

## **Psychological Effects of Carcinoid Disease: A study for carcinoid Patients and their Caregivers**

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First, I'll give you some background on how I began to study Carcinoid. Then I'll provide you with our major hypotheses, methods, results, and I will talk about levels of coping with depression, predictors of depression and unique aspects of the carcinoid experience. Actually, that is where Dr. Smith will take over because qualitative research is her area of expertise. I will then talk about implications and hopefully have time for questions at the end if everybody is not too tired.

The question of why a psychologist would be interested in chronic physical illness often comes up, and I have a long history in this area. I don't have carcinoid disease myself, but I am primarily interested in it from a scholarly perspective and also from a personal interest in connections between the mind and the body and in better understanding the ways in which psychological factors and disease factors interact. I have been spending the past eight years of my faculty position exploring those issues primarily in pediatric patients. Then Rick came in.

I was doing work in pediatrics at Oregon Health Sciences University in the Department of Pediatric Hematology/Oncology, and Rick Peterson, who is from Manzanita, Oregon, a beautiful town on the Coast, contacted my university asking whether anyone had ever heard of carcinoid disease. At first I thought it was a joke, so I kept reading and he said it was a rare disorder that is kind of like cancer and nobody seems to have done psychological research on it. He said it is a very complicated disorder and perhaps someone would be interested. Always looking for new challenges, I decided that I would meet with Rick. I actually preferred to go to the coast from where I am, but he was kind enough to come and meet me. We put together some ideas, and I thought we'd do a pilot study that would have 20 or 30 subjects in it just to get things going, and we ended up getting more like 300 people participating. To me it was very clear that there is a need. There is a lot of information that needs to be disseminated, and today I will talk about some of the primary findings from this study.

I have been working in psychosocial aspects of chronic illness in my faculty position for eight years following my graduate training. I have also been working on several NIH funded longitudinal studies on family adjustment to pediatric cancer, primarily leukemia. I have been examining the effects of steroids, specifically the neurocognitive effects, as well as behavioral effects of steroid medications.

The foci of this study involving carcinoid patients and caregivers were on psychological distress and coping. I want to relate this work to research on adjustment of other cancer patients, primarily so I can get this published. To me the work is only important if people will read it, so my goal was try to tie this in to what has already been done with other cancer patient groups, but also to examine unique aspects of carcinoid experience. That is why I invited Dr. Smith to work with me because her area of expertise is in qualitative work. Through this work, I hope to identify areas of further research and intervention needs.

Prior psychological research on adjustment in cancer patients has examined psychological

dimensions and distress. What we like to do as psychologists is try to predict who is going to be at highest risk for psychological distress and this is important for a number of reasons. We look at things like individual psychological and physical factors. For example, does cancer severity relate to greater psychological distress? If you examine the available psychological literature, you will find a very weak relationship between cancer severity and mood outcomes. But when we look at psychological factors such as level of optimism, coping strategies, availability of social support, we find those factors have much stronger correlations to depression and other kinds of distress outcomes than some of the physical variables.

Our goal is also to identify who may be at high risk for adverse psychological outcomes so that we may target interventions to appropriate groups. Today I will be discussing depression, although we examined many psychological outcomes.

It is hard to define depression when working with cancer patient populations or with any chronic illness population because of the obvious overlap between fatigue and depressive kinds of symptoms. Also, there are the effects of the disease process itself. How we tease these factors apart can be especially challenging, and I will talk a little bit about how we are trying to do that better.

Another reason that I am particularly interested in depression in cancer patients is a study that I recently read, which was a survival analysis of patients who have been treated in the VA system over the past forty years. We have depression measures that are scored by points; for example, a person may obtain a score of 10 points versus 11 points vs 12 points and so on. For each one point increase that an individual obtained on the depression measure, meaning they were more depressed, it was found that their survival decreased by one year or more. So, it can be concluded that depressive symptoms are related to survival. What causes what? That remains to be established -- give me twenty-five years and maybe I'll be able to tell you.

Depression is the most common psychological symptom in cancer patients and according to the literature, the rates range from 4.5 percent to 50 plus percent of patients. That is a very wide range, and it varies from study to study different reasons. Estimates vary widely depending on where the cancer is located. Head and neck cancer patients have the highest rate of depressive symptoms, as do liver and pancreatic cancer patients. It depends also on when cancer patients are assessed. If we are assessing patients who are in the terminal stages of a disease we tend to find a higher rate of depression. It depends on the type of assessment we use, and it depends on who we ask.

If we take 100 patients, for example, and they have all been identified with depression through a variety of measures and we ask nurses to identify which of those patients they think are distressed, the nurses typically are in about the 50% accuracy range. If we ask physicians, their accuracy ranges from 13 to 28% when asked to identify patients who have elevated depressive or distress symptoms. These rates make sense to me because physicians and nurses are looking for different things, and not always necessarily psychological distress. Towards the end I will give a few key questions that health care providers can ask in a very short amount of time to assess for depression.

There seems to be an assumption that cancer patients should be depressed and therefore it may be assumed that there's no reason to do anything about it. But if we look at information relating depression, the course of disease, and survival, it is important to do something about it. From a psychologist's perspective, cancer patients are given very serious information, and in many cases, there are few opportunities to follow-up on how their quality of life has been impacted. In addition, patients often speak of the lack of professional support they perceive as necessary to get them through what is obviously a very difficult period.

