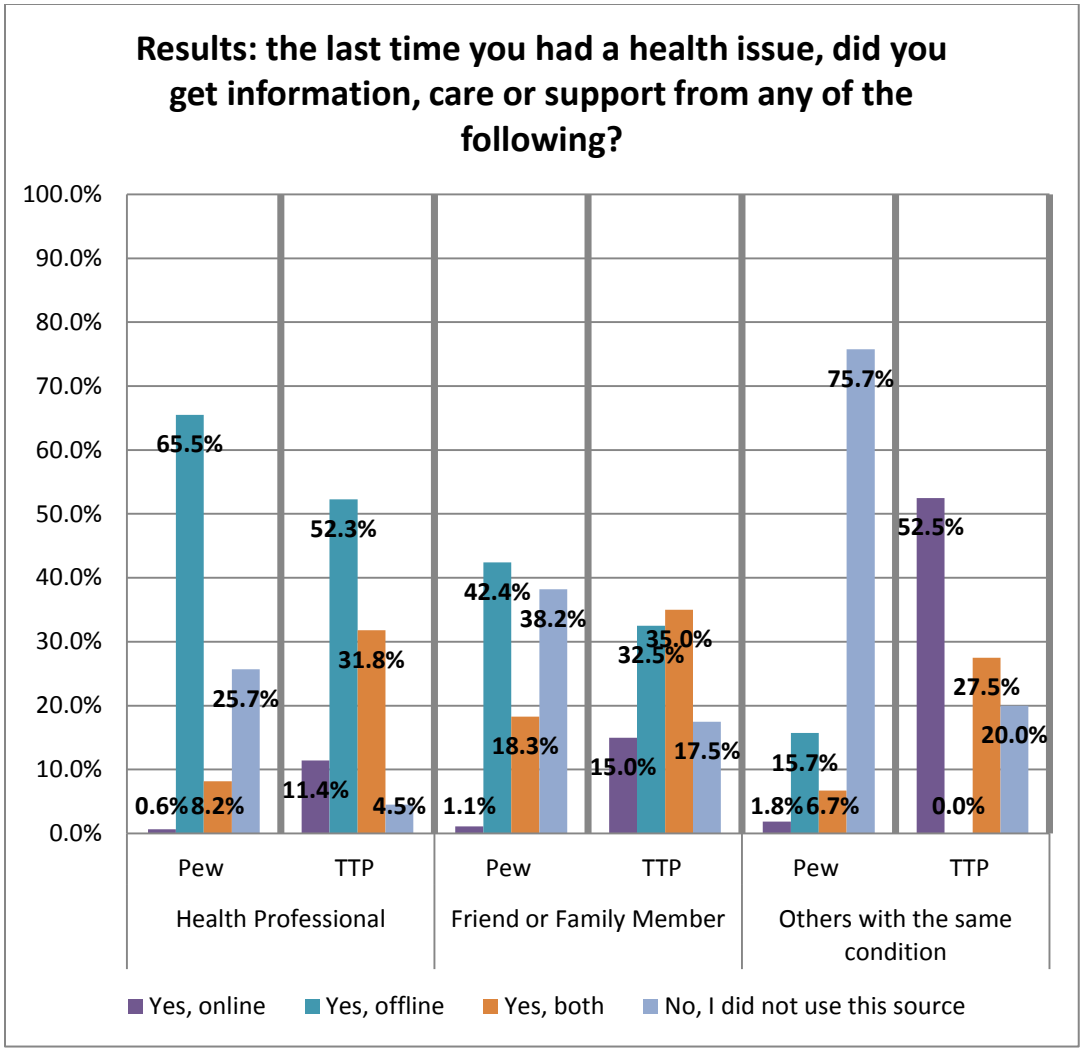


Figure 24 Comparison of results from Pew/NORD survey of rare disease patients and respondents for the TTP case study

Combining strengths. Kreps (2005) discusses the exciting opportunities presented by eHealth communication, especially the ability to tailor interventions to meet the needs of specific communities and reduce the effects of marginalization that are often experienced by members of communities with special needs. Chapter Four outlined many of the limitations of RareConnect.org stemming from a reliance on "best practices" for

health communication instead of health communication that is done well, including the strategic elements such as purposeful placement, optimization, message testing, and an interpersonal feel, that were identified in the literature review. The resulting lack of understanding of patient needs impedes the development of a community identity and norm of reciprocity, so activity is low. It seems that an application of good health communication principles to the resources that are currently available, such as NORD and other advocacy organizations, would lead to fruitful communities that would provide the benefits that patients report from the facebook groups, while leveraging capital and resources of large organizations. From the analysis of existing advocacy groups, it is known that well-heeled stakeholders are already heavily invested in providing resources for patients with rare diseases. However, the lack of formative research is hindering the utility of these endeavors. While they may fund research, the rarest of rare diseases are still marginalized, and patients' experiences are not improved – they are still being treated with repurposed technologies and medications:

