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Monica M. Tronsky (Burlingame Center for Psychiatric Research and Education, Institute of Living, Hartford, CT) Anxiety and Depression: Exploring Associations with Suicidality

ABSTRACT

The purpose of this study was to examine if anxiety diagnoses were associated with increased risk for suicidality and to examine if comorbid anxiety and depression diagnoses have a synergistic effect on suicidality. In a sub-analysis, we assessed associations between anxiety and/or depression symptoms (versus diagnoses) with suicidality in order to inform a future study.

Completed at the Burlingame Center for Psychiatric Research and Education at the Institute of Living (IOL) in Hartford, CT, this quantitative, cross-sectional study involved 20,823 adult inpatients admitted for psychiatric care from 2000-2009. Estimates of effects calculated were odds ratios (ORs) qualified at 95% confidence intervals (CIs). Descriptive, bivariate, and stratified statistics were utilized in the study. Through analysis of two-way interactions, we judged evidence of synergism or antagonism. Finally, we constructed binary logistic regression models to assess the anxiety - suicidality association.

We found that anxiety and depression diagnoses were associated with approximately 40% and 160% increased risk of suicidality after controlling for demographic and clinical confounders. Furthermore, our analysis provided evidence that

the effects on risk of suicidality of these two diagnostic groups were independent, neither synergistic nor antagonistic in this population. Preliminary analyses suggest that anxiety symptom information may be a better predictor of suicidality than the presence of a *DSM-IV* diagnosis. Additional research is warranted to examine the nature of anxiety symptoms that precede suicidal behaviors and to examine if symptom clusters work synergistically to increase suicidal risk as well as what symptom clusters present the greatest suicidal risk.

ANXIETY AND DEPRESSION:

EXPLORING ASSOCIATIONS WITH SUICIDALITY

A thesis based upon an investigation in the Burlingame Center for Psychiatric Research and Education at the Institute of Living (Hartford, CT) in collaboration with Dr. Stephen Woolley, submitted in partial fulfillment of the requirements for the degree of Master of Social Work.

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I dedicate this work to my children, Juliana and Cole, for the magic and sparkle they bring to the world; to my parents who were my first teachers, and to my loving husband who always finds a way to let me live my dreams.

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CHAPTER I

INTRODUCTION

Scope of the Problem

Suicidality is a global concern. In fact, on September 10, 2009, during the World Suicide Prevention Day, Mishara stated:

We live in a world where the media bombards us daily with stories of violent deaths occurring in the context of wars, terrorist attacks and homicides. Yet, worldwide each year, more human beings kill themselves than are killed in all wars, terrorist attacks and homicides combined. (p. 1)

The World Health Organization (2008) estimates that every 40 seconds someone in the world dies by suicide, which adds up to 1 million suicides across the world each year. The National Institute of Mental Health (NIMH) (2009), using data from the Center for Disease Control (CDC), reported that in 2006 suicide was the eleventh leading cause of death in the United States. In that year, the incidence of suicide was 10.9 per every 100,000 people, amounting to 33,000 deaths in the US alone.

Table 1. Number of Suicides by Age in the United States in 2006 (Adapted from Heron et al., 2009.)

Population by age in years	Number of deaths by Suicide
5-14	219
15-24	4,189
25-34	4,985
35-44	6,591
45-54	7,426
55-64	4,583
65-74	2,384
75-84	2,075
85 and over	840
Not stated	8
Total	33,000

Astoundingly, for every suicide death the NIMH (2009) estimates that there are 12-25 nonfatal suicide attempts, accounting for as many as 825,000 attempts per year in the U.S., a rate of approximately one for every 37 citizens. When you factor in the number of attempts and the number of people plagued by suicidal ideation, the toll in human suffering is immeasurable. The problem has become of such importance that suicide prevention has been identified as a national and world imperative by the Institute of Medicine National Academies (Goldsmith, Pellmar, Kleinman, & Bunney, 2002), the U.S. Surgeon General (U.S. Public Health Service, 1999), and the World Health Organization (2008).