There have been two prior studies on carcinoid patients and Monica Warner also brought me a dissertation that came from a researcher in Sweden. Both studies I found came out of Sweden, and they had have small samples, but there were very interesting findings in those studies. The researchers found that carcinoid patients' depression rates were elevated compared to typical populations. They also correlated depression with a number of biochemical markers, and the correlation between depression and chromogranin-A was significant.

In my study, I looked at the following. First, what was the duration of symptoms and other diagnoses

prior to the carcinoid diagnosis. Next, I examined depression and coping in patients and caregivers, and I wanted to identify physical and psychological predictors of distress. I wondered whether a longer duration of symptoms prior to diagnosis would be associated with greater levels of depression. If you have been through what for some carcinoid patients describe as a traumatic experience, that is, years of aversive symptoms without being adequately diagnosed, I hypothesized that it would lead to higher rates of mood disturbance.

I also looked at the number of overall current symptoms and specific symptom type and coping as predictors of depression. We hoped to identify the unique aspects of the carcinoid experience using qualitative assessment and Suzanne will present that. Our method involved using a series of on-line self-report questionnaires. Thank you to the Carcinoid Cancer Foundation and also to Susan Anderson who posted announcements on the websites.

We included both carcinoid patients and caregivers because carcinoid affects more than one person. It affects the whole family. We used widely known quantitative measures. Today I will be presenting information from the Hospital Depression Scales. We also used the Cope Scale, which is used in all kinds of settings. We also used a measure of optimism. We used a measure of anxiety and we had another depression measure which I don't have time to present today. We had some tailored qualitative measures. The people who participated were fairly well educated. We had an under-representation of men and ethnic minorities. Lots of people were married which is typical for folks in this age group, who were an average of 52 years old. Average duration of diagnosis was 5.9 years. There is a remarkable similarity between patients and caregivers; 226 patients, 77 caregivers. What is interesting is that these folks were not related. I did have a question on the survey asking, "Are you related to somebody who is responding to this questionnaire," which has some bearing on results.

In terms of question #1 -- what was the duration of symptoms and other diagnoses prior to the carcinoid diagnosis -- I am so glad that my talk came after Dr. Kvols' because there is an interesting outcome. The average symptom duration pre-diagnosis, as reported by these 226 patients and 77 caregivers, were remarkably similar to the figures Dr. Kvols presented this morning. It scares me a little bit. I asked Dr. Kvols where he had gotten the information he presented, and whether it had been published. He provided me with references from 1961, reported again in 1987. Things have not changed very much in the forty year time period which I find unfortunate. As long as we keep working in this area and trying to get our work published, I hope the situation will improve, but I am shocked that duration of symptoms does not seem to have changed in a forty year time period.

87 patients gave me misdiagnoses that they received. Not all patients from the original 226 actually reported their misdiagnoses. In fact, going back to the previous slide that described symptom duration, most folks diagnosed within 0 to 11 months had their carcinoids diagnosed during surgery for something else, such as gallbladder surgery or appendectomies. In some cases the surgery was necessary. In some cases it was not, but most of those folks were diagnosed early were receiving surgery for some other condition.

The most frequently occurring misdiagnosis was irritable bowel syndrome. Does this sound familiar? Irritable bowel syndrome was reported by 23% of folks, but just as frequently as irritable bowel syndrome was reported, and here is where my interest as a psychologist comes in, was psychosomatic causes. Some patients were diagnosed with anxiety and panic attacks, depression, or stress. That is another 23% of the group. Crohns disease was reported by 8.1%; also reported were asthma, menopausal symptoms, appendicitis. Diagnoses reported by fewer people that are fairly serious were: multiple sclerosis, lymphoma, adenocarcinoma, gallbladder disease, pernicious anemia, bleeding ulcer and pneumonia. There were a lot more, but I did not have room on the slide to present them all.

Question #2: Results for levels of coping and distress in patients and caregivers. I wanted to show you what the coping scores were. The types of coping that people use are associated with psychological distress and also with some physical health outcomes. Active coping is problem solving kinds of things - what do you do to actively cope with your illness. I have three groups here: Carcinoid patients, caregivers and a comparison group of breast cancer patients. They looked similar all the way down, but what we tend to find is that carcinoid patients are active copers. I don't think

that should come as any surprise because looking at the qualitative data, patients often feel like they are responsible for their own care, responsible for gathering information, responsible for communicating things to physicians who they feel sometimes are less familiar with their disorder than they are. Other things were fairly similar between carcinoid patients.

Next, I examined the percentage of the total sample that was affected with depression. As can be seen in my graph, the percentage of people in the normal range was from 65 to 70%. Caregivers and carcinoid patients who had no relationship to each other had remarkably similar rates of depression. 15 to 20% of patients scored in the at risk range, and slightly more caregivers were in the at risk range than were in the carcinoid patient group.

Next, we will see how many folks were in the "clinically depressed" range. This does not necessarily mean that someone has a diagnosis of depression, but it is very likely that if we took these folks and gave them further evaluation such as a standard semi-structured psychiatric interview, they would be diagnosed with some kind of depressive disorder. What we find is that about 5% of carcinoid patients and about 5% of caregivers are in the depressed range.

The scale I used -- the HADS, or the Hospital Anxiety and Depression Scale - is specifically designed to measure loss of interest in life activities, known as anhedonia. Many researchers assess depression by asking about vegetative, or physical, symptoms, such as I don't feel like getting out of bed, I don't feel like eating, my appetite has changed, my weight has changed. Because these things co-occur with many chronic illness conditions, we may be more accurately measuring depression in cancer patients by looking at the anhedonia only.