Ginny	What do you call it? Rituxan. That's what's finally got it to turn around. Rituxan was not made for us—I met the guy that—actually met the guy that developed it.
Lindsay	Oh did you really?
Ginny	Yeah, in California. It was so cool. You know we were at a conference and we were going to Disneyworld or Disneyland or whatever. He had a shirt on and a hat with Rituxan. I said, "Do you work with the company that makes that?" He goes, "I'm one of the developers of it. You know we're having a conference here." And I ran up and gave the guy a hug. And I said, "Oh I'm sorry. I'm sorry. I said, "You

> saved my life." He goes, "Do you have cancer?" I said, "No, I had TTP." And he looked at me and stepped back and he went, "Oh my God." He goes, "You have no idea." And he started crying, because he was like, "We didn't make that for TTP. But we're hearing more and more people are being saved by using that drug and it wasn't made for that." He said, "And we're just so happy that it's happening that way."
>
> So then he gave me a hug because he was really happy. We exchanged names and things like that. But he was one of the developers of that drug. How cool was that? Yeah, I just thanked him for saving my life because I just thought he worked with it. It turns out he was one of the people that developed it. But, anyway, I forgot your question. I digressed.

(Ginny Chambers, Personal Interview, February 10, 2013)

Next Steps

The research questions that have been answered in this study provide an important understanding of what patients' needs are, how and when they consume information, and enabled an applied understanding of some of the unique challenges encountered by rare disease patients, many of whom are "recovered" and suffering more from side effects than from the initial illness. A patient-centered model, built and evaluated using the theorietical frameworks herein, would enable the community building, information sharing, isolation reduction, and development of strategies to enable effective coping, much like facebook. However, the scope of this community must not be limited to a discussion forum. Patients and HSOs desire a comprehensive destination where they may learn about treatment options, gain social support, engage with emerging findings with

the guidance of skilled health communicators to reduce the feelings of uncertainty that may arise in the face of a debate about new or potential findings, and where they may also organize to make their presence known and advocate collectively, enabling the reduction of the individual battles so many respondents reported fighting constantly, as a matter of course, due to the lack of understanding of their disease. One of the primary barriers to the success of RareConnect.org is the overabundance of a handful of moderators and the implicit lack of delineation between diseases, but that is not to say that an ideal community would not be moderated. In fact, the lack of moderation on facebook is one of the limitations to its credibility. Rather, moderators could be comprised of subject matter experts, health professionals, and (appropriately knowledgeable) survivors.

Although some formal support groups and meetings have developed in a few cases, most patients report major feelings of alienation offline, particularly isolation from the scientific and medical community. Participants were extremely grateful for my research, offering profuse thanks and negotiating continued involvement. However, a few also noted that my interest in their disease was motivated by personal experience with TTP, articulating their feelings of insignificance to the larger scientific community or the "outside" world.

It is clear that patients have a desire to organize, but the current model that is applied to rare disease communication is ineffective. Frydman (2009) states that patient-driven research is especially prevalent for rare and orphan diseases, due in large part to the lack of consideration given to the breadth of challenges imposed by a rare disease,

such as the requirments for funding by the OOPD that are practically impossible to meet in cases where diseases are extremely rare. As some particiapnts observed, this limits interested researchers to those who have a personal investment in the disease. This cannot change without intense advocacy by vocal and influential stakeholders.

To best meet the needs of patients and the reported goals of the rare disease advocacy organizations, I propose the development of a comprehensive social community that synthesizes the strengths of each formal and informal rare disease communities examined. Such a community should allow for purposeful linkages with the scientific community and relevant, powerful, stakeholder groups. Fortunately, the pharmaceutical industry and insurers have already bought into the idea that they must support rare diseases, but the model that they are following is ineffective. Results from this study demonstrate that top-down model used by advocacy organizations reduce user-loyalty, and result in the failure of these communities to attain their expressed goals.

Coupled with the benefits that stakeholders in the pharmaceutical and insurance industries could achieve by including patients more actively (discussed in Chapter 2), findings from this study make a compelling case for the redirection of investment to a patient-centered model that would result in greater return on investment for these stakeholders, as well as improved outcomes for patients. I suggest an approach that begins with patients and their identified needs, such as access to credible information and a social network of peers with similar experiences. This premise is critical, and enables a foundation for advocacy and material outcomes, such as improved treatment options,

appropriate assays, and dissemination of findings. These considerations should be the dominant driver behind the design of the community.

Conclusions and Limitations

This study provides a valuable model for public health research design that leverages grassroots mobilizing with more conventional advocacy strategies that are successful in the context of more prevalent diseases. The use of strategic communication principles and the development of communities prioritizing patient input are crucial to enabling successful rare disease communication. Current advocacy organizations must evaluate their current structures, which are based on mainstream models that marginalize patients. These findings point to a need to rethink the engagement of patients, and eventual applications will benefit people other than rare disease patients, including stakeholders, physicians, and otherwise healthy people who would like to seek health information online.