Question #3: What were the predictors of depression. In looking at predictors in carcinoid patients, I controlled for sex (male or female), age, and education. Females are generally at higher risk for depression, as are younger patients and those with lower education. The next thing I looked at was Sandostatin dosage. I expected that Sandostatin use would predict lower depression.

The next variable was duration of symptoms before diagnosis and the total number of reported current symptoms. Specifically, does a specific type of symptom relate to more psychological distress? The symptoms that I was able to code from my data were diarrhea, fatigue and pain. I conducted what is called a regression analysis. This allows the researcher to determine whether there is a statistically significant relationship. I don't want to bore you with the details, but I do want to tell you that the overall equation was significant so it does mean that there is relationship among these variables. I also want to clarify which specific variables were associated with depression.

Another thing regression analysis allows me to do is to look at the relative strength of association among the variables. For example, is Sandostatin dosage more important than some of the psychological parameters? I found that a higher rate of physical symptoms related to higher depression, with a strong relationship shown by these indicators. Fatigue and depression were also related, but not quite as strongly as physical symptoms and depression. There were no effects for any of the demographic variables, for Sandostatin, for pain or for diarrhea. So, what this says to me is that the total number of symptoms is important, but the specific kind - for example diarrhea vs. fatigue - is not the determining factor of depression.

Next slide: how does coping predict depression in carcinoid patients and caregivers. I'd like to point out this figure, called the total R. It is 0.597. What that means is that this is a strong relationship. Psychologists generally say that anything over a 0.3, is good. In looking at the previous slide, we see that the total R for physical parameters and depression is 0.291. This is statistically significant, but from the usual indicators that we use to evaluate how important specific factors are, coping factors are stronger predictors of depression than physical symptoms. I consider this good news. Coping mechanisms are something that are somewhat under your control. Individuals have less control over physical symptoms.

The amount of effort that people put in taking a negative situation and framing it in a positive way had a strong relationship with depression. So the more re-framing and individual does, the lower the depression. The higher the amount of distraction, for example, TV watching, and the avoidant type behavior, for example, not wanting to think about having carcinoid, related to higher depression. It

was a relatively strong relationship using our typical indicators. Higher rates of self blame, for example, believing that you somehow caused the disease was associated with higher rates of depression. In this particular equation, Sandostatin did come out as a predictor of higher depression. It is not a strong relationship, but it is there.

Next, I looked at coping as predictors of depression in caregivers. I found no significant relationships between any coping variables and depression. That is where it is really good to have a colleague who can step in to help us better understand what is behind the distress in caregivers, which appears to be different than in patients. This is where Dr. Smith will take over.

Dictation by Suzanne Smith, Ph.D.

Again, I just want to say real quickly, the kinds of things that Dr. Soliday has been presenting so far dealing with your answers to question - how often do you feel this on a scale of 1 through 5. We know that you are while that provides us extremely viable information and helps us figure out what we need to do next it does not tell us individual people's experiences or how they think and feel and may be we did not ask a question that relates to them so they have something extra that they want to tell us. At the end of the questionnaire, we ask them 10 open-ended questions and the questions range from anything to how has carcinoid changed you feel about yourself, how has it changed how you feel about your family, and may be how your family feels about you. We ask things like what is the greatest challenge you faced since being diagnosed with carcinoid. What was the process of diagnosis like for you and what was that process like for your family and what would have made the diagnosis process easier?

The general questions that we will focus on today or that I will talk about real quickly - what have your interactions with medical professions been like because if you have symptom duration of 0 to 25 years you have probably seen a lot of medical professionals throughout that time period so how have those interactions have been like for you. I ask the question if you were able to train medical professions to deal with carcinoid patients what would you want them to know, so what makes you different from other patients that they deal with that these doctors need to know about and other practitioners.

Finally, we ask how do you cope with the psychological and emotional side effects of being treated for carcinoid so we have a lot of research out there on the physical effects of carcinoid, but what are you doing to cope with the psychological effects of that because that is something that is not often addressed. What happens here is that the question is listed and the person just types in their answer.

I have been a qualitative researcher for fifteen years and generally you are thankful if you can get a couple sentences out of someone when you are asking them to write down their answers. I was very happy to say that we were overwhelmed with information. It was a beautiful thing. For each question we received approximately 25 pages of response per question. That is 25 single spaced pages. The thing that is especially interesting about this is that some of the questions that we asked were things like what three words best describe your experience with carcinoid. Some of the questions had three word responses and then some if you have a 25 page average that means some had 40 and 50 pages of single page text. That is a lot of information. We were extremely thrilled to get this kind of response. That is 25 pages per question. I have several 3-inch binders full of your knowledge that you have shared with us and we are greatly appreciative for that.

What do we do with all that information? The first thing that we have to do is code responses. What that means is let's say I ask you how has living with carcinoid affected your family. You might give me 40 lines about how it has affected your family and each line may have something totally separate to say. First thing I want to do is take your response and put it into sentences or sections based on topic so that each line has a different topic. That takes the pages to about 100 once you do that. Then what you want to do is go back and label each topic that is talked about so that you can see if people talking about similar topics. What are the commonalties here? So coding response simply means, okay, this person said I feel sad sometimes so I am going to code that as sad. That code descriptor explains what they said. Once we have done that we develop a classification system. This is really how you tell a story. How do I make 150 pages of information at this time into

something that represents everyone's experience and their commonalities and similarities. This usually ends up looking kind of like an outline. Here are the ten topics that everyone mentioned and here are the categories that fit under that. I will be giving you some of these classification systems and I am going to be the only one to use notes because I am going to read you some direct quotes from patients so that you can hear in other people's words rather than my own what they feel about these topics.