Future Research

This study illuminated many areas that will require further inquiry. Due to the sampling frames, limited information about information avoidance was able to be surmised. This should be explored in greater detail so that communication may also focus on the receiver (Neuhauser & Kreps, 2011). The myriad mental health difficulties expressed by respondents points to a definite need to understand and improve the treatment of **all** side effects of a disease, not just those with symptoms that are within the expertise of the primary specialist. The role of gender, caretaking, and auto-immunity

must be explored further; since TTP disproportionately affects women, HSOs consulted were exclusively male spouses. It would be interesting to learn of HSO desires when the HSOs are women or people occupying a role other than spouse. The most obvious need for further research will also be the most challenging: scientific inquiry toward more effective and targeted treatment and increased "consistent" information. However, by advocating for regulations that account for some of the restrictions of truly rare diseases, it would be possible to move toward this. In addition to what has already been discussed, numerous themes arose from this case study which will warrant future study. A few patients reported similar environmental factors that may lead to auto-immune diseases; this is something that I intend to explore further. Finally, all survey respondents were idiopathic acquired – none congenital. This says something about information seeking, rhetoric surrounding auto-immune diseases, and the influences of inconsistency in the rhetoric that merits some further exploration.

By understanding how patients are currently using resources to organize and cope with equivocal situations, we can move toward a model that encapsulates the needs of patients and HSOs, will be more cost effective for stakeholders, and ultimately enable improved material outcomes.

APPENDIX 1: CODER CONFIDENTIALITY FORM

Confidentiality Agreement

This study, "One in a Million: Navigating Health Information and Advocacy in Rare Disease Diagnosis and Treatment" (#8459), is being undertaken by Dr. Gary Kreps (faculty advisor) and Lindsay Hughes, MS (student researcher) (referred to hereafter as Principal Investigators) at George Mason University.

The study has several objectives:

1. To examine when and for what purpose patients (and HSOs) are most likely to use online communities focused on their specific rare disease?
2. To understand what are high equivocality situations for patients and HSOs engaged in rare disease communication?
3. To learn what patients and HSOs report as their information needs regarding online communities?

Data from this study will be used to increase understanding about how communication influences the creation and refinement of patient communities of advocacy in which information can be shared, accessed, and discussed. Findings from this study can be used to help enhance programs for communicating about rare diseases that can have positive influences throughout healthcare fields, including improved health outcomes, increased symptom reporting aiding in diagnostics and long-term disease management, increased efficiency in drug and treatment development, and patient empowerment.

I, _____, agree to:

1. Keep all the research information shared with me confidential by not discussing or sharing the research information in any form or format (e.g. disks, tapes, transcripts) with anyone other than the Principal Investigators and other Research Assistants;
2. Keep all research information in any form or format secure while it is in my possession;
3. Return all research information in any form or format to the Principal Investigators when I have completed the research tasks;
4. After consulting with the Principal Investigator(s), erase or destroy all research information in any form or format regarding this research project that is not returnable to the Principal Investigator(s) (e.g. information sorted on computer hard drive).

Research Assistant:

_____	_____	_____
(print name)	(signature)	(date)

Principal Investigator:

_____	_____	_____
(print name)	(signature)	(date)

If you have any questions or concerns about this study, please contact:
Lindsay Hughes
George Mason University
410.382.7306
lhughes5@gmu.edu

The faculty advisor is Dr. Gary Kreps at George Mason University, and he can be reached at 703.993.1094.

This study has been reviewed and approved by the Research Ethics Board at George Mason University. For questions regarding participants rights and ethical conduct of research, contact the George Mason University Office of Research Integrity and Assurance at 703.993.4121.

APPENDIX 2: CODER CHARACTERISTICS QUESTIONNAIRE

Thank you for helping me with my research. Now, please answer some very personal questions about yourself so that I can contextualize coding patterns.

If it's any consolation, responses are not tied to your name. However, I recognize that the sample is pretty small so please feel free to select "pass" on any question you don't want to answer - questions that don't have the "pass!" option, you can still skip. Please don't lie though!

In case you were wondering about how some of the questions may relate to this particular project - this is a survey that will be/has been administered to anyone involved in content or qualitative coding, so the questions are meant to gather a comprehensive picture of coder background to understand whether factors influence interpretation, and to establish the heterogeneity of the coders.

1. What is your coder ID? _____
2. What is your age?
   - Under 21
   - 21 – 25
   - 26 – 30
   - 31 – 40
   - 41 – 50
   - 51 – 60
   - 61 – 70
   - Older than 70
   - Pass!

3. What is your sex?
   - Male
   - Female
   - Intersex
   - Pass!

4. What is your gender? _____

5. Have you experienced a life event that you would consider to be exceptional or significant? No right or wrong answer, but something atypical that has shaped how you view things (i.e. you view them differently than before).
    Yes
    No
    Pass!

6. What is the highest level of education you've completed?
    Less than high school
    Some high school
    High school graduate
    Some college
    Associates degree
    Bachelor's degree
    Some graduate school
    Professional degree
    Master's degree
    Doctorate
    Multiple graduate degrees
    Pass!

7. What is the highest level of education either of your parents has completed?
    Less than high school
    Some high school
    High school graduate
    Some college
    Associates degree
    Bachelor's degree
    Some graduate school
    Professional degree
    Master's degree
    Doctorate
    Multiple graduate degrees
    Pass!

8. What is the highest level of education anyone in your immediate family has completed?
    Less than high school
    Some high school
    High school graduate
    Some college
    Associates degree
    Bachelor's degree
    Some graduate school

Professional degree
Master's degree
Doctorate
Multiple graduate degrees
Pass!

9. Turning to your youth, with whom did you grow up (please apply to your youth - from birth to age 11)?
   With biological parents
   With biological mother
   With biological mother and partner
   With biological father
   With biological father and partner
   Adopted by other family members
   Adopted by non-relatives
   Pass!
   Other (Please enter an 'other' value for this selection.)

10. Turning to your adolescence, with whom did you grow up (please apply to your adolescence - from age 12 - 18)?
    With biological parents
    With biological mother
    With biological mother and partner
    With biological father
    With biological father and partner
    Adopted by other family members
    Adopted by non-relatives
    Pass!
    Other (Please enter an 'other' value for this selection.)

11. What is your sexual orientation? _____
12. What is your race? _____
13. What is your ethnicity? (Ethnicity is the heritage(s) or culture(s) that you (or your family) identify with.) _____
14. How religious do you consider yourself?
    Sliding scale. Left: Min = 0 = Not at all religious Right: Max = 100 = Very religious

15. How religious do you think others who know you very well consider you?
    Sliding scale. Left: Min = 0 = Not at all religious Right: Max = 100 = Very religious

16. How religious do you think your friends consider you?

Sliding scale. Left: Min = 0 = Not at all religious Right: Max = 100 = Very religious

17. How religious do you think people who don't know you very well consider you?
    Sliding scale. Left: Min = 0 = Not at all religious Right: Max = 100 = Very religious

18. What is your religion? _____
19. When people talk about their problems, I think that it is:
    Slide the scale closer or further away from each word, depending on how much you agree with it.
    Programming note: participants see a column of words on the left and an unmarked slider to the right of each word. The slider has a minimum (left) value of 0 and a maximum value (right) of 100.

    Useful
    Weak
    Helpful
    Brave

20. Have you ever had a severe illness or chronic medical condition?
    Yes
    No
    Pass!

21. Do you have plans to continue your formal education?
    Yes
    No
    Considering it
    Pass!

22. Is prayer powerful?
    Yes
    No
    Other
    Pass!

23. Please elaborate if you choose: _____
24. Do you have experience with mental healthcare, therapy, or counseling?
    Yes
    No
    Pass!

25. How often do you use the internet?

Constantly – it's the first thing I look at in the morning and the last thing before bed.
Daily
A few times a week
Infrequently
Almost never
Pass!

26. How often do you use the internet – not including email?
    Constantly – it's the first thing I look at in the morning and the last thing before bed.
    Daily
    A few times a week
    Infrequently
    Almost never
    Pass!

27. How often do you use the internet – not including use for work or school?
    Constantly – it's the first thing I look at in the morning and the last thing before bed.
    Daily
    A few times a week
    Infrequently
    Almost never
    Pass!

28. Your politics: Please answer which questions you choose, however you choose.
    Politically involved? _____
    Politically informed? _____
    Fiscal Ideology (e.g. liberal, socialist, conservative (pre-1975), conservative (post-1980), libertarian): _____

    Social Ideology (see above for examples): _____

    Affiliated with a party? _____

APPENDIX 3: CONTENT ANALYSIS CODING INSTRUMENT

Data Dictionary/Coding Instructions

Not all of these questions will appear for you each time. Depending on your answers, some of these questions will not be asked, and they will automatically be entered into the database as NA.

1: What is your Coder ID?

You have been assigned a coder ID. Consult with Lindsay to confirm.

2: Which community is this thread a part of?

01. Multiple System Atrophy
02. Alternating Hemiplegia
03. Pulmonary Hypertension
04. Alkaptonuria (AKU)
05. Narcolepsy
06. Waldenstrom Macroglobulinemia
07. Mastocytosis and Mast Cell Activation Disorders
08. Evans Syndrome
09. Familial Mediterranean Fever
10. Coats Disease
11. CAPS
12. Neuroacanthocytosis
13. Ehlers-Danlos Syndrome
14. Alstrom Syndrome
15. Lipoprotein Lipase Deficiency
16. Atypical Hemolytic Uremic Syndrome
17. Multiple Myeloma
18. Cystinosis
19. DysNet
20. Rett Syndrome

21. Von Hippel-Lindau
22. Fibromuscular Dysplasia
23. Epidermolysis Bullosa
24. WHIM Syndrome
25. Moebius Syndrome
26. CDG
27. Hereditary Spastic Paraplegia
28. Glut1 DS
29. Dravet Syndrome
30. Trimethylaminuria
31. Paraneoplastic Neurological Syndrome
32. Behçet's Syndrome

3: Is this from an Overview or Detail screen?
On the first page of each screen packet, you'll see a letter followed by a two digit number. O_ _ or D_ _ handwritten in the upper right-hand corner. The O or the D indicates whether this is from an overview or a detail screen.

Detail = 01
Overview = 02

4: What is the screen ID?
The screen ID is the numerical part of the code described above.