Why is this important? Because we are looking for potential sources of distress. This cartoon says don't worry. Fantasies about devouring the doctor are perfectly normal. I choose that because while 28% of the patients and 25% of the caregivers said they had wonderful perfect care. They had absolutely no problems with their doctors or medical professionals and they are very pleased with what is going on. The rest of those people faced some problems when dealing with medical professionals in some way or another. Again, the purpose here is by no way or means to place blame on anyone. We also recognize that we are not talking to the people that we need to talk to with regards to medical professionals here because the people that are in this room are the people that are caring and concerned and are going above and beyond what you would ever expect any caregiver to do. The point really is to say that these are problems that the majority of the carcinoid patients and caregivers that participate in our study are facing with. It allows you as patients yourselves to see that you are not alone in your experience. When you are having problems in your interactions with medical professionals it is not just you. It is the person sitting next to you and it is the person sitting in front of you. This is a common experience.

It also has been found that it is a way to empower patients to be more active in their own care if they see that they are not alone in this battle. What are some potential sources of distress? In our study, the patients and the caregivers reported, so this is their reports not me, the need for medical professionals to do some of the following things. The most commonly reported item that patients mentioned was to please listen to their patients. They often feel like they are not being heard by their physicians and that being heard would help make their diagnosis process easier and the treatment process easier. For example, one patient stated "I have suffered for years because I could not find anyone to listen to my symptoms. It seems they were written off rather than listen to." Another person stated "I am usually very pleasant, but I hate when people think that they know all about me simply because they read my medical chart. They also need to listen to my words. I am more than a piece of paper." Finally, one person stated "Most of the doctors I have seen in the past six years were not listening to my valid complaints. At 43 years old I do not think everything should be attributed to women's health issues, depression or menopause. One even suggested that perhaps it was a mental health issue. Please listen to what I have to say.

Another common issue that was brought up was the need to speak in lay person terms. This was mentioned over and over again that even sometimes when the conversations are taking place they don't understand what the conversations mean so they are leaving scared more than anything else because they have been told they have this diagnosis and these likely symptoms, but they do not know what those mean. The need to speak in layman's terms was very pronounced. For example, one person stated "I wish the surgical oncologist would help me understand more about carcinoid. He keeps telling me there is clear documentation of carcinoid and that basically we just have to treat the symptoms as they occur, but I don't even know what the clear documentation is, what the other treatment options are. We really need to understand." Again, knowledge is power in this community.

Spend more time with them. Spending time means things like time doing the appointments as well as returning phone calls. A lot of people actually mentioned that they would rather have their doctor present the serious diagnosis to them than the nurses because the doctors are the ones that they have the relationship with so far.

Returning test results. The majority of our patients said that the hardest part about the diagnosis and treatment process is waiting for the test results to come back. They often called in to see where they were in the process to be told that the results have been back for some time, but information was just not out there yet.

Other frustrations include things like this is a quote from one patient caregiver "Her doctor sees her only a few minutes after her chemo and at no other time. She is too passive to insist on seeing him

in the office when she is feeling better." Another patient said "I ask questions, but I guess not the right ones. They don't say much unless I ask and since I don't know what to ask they are in and they are gone and I know nothing."

Another issue is to be honest but compassionate. People kind of fell on both sides of the continuum on here. Some people wanted to know everything they could possibly know and they wanted their doctors to say you give me as much information as you can and some people said I want you to tell me the truth, but I don't want to know the whole truth. So, people fell kind of on both sides of that. One patient said, "I wish they were not afraid to come right out and tell you the truth just like it is. Not just the things that they want you to know, but answer the hard questions too."

Provide caregivers with information as well. Again, this seems to be a pretty typical comment that was listed by caregivers. One caregiver said for example "Since I am the one taking care of her it seems I should know what she is told. Sometimes it stresses her out to be told everything, but I found that if she does not want to be told that means that I can also not be told and I want to be. After all, I am the one giving the shots." So, again, this just points to the idea that this is a family disease, not just an individual disease because everyone is going to be involved in this regardless of the fact that just one person might have the carcinoid.

Diagnosis process. Again, one of the questions that we asked is what was diagnosis process like, what could have made it easier, and how does this affect your family so will just cover a few of the things that the patients talked about. First of all, acknowledge the symptoms. This means this gets back to the idea that people go twenty to twenty-five years without diagnosis but having presenting symptoms. One caregiver said, for example, "If a doctor would have taken my mother's complaints seriously and ordered tests this could have been found earlier on and treatment could have begun much sooner." One patient very insightfully I thought stated "I wish that all doctors ask the question what unusual symptoms have you been experiencing in the recent past which you did not experience before when your treatment does not seem to be working." So if you are being treated for the same thing over and over again, okay, what is different now than it was before and try to figure out how we can treat better and make that different.

Something that I have heard a lot today from talking with some of you is the ability to seek help from specialists, seek outside help from specialists. Because of the rarity of this diseases I think Dr. Soliday mentioned earlier people sometimes feel as if they are being treated as the rare case as opposed to an individual. So, this is, you know, I've got a carcinoid and I'm not going to give her up because this is something that would be good for me. That is really the time if you have not treated a carcinoid before when patients feel like that outside help should really be sought at this time. One patient said "My doctor admitted he remembered learning about carcinoid in medical school, but had never seen a case in his twenty years of practice so he never even considered as a diagnosis. Thus my husband's rosacea that was not responding to treatment almost went undiagnosed indefinitely because he was not sent to a specialist, but for six years instead was told lets just give it some more time."