5: What is the thread number?
The threads have been numbered for you. Count each thread sequentially, if it has a solid black dot bullet point next to it. The outline bullet points are responses within the thread. In some cases, a thread will be crossed out. This is because there were more responses than could be displayed on this webpage. Do not code the thread if it has been crossed out. It will be coded separately on a detail screen. Detail screens have only 1 thread. Overview screens usually have about 6 or 7.

6: Is the original post in English?
If the original post is not in English, you will be directed to the end of the survey. Because we cannot be sure of the quality of the translation, and this is communication, we will throw out these responses. (See further explanation at the end of this document.)

7: What is the purpose of the original post?
To the best of your ability, select what you think the purpose of the original post is. You can select more than one option.

1 = introduction or to join the community
2 = seek information or support
3 = advertise external event or resource
4 = venting or sharing (personal) news [so this would be something that occurred to the patient,
not results from a study]

5 = other information sharing
88 = other please enter what the other reason is

8: What is the identity of the original poster?

1 = patient
2 = patient's family member, friend, or significant other
3 = health care provider (doctor, nurse, they do not have to explicitly identify but if they seem to be posting from the perspective of a professional caregiver)
5 = advocate (someone who is a representative of an advocacy or fundraising organization, for example)
4 = moderator (they will usually identify themselves as a moderator in the post or fairly frequently throughout the screen. If you mistakenly code someone and later realize they were a moderator, you do not have to go back and correct this, but it would be good to skim through a screen or two before you begin a community to see if there are any moderators you should be aware of (there's a list of the one's I've found so far attached to the end of this document).

9: What is the gender of the OP? (Answer only if the OP explicitly says, their avatar is explicit, or their name is explicit. When in doubt, say unknown.)

10: Does the OP reference a patient (whether it's themselves, a friend, or a generic case having to do with a particular health problem)? *This question is trying to capture why the person is posting. Are they just randomly interested in this disease, or are they (or do they know) a patient. So, for example, "I have been having symptoms for 3 years now" would be referencing a patient – themselves. "Come to this awesome event" or "check out this study article link" would not).*

11: What is the age range of the patient referenced in the original post?
(These are purposely broad. There was too much variation in interpretation, because people rarely give exact ages. You should be able to interpret whether someone is talking about a child, an adult (which can include a young adult), and a senior (who would be identified because they'd have different needs than other adults. Otherwise, say unknown if you do not feel you have enough information to decide.)

1 = Child
2 = Adult
3 = Senior
44 = unknown
88 = other

12: How urgent is the original poster's tone? Think back to the video about how to conceptualize urgency. Stick to 1, 3, and 5 most of the time, and only use 2 and 4 if you really can't choose.

13: What words were used that made the OP seem urgent? If there were any words that made this seem urgent to you, record them here. Otherwise, leave it blank.

14: What was the theme of this post that made it seem urgent? If this post seemed urgent, briefly describe the theme of the post that made it seem urgent to you.

15: How uncertain is the original poster's tone?

16: Record words that the original poster used to indicate uncertainty? (e.g. this could include but is not limited to: scared, confused, concerned, terrified, 'don't know what to do')

17: Record the theme of the post that makes it seem uncertain? (e.g. this could include but is not limited to talking about conflicting reports from a doctor)

18: How complex is the issue conveyed in the original post?

19: Record words that the original poster used to indicate complexity.

20: Record the theme of the post that makes it seem complex

21: Including the original thread post, how many unique posts are there (so, the original thread post plus all of the responses to it. On an Overview page, this should be no more than 4. On detail pages, there can be quite a few).

22: Are mental health issues mentioned at any point, in either the OP or in responses? (This could include depression, anxiety, changes in mood, etc).

23: How is mental health discussed? (Please summarize in the text box).

24: Does anyone (either the OP or a respondent) mention seeing a mental health professional?

25: If a mental health professional is mentioned, what is the nature of the discussion (can select more than one response, or select other and fill in the blank)

1= wants to seek therapy
2 = does not want to seek therapy
3 = does not need to seek therapy because other physician is prescribing psych. medication
4 = skeptical
5 = other _____

From here on, you're just counting for a little while.

26: How many responses are there under the original thread post? (Do not count the original thread post)

27: How many responses under the original thread post are by a moderator (identified as a RareConnect.org staff member within their post, username, or as indicated during training)?

28: How many responses under the original thread post are by the original poster?

29: How many responses were reassurances, agreements, or something motivational or calming?

30: How many responses were asking for clarification?

31: How many responses asked general questions?

32: How many responses offered specific recommendations (including medical recommendations)

33: How many responses offered medical recommendations?

34: How many responses offered solutions or answered the OP's question?

35: If applicable, what response number(s) suggest a solution?

36: How many responses include a link to or reference scientific findings?

37: If applicable, what response number(s) reference or link to scientific findings?

38: How many responses include anecdotal evidence or evidence derived from personal experience?

39: If applicable, what response number(s) reference anecdotal evidence?

40: Including the original thread post, how many unique posts are there?

41: Were there other notable types of responses? Insert description and frequency.

42: Does a statement indicating a rule, strategy, or system to address a problem appear at any point in the thread?