Again, many refer to the fact that they wish they had been sent to a specialist earlier. We have not really figured out how to solve this problem, because, again, presenting symptoms are what they are and doctors do what they can with that information. Perhaps what Dr. Soliday and I are hoping to do with this information and other people in this research just the get the information out there. If you get these symptoms in a patient consider this test. Consider this as another option just so that more people are aware of the fact that there are other tests that could be run which leads to the next point is make appropriate test known available. I am having tests checked at hospitals all over the country. These tests are very easily available and very inexpensive if you know what to ask for and so that is what we are working on now is getting that information out there.

The importance of early diagnosis is pretty self explanatory. Most of the patients said that their lives would have been different if they were diagnosed earlier and knew how to deal with those things, that the family would have had a better understanding of what was going on, and with more understanding is a better way of coping with and dealing with that.

Once the diagnosis is made, however, one of the things that they hope is that they are able to find a

doctor that has knowledge of the disorder, knowledge of carcinoid. The first thing that they want their doctors to do is learn about carcinoid. I love this quote by one patient "I wish doctors had a better understanding of this disease. They need to learn about this relatively rare disease before treating their patient. Visit the Carcinoid Foundation webpages. Follow the lists of discussions to see problems patients are having. Make sure you understand the medications and treatment options and how to give them. Read the research that is out there. Bottom line, don't just treat this like any other cancer because it is not."

A lot of patients reported that they were the ones who were learning about carcinoid and trying to pass that information on to doctors who were receptive sometimes and sometimes not. Because of the lack of knowledge, again, except for the people in this room obviously and many other people like you, patients often feel like they are responsible for their own care which means that they feel like they are doing the research, coming into their doctor saying here is what could be going on, what can we do about it or what should we do about it. In many cases they are actually saying here is what tests need to be done, here is what we are going to do. As one patient stated "I show our doctors that I am very interested in learning about the disease and I expect him to care and be aggressive as well. Please at least read the things I bring in to you." Another patient said "Sometimes it is like they don't believe me. I know more about this than they do, but I have to get for tests to keep up with the process of the disease." Carcinoid patients have got to be proactive and assertive to get proper care which I think is kind of the bottom line of all of this if you are not fortunate enough to be able to see one of the specialists is that you have to be proactive and be willing to do the research and ask for what you need.

Discuss treatment options. One patient said, "I wish that they knew how to treat this disease better. I hate the watch and wait attitude, but I understand that they often truly don't know enough since this is a rare disease. I am not expecting them to know everything because we are in the early stages, but I would like to at least be given some options that I feel like I have some power in this decision." Here are your options and here is what may suggestion is so they feel like there is something that they can do.

The most important for most of our respondents was to share the non-medical side effects of carcinoid. One patient said "This is much more than a physical disease. The psychological pain is much worse." So, here is the diagnosis, here is how we are going to treat it medically, but then they never get the how do we treat this psychologically and emotionally, how do we treat your family members when you tell them what your diagnosis is, how do you encourage the people to be supportive of that. One patient also said, "Cancer is not only a physical disease. It affects the body, the mind, and the spirit. It affects the whole family dynamic and each family member suffers because of the disease. Physicians should strive to address these issues. This would undoubtedly benefit the cancer patient in many ways. The least being helping the patient feel she is not alone in this, the fight of her life."

This brings us to so if they need to figure out how to cope with this what are some things that our patients were doing and our care givers. Lots of things this community was doing to deal with cancer. The first was just focusing on the self. This included things like doing things for themselves, keeping a positive attitude. I was just blown away reading your responses of the number of people that said, "I just enjoy every minute of every day that I have. If I have one more day to spend with my family than that is a perfect day." That positive attitude is what Dr. Soliday referred to earlier was a highly powerful coping mechanism for this group. Using God, religion or something of spirituality to help focus on the self and the family was also very powerful for this group.

Outside support. By this group specifically, I mean things like support groups and support means not just the carcinoid individual, but the family members as well particularly children, professional help meaning a counselor, may be bereavement counseling, getting information was one the things that carcinoid patients use the most. How do you cope with this disease. I copy by learning everything I possibly can and that was primarily done through going on line and getting information off of the web. Outside support also meant relaxation techniques, yoga, taking a hike, going for a walk, those kinds of things.

Some people did use distractions. Distractions are anything that you can imagine; hobbies, TV,



movies, eating for some people, exercise, keeping a journal. Lots of things that people do as a means of distraction. Interestingly enough, Dr. Soliday talked about this as being a very negative way of coping. The connotation that was used as people's written answers was a very positive way so we are not sure how to tease it out. It is a perfect example of why you need both because while it looks like some of those things are negative we actually found them to be positive in this way.

Family and friend support is very important as well and the high level of activity. Keeping busy. Trying to keep as much of a normal life as possible.

The final means of coping was negative emotions or none at all. Primarily this was the patients and caregivers who were so bogged down in the depression that they were not able to figure out how to respond to this disease. They either responded to it negatively in a depressive way or they simply refused to acknowledge that the carcinoid even existed.

Now we are going to talk about some of the limitations of our study and Elizabeth will do that.