43: If yes, who first raised the rule, strategy, or system?
1 = Original poster
2 = Respondent (aka anyone other than the original poster, unless it's a moderator)
3 = moderator

How can I tell if the post was originally in English and why aren't other languages included?

If the original post isn't in English, we're throwing it out. I don't know who this third-party service is, but I want to make sure we're not missing nuance. This is less of a concern in the responses, because we are interested in the type of post that elicitsa lot of responses. We're less interested in the content of the responses themselves.So if a post other than the original post was translated, that's fine, keep it. But when you answer that the post was not originally written in English, you will be redirected to the end of the survey.

raquelr-pg | Episodes, General Information | published 8 months ago | Originally written in Spanish **IRENE STARTED READING.**

About 2 or 3 years ago, the attacks overwhelmed our family everyday. The attacks occurred so often and lasted so long that there were very few moments of normalcy in our home.
The despair became almost unbearable; I thought I was going insane.
The days, months and years went by and the girl did not get better at all. I never imagined a moment of peace would come. I went so far as to think all that suffering would kill me.

But regardless of the terrible moments, you hang in there and get the strength out of thin air, because your child is everything to you, and there is no greater or purer love than the love a parent feels for his/her child.

Finally, some decisions were made in my household. They were hard decisions, surely, but they were key to Irene's improvement. These decisions, hard to understand maybe, meant a few fight between my husband and I, since each of us lives and sees the disease from a different perspective, although we are together every day.
I suppose we are not all prepared in the same degree to understand and, more importantly, face the disease. I guess it depends heavily on each one's personality, on whether you're an optimistic or pessimistic person and on the experiences you've had in your life. The decisions we took were not taking Irene out of the house under any circumstance.
This way, she stopped going to school, to the park, shopping... and we also stopped turning the TV on in the house.

I must clarify that both going out and watching TV have always had a negative effect on Irene. Both of these caused her excitement and meant several attacks that would last up to 15 days, with just 4 or 5 days of calm in between.
Irene has gone from having 152 days of paralysis in 2010 to just 16 days in 2011.
This is allowing her to learn quite a few things.
Although she had had to become a leftie, she is now able to write almost all the letters in the alphabet, and also some numbers, and she's beginning to read her first words.
I recommend that you use several methods, the Dolman and Syllabic methods work best for me.
I am afraid of her suddenly getting worse like she used to, I am terrified of it, but I am trying to enjoy this time because it is wonderful, and I see that my little girl is very, very happy.
All the best to everyone!!!
Raquel (Show less)

Notice: This text content has been translated automatically by a third-party service.

Moderators:

Anyone who identifies as working for NORD, EURORDIS, being a "community manager", or a moderator should be coded as a mod. If you realize someone is a moderator after you have submitted the code for a thread, do not submit a duplicate thread to correct this as this will result in duplicate answers. It might be a good idea, however, to skim through the first few pages of a "screen packet" to see if there are any moderators in addition to those I have listed here.

robpleticha

I think he is the main moderator. He's from EURORDIS and he's in every community.

AllieFreitas

She is Rob's NORD counterpart. I think she's a bit newer, so you'll see her a little bit less than Rob but more than others.

patricia

She identifies herself as a "community manager". She works for NORD, so she counts as a moderator.

Sometimes they have that moderator tag under their name, so that's obviously helpful. This is Marcus and he is a moderator.

Rob got a new picture when he got the moderator tag. Unfortunately, these tags were being rolled out just as screens were being captured, so you will see them infrequently.

“English language moderator”

Toyre – moderator

I have only seen Niko once, and I believe he was one of the original moderators before there were actual moderators.

Monica – MODERATOR

Constance - MODERATOR

Karend - MODERATOR

RDC-team - MODERATOR

(I’ve only seen her in FMF, so if you see a faceless Nancy elsewhere, make sure it’s NancyS before you code her as a mod).

Paul P - MODERATOR

APPENDIX 4: TTP RECRUITMENT SURVEY INSTRUMENT

Programming note:
Every question should have an open text box with no character limit.

Introduction

I am a PhD candidate studying Health Communication at George Mason University, and I am collecting information for my doctoral dissertation. I am interested in how people with rare diseases and their loved ones access information, and I hope to learn about your personal experience learning about TTP. I first learned about TTP and the role of communication in understanding one's health through my significant other, who was diagnosed with idiopathic TTP in 2008. The answers that you provide will be included in my dissertation, which is being written with the goal of designing online communities where people can access the health information that they want and that will be useful to them.

The survey consists of 14 questions. I am especially interested in your personal stories, so please feel free to make your answers as long as you like. There is no need to answer all the questions – please skip to the questions that are most interesting or important to you. At the end of the survey, you will be asked if you are willing to participate in a one-on-one interview with me, a focus group discussion with other TTP patients and their loved ones, or both. There is no requirement to do so, but these conversations will build on your survey responses and we will have the opportunity to get some more detail on your opinions and experiences to apply them to a solution. These interviews and focus group discussions would also take place online or over the phone. If you only want to participate in an interview and/or focus group and prefer to skip the survey, that's fine too. Please just leave the survey blank and skip to Question 14.