Elizabeth Soliday

Now I will discuss the implications of this work. First it seems important to screen for depression at medical visits if possible. This may be the only opportunity that a lot of individuals have because not all oncology teams have a mental health professional or social worker or medical social worker as part of the team. Medical folks are involved in other responsibilities, but screening for depressive symptoms can be fairly easy by asking one or two questions about interest in life activities. How are you in terms of doing the things that you used to do? Knowing what the person did before the onset of the disease, the kinds of things that they used to do. Did you read? Did you have specific activities? Did you spend a lot of time with family? Are you as interested in those kinds of things as you used to be? Well, you might not be capable of doing all those kinds of things, but do you still have the interest and the desire in doing that? That is a pretty quick and dirty way to assess for depressive symptoms.

Also, history of psychiatric problems is really important. What we are seeing is 5% of these folks are in a depressed range of scores, but that might have been going on before the individual was diagnosed with carcinoid, and we don't really know for sure so asking a person about history of psychiatric problems is important as is use of validated measure where possible. That can be difficult in busy medical settings, of course. I have worked in home/onc units for a while, so, again, that one question can be very useful. Where it is possible, the hospital anxiety depression scale has seven questions assessing depression. It is a highly valid measure.

Risk factors for carcinoid patients: this is a summary statement about risk factors for depressive symptoms. The more physical symptoms, the higher the person's depression. Also, fatigue and also self-blame were risk factors. These are things to assess with carcinoid patients to see at what degree of risk they might be for developing depressive symptoms or even a depressive disorder. We want to know these kinds of things again because depression itself is associated with survival.

Is Sandostatin a risk factor for depression? I found it interesting that it was a significant predictor of higher depression. When this occurred, I looked through my resources to see what the adverse effects listed were and found a fairly consistent possible adverse effect to be depression for Sandostatin. The effect of Sandostatin is diminished when physical symptoms and fatigue are included in an equation, but the effect remains if we are looking solely at psychological factors. In my estimation, it is worth doing systematic research on Sandostatin mood and quality of life effects because there is obviously a balance to consider. Most patients, in the qualitative data, said Sandostatin has really helped them get things back on track. For example, I can go out now. I can see my friends, etc, etc. Does it cause mood disturbance, is it related with mood disturbance in a significant number of individuals, what is the cost benefit ratio possible effects, and who might be at highest risk for that kind of adverse response remains to be determined scientifically. This is the kind of work that I have been doing with pediatric patients for a good stretch of time now and I think that this question remains to be asked also with Sandostatin. I have been reading lately that pharmaceutical companies are becoming more and more interested in examining quality of life outcomes related to medication use. I think there is room for more work in that area.

Next slide: managing depression in carcinoid patients. Multiple avenues for treatment must be considered because it is a rare disorder and we are not talking just about medications that might be available although that can be very effective for certain folks who have depression. We are also talking about appropriate support systems and depending on the severity of depression; a number of behavioral changes and behavioral modifications can be very effective and that has to be considered for carcinoid patients because of some of the unique features of the disease that may preclude the prescription of certain anti-depressant medications, which I will talk about in a second.

It can be hard to tease out depression verses illness and treatment related reactions. The bottom line is in terms of treating depressive symptoms, in many cases we do the same things whether it is related to the illness or whether it is related to something that is more psychological in nature. We do the same things in terms of helping folks learn to reframe things using their cognitive and coping abilities. We do the same thing no matter what the source of depressive symptoms. Mild exercise is something that can be indicated when symptoms are mild. It is hard to get folks to start exercising when they have not been doing that before and especially if their depression is severe, but if they have mild symptomatology or mild distress, mild exercise was discussed last night in one of the presentations. One cancer patient spoke of the difficulty walking given her Fatigue, so she started by making herself walk from her house to her mailbox, and working up from there. Taking short walks can get a person started in regular exercise that has been found fairly consistently in cancer patients to alleviate depressive symptoms.

On the other hand I think medical professionals and all of us can do a lot to normalize that carcinoid patients have been given a serious diagnosis. Not that you should be depressed, but let's set reasonable expectations. If you are going to be undergoing surgery what is a reasonable recovery time? How much help might you need during this recovery? What kinds of resources and support do you have during this particular time? Are you going to be able to do everything that you did before the disorder? Rick Peterson told me that his oncologist told him "I have got two things to tell you. First of all, you have cancer. Secondly, your life will never be the same." It sounds like something that he never forgot and I have not forgotten it either, but I think that is a part of whole process of helping an individual set expectations for how this might change one's perspective on life because these patients are still living so we are going to try to do everything to enhance life. Again, mild symptoms respond well to physical exercise.

Next slide: Developing referral lists. This issue came up at a symposium that was held for patients by Novartis last November. The patients who attended that particular symposium said that none of their or very few of their medical providers had any idea that there were support organizations out there for carcinoid. What we have instead are extremely active carcinoid patients who are working really, really hard to disseminate information about their ongoing support groups, but it is a very slow process and it slows down when folks are not aware of this information. I think one thing that can be very useful in the medical setting is to develop a referral list for folks who might be able to intervene and also support organizations that exist.

SSRI's may be contraindicated for depressive symptoms in folks who have carcinoid. SSRI's are selective serotonin reuptake inhibitors. Carcinoid is associated with elevated systemic serotonin, and it has been reported that SSRIs may elevate serotonin to a level that increases psychiatric disturbance. Before I came here, I checked a list of medications that I had asked people in this study to provide. About 10% of the sample was taking SSRI. What I really want to know is whether there are adverse responses associated with that. A couple studies have been published in which adverse responses were noted when a person was taking an SSRI who had carcinoid and this was described as the serotonin syndrome, where the individual actually developed some psychotic symptoms as well as a number of physical symptoms that were very difficult to treat. SSRI may be contraindicated, but there are people who are getting that medication. Again, these are things that folks in this audience probably know about and we need to take our show on the road and get the information disseminated and hopefully that will start through the process of publication. What we have now are two papers under review and a third that will go out shortly upon our return.

Continuity of care and follow-up seem to be particularly important when we talk about treating psychological distress. Sometimes a person might be seeing a mental health professional. They also

might a anti-depressant that is being prescribed by primary care provider. Does the specialist know that? That is especially important when we talk about specific anti-depressant medications that may be contraindicated for the carcinoid population. Continuity of care and that communication among providers really needs to be there.

Also, building on existing strengths. Support groups seem to be an importance resource for folks with carcinoid disease and this is also an important resource for folks who have mild depressive symptoms. The interest in reaching out to other folks is extremely beneficial. Coping strategies, including acceptance and re-framing, were significant predictors of lower depression. When I think of re-framing, I am reminded of the master re-framer, whom you can see here in this picture.

This is Rick Peterson and this is his wife, his wife Esse. They are enjoying one of the few beautiful days in Manzanita, Oregon. Again, Rick was told sixteen years ago that he had six months to live. Having been very active in reaching an adequate diagnosis and appropriate care he has lived eighteen years past that initial diagnosis. He was initially diagnosed in 1984 with adenocarcinoma, but he is very active in his care. He is in endostatin trials now. He says he is feeling better than ever. He has gained a lot of weight back that he lost following a surgical procedure, chem-embolization. This summer he intends to take his sailing yacht and go to Alaska. I think he has done quite a bit to get the most out of life and to involve his spouse in that process. I think in terms of coping, finding ways to cope helps work against depressive symptoms that have a tendency to set in when a person has a diagnosis of the chronic illness. Rick is a very good example to follow.

## QUESTIONS

Dr. Kvols

Q: My question is related to one of your conclusion slides that increased symptoms correlated with increased depression, but then you went on to say that there was no correlation between pain, fatigue or diarrhea. If I view of three of those as symptoms, so if there is no correlation with those what were the symptoms that correlated with increased depression?

Dr. Soliday

A: It is the total number of symptoms. I analyzed this two different ways. I looked at specific symptoms, yes or no, does the person have that symptom and whether that individual symptom predicted depression. If we look at only pain, we look at only diarrhea, and only fatigue those were not significant predictors. If we sum total people's symptoms, for example, if the person has five symptoms versus zero, the total number of symptoms, in fact, did significantly predict depression rather than any specific individual symptom. The reason I did that is my bias from reading the qualitative data: it looked as if diarrhea was a significant inhibitor for folks being able to be involved in activities that they were prior to their carcinoid diagnosis and I thought that specific symptom may have some association with depressive symptoms, but it did not.

Dr. Kvols

Q: The second is more of a comment. I think we need to really look very, very carefully at your conclusion about depression possibly being related to Sandostatin. I have probably administered more Sandostatin than anybody in this country and what I hear from patients is that it is a feel good drug. The patients don't come back until "My gosh, I was fine before you put me on this and now I am feeling so depressed, doctor." The contrary was that majority of patients will come back uplifted, new outlook on life, they skip a day of two of shots then they may get depressed. They may feel better even mentally within an hour of taking a shot so I really question that conclusion.

Dr. Soliday

A: Yes, to reiterate statements I made at the end, in terms of that association it is inconsistent with the qualitative data. In the qualitative data, folks wrote about how Sandostatin has really saved my life, I can get back out and do the things I was not doing before; that was really clear. When we look at quantitative, just Sandostatin dosage versus depressive symptoms, we simply found that a higher

dosage was related to higher severity of symptoms. We assessed a heterogeneous group of patients so it could certainly be that folks were completing assessments at a time when may be that end point, if they were taking the LAR, the last day of the third week or the fourth week as it was wearing off. It is hard for me to determine these kinds of things and that is why I want to reiterate my qualification by saying that it is really important to pursue this issue more systematically with a homogeneous group of patients and probably prospectively before folks ever start and then repeatedly during the process of administration. Absolutely.

Dr. Kvols

The comment was when you are taking Sandostatin three times a day subcutaneously you are constantly reminded three times a day that you have cancer. I remember when we first started using Sandostatin long-acting release. That was one of the things that we heard most commonly and we still hear it "I can get a shot. Hurts. I have pain in the butt for a day or two, but then the rest of the month I forget I got carcinoid." It is a godsend for some people for that very reason.

Dr. Soliday

I'll take a look at my data because I do have it divided up daily versus monthly and then some people were doing both and so I'll take a look again and see if there are any differences with those three subsets of folks, but thank you for that point.