The answers that you provide will be confidential. After each question, you will be invited to explain or expand on your views in the text box, or to provide feedback on the question. If you provide your name at the start or end of this elaboration, I will be able to give you credit for the answer – please do take credit if you desire!

If you have questions about the survey, or if you'd like to send us additional input later, please contact Lindsay Hughes at lhughes5 (at) gmu.edu.

1 Are you the patient? If not, what is your relationship to the patient?
a. I'm the patient

I'm the patient's…
b.Parent
c. Spouse/partner
d. Child
e. Sibling
f. Other family member
g. Friend
h. Other

2 When were you diagnosed with TTP?

3 How long did it take you or your loved one to get a diagnosis?
a. Within 1 year
b. 1-3 years
c. 3-5 years
d. 5+ years
e. Other

Please explain further if you would like:

4 If you wish, please tell us how you found out about this condition. Was the diagnosis process difficult? What did you learn that you would share with someone facing a similar situation?

5 Had you ever heard of TTP before you (or your loved one) were diagnosed?
a. Yes
b. No

6 What treatments have you (or your loved one) undergone?
If you would like, please give us some information about your search for treatments. Has it been pretty easy or pretty difficult? And how about the treatments themselves? How are they going? How did you learn about these treatments? Where did you get information about the treatments?

7 Do you think your doctor knows very much about TTP?
a. Yes
b. No

Please explain further if you would like:

8 Have you used the internet to find specialists?
a. Yes
b. No

So others might benefit from your experience, please list any websites or resources you have used to look specialists:

9 Have you participated in any of the following activities online? [Respondent will see a grid]

a. Consulted online rankings or reviews online of doctors or other providers
b. Consulted online rankings or reviews online of hospitals or other medical facilities
c. Consulted online reviews online of particular drugs or medical treatments
d. Posted a review online of a doctor
e. Posted a review online of a hospital
f. Posted your experiences with a particular drug or medical treatment online

1 Yes
2 No

What other online activities do you find useful? Please share anything that comes to mind (and remember, please sign your name if you would like credit):

10 Thinking about the last time you had a health issue, did you get information, care or support from any of the following? If so, please tell us if you interacted with them ONLINE through the internet or email, OFFLINE by visiting them in person or talking on the phone, or BOTH online and offline? [Respondent will see a grid]

A doctor or other health care professional
Friends and family
Others who have the same health condition

1 Yes, online
2 Yes, offline
3 Yes, both online and offline
4 No, did not use this source

Please explain further if you would like:

11 Overall, who do you think is more helpful when you need each of the following kinds of information or advice – health professionals like doctors and nurses, OR other sources, such as fellow patients, friends and family? [Respondent will see a grid]

a. An accurate medical diagnosis

b. Emotional support in dealing with a health issue
c. Practical advice for coping with day-to-day health situations
d. Information about alternative treatments
e. Information about prescription drugs
f. A quick remedy for an everyday health issue
g. A recommendation for a doctor or specialist
h. A recommendation for a hospital or other medical facility

1. Professional sources
2. Other sources
3. Both equally

I am especially interested in any stories you can tell related to this question. Please share your experiences and insights (and remember, please sign your name if you would like credit):

12 Have you or your loved one been helped by following medical advice or health information found on the internet?
1 Yes, major help
2 Yes, moderate help
3 Yes, minor help
4 No

If a particular story comes to mind that you haven't written about already, please share it here:

13 What else can you tell me about yourself that would help to understand your experience?

14 Many thanks! Just one more question: Would you be willing to participate in a one-on-one interview with the researcher over the phone or online? Would you be willing to participate in an online focus group discussion with other TTP patients and their loved ones? Would you be willing to have me contact you solely for follow-up questions about your answers? If so, please check the box next to each of these that you are willing to do and tell me your name and the best way to contact you in the text box (e-mail, phone, etc.).

APPENDIX 5: IN-DEPTH INTERVIEW SCHEDULE

Sample script:

Opening: I'd like to begin by thanking you for agreeing to participate. The goal of this interview is to get your perspective on the process that someone goes through when trying to find information about TTP.

I am a PhD candidate in Health Communication at George Mason University. This research is for my doctoral dissertation, and my goal is to gather in-depth information about communication and rare diseases from the perspective of you, the consumer. This information will lead to an intervention to improve access to information and support for people with rare diseases in a way that would actually be useful. Since a goal of the intervention is to enable self-advocacy of patients, I hope that it will also lead to increased drug and treatment development for rare diseases, better and more evenly applied screening tools, and ultimately improved health outcomes. My partner has TTP, and he has told me about his process while trying to learn about his disease and some of the side effects of treatment and what that will mean for the rest of his life. I have similar experiences from my own quest for information about this disease and its affects on a loved one.

I cannot offer you financial compensation for participating in this study, but you should know that your contribution will certainly be very important in helping other TTP patients and their loved ones, along with others who have rare diseases like TTP. Depending on your preference, I'd like to acknowledge your contribution by name. You can choose whether or not any answers are tied to your name, and if you'd rather not be acknowledged, or acknowledged by a pseudonym, please just let me know. I suspect that this interview will take between 30 minutes and an hour. If you become tired and you want to stop the interview, that is fine; we can always revisit it later. If there is something that you do not want to talk, please just tell me if you'd like to move on or return to the item later. Are you comfortable with the timing? Do you have any scheduling constraints that I should be aware of, in case our conversation runs long? Do you have any questions for me before we get started?

Transition: Let's begin by making sure I have all of your background information right.

Topic – Demography (general and disease) [*5-20 minutes*]

Where do you live? *(can be specific or give region and proximity to a major city) Confirm information from Survey Questions 1 (role), 2 (time of diagnosis), and 6 (treatments) if provided. If not provided, ask specifically.*

How old are you? (*if HSO or anyone other than patient, also ask patient's age*)

Transition: Now I want to move specifically to talking about how you looked for information. Before we do, is there anything you think I should know about your basic background information that you didn't provide on the survey or that I didn't just ask?

Topic – Information Seeking [10-30 minutes]

Follow up on stories about looking for information provided from survey as necessary/appropriate.

You mentioned that you were diagnosed _____ years ago. Have there been certain points in the last _____ years that you found yourself looking for information more than at other times? When? Why? What events did this correspond with? Where did you look and with whom did you interact as you sought information?

Have you experienced similar events since? Did you go through a similar process as the first experience? Did you develop any strategies for dealing with these events?

Turn to Survey Questions 8 (specialists) and 9 (online activities grid) if available. If not, ask about online activities and prompt if they don't mention one or more of the activities in grid. For each used, what was good or bad about it? What did you like and what do you wish had been different?

Transition: Now that we've discussed your experiences with looking for information, I'd like to spend the rest of our time talking about your ideal scenario as far as finding information and how you'd use a community – even if that community doesn't exist currently.

Topic – Personal Opinions on Information Availability [10 minutes]

How would you like to use online resources to interact with TTP? What would you want a TTP community to include? Is there anything you would <u>not</u> want it to include or to be kept separate from other parts? (*inform from Survey Question 11 and any narrative provided. Possible probes would be community building, learning, referrals, advocacy, etc.*)

Transition: We have covered all of the questions that I had hoped to. Let's spend a few minutes wrapping up.

Closing:
First, I'd like to make sure I understood everything correctly. In your ideal world, you'd use online resources in the following ways: _____. You've previously used: _____ in the _____ years following your diagnosis/the diagnosis of your (role).
Thank you so much for taking the time to discuss this with me. Is there anything that you think would be useful to me to know that we haven't discussed?

At this point, I have some of your medical history and your opinions about what exists currently and what you would like to see. I will be interviewing other people like you, and the next step of my process is to hold online focus group discussions with folks where they can speak with each other about what possible interventions would look like. Is this something you would be willing to do?

One last question: I think I have a clear understanding of everything, but in case I have any follow up questions on what we've discussed today, would it be okay for me to get in touch with you? What is the best way to get in touch? Can I credit you? How would you like to be cited?

Please feel free to follow up with me if you have any questions via email at lhughes5@gmu.edu.

APPENDIX 6: FOCUS GROUP GUIDE

Sample script:

Opening: I'd like to begin by thanking you for agreeing to participate. The goal of this discussion is to generate some ideas about improving access to health information and communities for people with rare diseases. The discussion will take place for an hour, and I will tell everyone when we are coming close to the end of our time.

I have spoken with all of you before and we have discussed your experiences with TTP and the various information-seeking processes you've encountered. I've also shared with you that I am a PhD candidate in Health Communication at George Mason University, and I became interested in rare disease communication because of my partner who has TTP.

This is the part of my research where I will develop actual ways to address the problems and limitations that we've all been talking about. Since a goal of the intervention is to enable self-advocacy of patients, I hope that it will also lead to increased drug and treatment development for rare diseases, better and more evenly applied screening tools, and ultimately improved health outcomes.

What you say is confidential. I will be recording this discussion and taking notes. I will ask you all to introduce yourselves momentarily, but you can feel free to use a pseudonym to allow for your privacy. If this is the case, we have agreed to a pseudonym during your in-depth interview, so please use that to refer to yourself. I hope to acknowledge everyone's contribution (but I will only tie specific comments to your name with your permission). If you are comfortable with this, please use your real name.

Please speak to each other, not to me. I will start the conversation with a question, but after this initial question, I will only jump in to get clarification, direct the conversation back on track should it go off-topic, or to raise an issue that we have not covered. Please feel free to disagree with each other or to offer alternate opinions. I am interested in your experiences and your opinions, and more ideas will give me more to work with.

Are there any questions before we begin?

Ask each to introduce self by name/pseudonym and to give role and brief background (e.g. patient/HSO, diagnosed X years ago, currently in treatment or not.)

Opening Question - I would like you to talk about how you would want to use online resources to get information and interact with other TTP patients or anyone else who may be knowledgeable about TTP.

Topics to cover:
Community (online and in person)
Advocacy (government, policy, FDA, advocate for tests with doctor, insurance)
Referrals
Current resources
What's good?
What's bad?
What's missing?
How would this be laid out or accessed?
How would you spread the word or find out about what's available?

When 10 minutes are remaining, give a warning and focus on any priority area. Close after 1 hour.

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