Dr. Kvols

My last comment relates to your statement that SSRI's, that stands for selective serotonin reuptake inhibitors, and that includes a whole class of drugs like Prozac, Zoloft, Effexor, Paxil. You state that you think that they are contraindicated and I have to totally disagree with you and I think it is a disservice to tell people with carcinoid that they are contraindicated because we have lots and lots of patients on them and have had very good success in treating their depression. Yes, you can have a serotonin storm..... [cut off]

Dr. Soliday

.....that was published in American Journal of Gastroenterology, describing a case. It was a case study describing serotonin syndrome and adverse responses to SSRIs by a carcinoid patient, and the study concluded by saying SSRI's were contraindicated in patients with carcinoid. Another study was published in JAMA in 1987 that was an overview of carcinoid treatment etc., and again in that article it was cited that SSRI's are contraindicated. Both of those gave the qualification that, yes, we are talking about systemic versus central nervous system serotonin, but both of those articles said that there have been cases of adverse responses described and so given that there are other classes of antidepressants to use it might be better to use those kinds of antidepressants. I think it is time to look at this and perhaps update the literature and I would love to be involved in such a study in terms of doing a systematic study of people's responses to SSRI's when they are also diagnosed with carcinoid. The literature currently published is what is available to primary care folks who may be reading this and they might decide, no, I am not going to use this. If they don't have access to a specialist and this is where they are getting their care then it might be appropriate time to update that literature. There may be something out there, just have not come across it in my reading.

Dr. Kvols

talking to audience.

Dr. Soliday

Well, I think given again that there is a reasonable subsample of folks who are taking medications and that the literature clearly needs some updating than it is probably time to look at this systematically and gather appropriate data to answer the question. Again, what has been reported are primarily case studies so to look at a larger group of folks systematically over time is clearly warranted.

What happens with groups over time remains to be established and published.

She said theoretical contraindications don't necessarily pan out in real world practice, correct?

What I also did with this group of folks who were taking SSRI's is compared them on a number of parameters. I don't have that many physical parameters because it was a fairly broad based study and really there were no differences in any of the physiological parameters that we have in terms of physical symptoms, years, diagnosis, etc, etc., so all that stuff came out to be fairly similar. Again, this sort of systematic study of that is yet to be done.

That is a really good question. I think most of that comes through in the qualitative data. The thing that was most striking was the process of diagnosis and the length of time that a person lives with symptoms before being diagnosed. The process of diagnosis, the stories that people have, it is pretty remarkable that people continue to pursue treatment after quite a bit of what sounded like frustration. Frustration with medical providers, frustration with caregivers sometimes too, who became frustrated with them, and frustrations with treatments that did not feel really effective. I think that is probably the most striking difference in this group was just that process of diagnosis. In a certain sense, it sounded traumatic and was similar to the kinds of things you hear people talking about when they describe posttraumatic stress symptoms. The whole process is very stressful for folks.

Carcinoid seems to have its own unique quality of life impact issues. Probably the most published data on quality of life issues is in the breast cancer population and folks have some serious quality of life changes with breast cancer also, but they are of a different nature. A lot of them are associated with body image so we are looking at different things.

We are talking about group data so we are talking about what is happening with 226 patients and sometimes an individual patient experience might get washed out by what is happening with a larger number of individuals. That is one thing that happens with group data is that it does not tell the story for each individual person within that group. The other issue is Sandostatin dosage might be a proximal indicator for all kinds of different things. It might mean that a person has more severe symptoms. It can mean all sorts of things in terms of its relationship with distress so we are looking at two things that are very broad indicators where we probably need to get down more to the nitty gritty and find out what that relationship is about. I have been trying to reiterate the message that more systematic research on that question has to be conducted. Again, it is listed in the adverse effects column in most drug handbooks that depression is a possible consequence. How many people wind up with that? I don't know. That is one reason why we try to tie these two things together, but we are looking at broad measures and we are looking at a large group of people so it needs to be looked at further.

Well, I think there are couple of ways and ultimately it is up to your mother, but I think as the caregiver, it can be hard to see that when your are on the outside. One thing that a lot of units have in place is a one-on-one contact kind of program and so you might check to see if they have that where your mom is getting treated. If an individual contacts your mom and they have some ability to connect over a difficult experience, that is certainly a lot less threatening than it is to seek help from a therapist. Maybe not. Shortly after diagnosis most people go into a difficult period and that is a tricky time for a lot of folks. It may be that an entree to that kind of treatment is just connecting with someone else who has a similar experience. Check out the websites that are available and maybe try and turn your mom onto those. Look at Susan Anderson's website, which is very beneficial for a lot of people. It often takes a child to do that, you know. In reading some of the qualitative data people are saying my son or my daughter does this for me and kind of helps me get there. Support organizations are in place depending on where you are and sometimes those can be less threatening where you can take your mom to those and especially those have more of a psycho-educational component. Meaning that if they have a physician come and talk about medication issues, for example, and a nurse will come and talk about post diagnosis issues. Where the focus is more educational. That can sometimes be an entree to help get the process of dealing with this started because there will be issues.

One of the messages that health care providers can often provide patients is to give them a positive framework. You know, this was a very different disorder thirty years ago you would have been treated differently. These days here is what is going on and here is what we can provide you, etc., etc. as setting a reasonable framework. Nonetheless, according to our results, a significant number of patients and caregivers do experience distress worthy of our concern.

Certainly, again, we have a quantitative relationship. We had anonymous data collection, so I do not know who did or who did not participate in our study. What we are seeing are the experiences of the 226 patients and 77 caregivers who did participate.

You are talking about multicollinearity and actually I did check for that. That is why I did two separate equations because we did not have a correlation that was high enough to kick it out, but certainly it is related at about 0.25 so the strength of the relationship was significant, but not significant enough to kick the variable out.

Again, our qualitative data really speaks to that and talks about folks feeling very empowered and I am able to engage in kinds of activities that I was doing before I was diagnosed, etc., etc. There is a quantitative relationship showing otherwise, but there is a qualitative piece of information that indicates this issue needs to be looked into further.

THE END

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