Predicting Suicidality

The relationship between psychiatric illness and suicidality has been discussed frequently in the psychosocial literature. (Suicidality is defined herein as the range of suicidal behaviors including ideation, attempts, and completed suicide.) In fact, diagnoses and incidence of suicidality have been studied in the past to determine if certain psychiatric diagnoses carry a higher risk for suicidal behaviors (Bernal et al., 2007; Nock et al., 2008), and some differences have been noted. However, despite the plethora of research available, much is still unclear about the exact components of mental illness that lead to suicidality. The fact that, compared to the risk of suicidality in the general population, the risk is elevated across individuals with psychiatric diagnoses suggests that a common element or elements in individuals with these diagnoses may be the root cause(s) of suicidality among mental health patients. Psychiatric disorders often share the same symptom(s) in their diagnostic profiles, although the prevalence of these symptoms may vary by diagnosis. Thus if a symptom or symptoms and not diagnoses are causative for suicidality, the variation in prevalence of

symptoms may explain why the risk for suicidal behaviors differs between psychiatric diagnoses. Isolating the exact components that are predictive of suicidal behavior is important for accurate assessment (in terms of sensitivity and specificity for the prediction of suicidality) and treatment. For example, because suicide attempts can occur in the absence of mental illness and can occur across a variety of diagnoses, suicidal risk cannot be based on current definitions of diagnoses alone. Although postmortem studies have indicated that 90% of all people who commit suicide have a psychiatric disorder (Yan, 2009), the World Health Organization (WHO) found that mental illness was prevalent in only 65.7% of suicide attempters in developed countries and 54.6% in developing countries (Nock et al., 2009). Furthermore, when looking at the diagnosis of depression, Yan (2009) underscored that in the multi-national study conducted by WHO, researchers found that although depression was strongly associated with suicidal ideation, it was not predictive of suicide attempts. This is a strong departure from conventional wisdom and the findings of many studies, and raises questions about the assumed necessary role of depression in the progression of suicidality (Nock et al., 2009). In fact, the WHO found that the only commonalities across diagnoses in both developed and developing countries that were predictive of the transition from suicidal ideation to suicidal attempts were anxiety symptoms and impulsivity (Nock et al., 2009).

An argument could be made for reformulating diagnostic criteria and taxonomy to better differentiate and screen disorders that also present with symptoms of anxiety and/or impulsivity. In light of the importance of comorbid mood disorders and anxiety, an affect disorder workgroup from the American Psychiatric Association is even debating whether to add a new diagnostic category called "Anxious Depression or Mixed Anxiety-Depression" (Fawcett, 2009) for the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition

(DSM-V) that will be published in 2012. The workgroup is also discussing whether to add a dimensional aspect to mood disorders in general that would assess severity across various symptom variables and/or whether anxious depression should be listed as a separate diagnosis. However, an important consideration is that symptoms of anxiety that do not meet the full criteria to warrant an anxiety diagnosis still may have important implications in suicidal assessment, particularly in patients with depression (Diefenbach, Woolley, & Goethe, 2009). Furthermore, although a change in diagnostics may help inform clinical practice and treatment plan development, the changes in diagnoses alone may not be the most effective way to promote understanding of the development and prediction of suicidality.

Suicide has been associated with multiple environmental/social and psychological causal pathways. Environmental/social triggers include major life events such as loss of loved ones, social isolation and employment problems. In the psychological arena, early psychoanalytic theory proposed that suicide is aggression or hatred turned inward against one's self (Gonda, Fountoulakis, Kaprinis, & Rihmer, 2007; Joiner, 2005). Multiple other psychological theories have been developed since then including theories about hopelessness (Gonda et al., 2007) or about what Shneidman termed "psychache" or "psychological pain" being the root of suicidality (Joiner, 2005). More recent theories include Linehan's biopsychosocial model that indicates that a biological predisposition, an oversensitive temperament, an invalidating environment and/or trauma work to contribute to an inability to regulate emotions (Joiner, 2005). This emotional dysregulation can result in self-injury or suicidal behaviors.

Although affective, anxiety, and impulse control disorders have each been investigated independently as predictors of suicidality, formal research is needed to consider

potential synergistic effects of the disorders. To address this issues, the study described herein considered the elements of the development of suicidality suggested in the literature described above by examining the crude associations of anxiety and of depression, (as diagnoses), independently and in combination with suicidality in a population of adult psychiatric patients treated in a community hospital. Ultimately, the purpose of this study was to explore in depth the mechanisms underlying suicidal ideation and suicide attempts by examining the joint effect of anxiety and depression in order to enhance risk assessment. Obviously, the relevance of the study to clinical practice is the impact that it will have on assessment of suicidality, treatment, and follow-up care.

Relevance to Social Work

The relevance of this research to social work is that it may support better outcomes for suicidal people by providing information that can inform screening protocols for suicidality and by informing therapeutic interventions. For example, if depression with co-occurring anxiety causes an increase in suicidality that exceeds the sum of the individual effects of these other two conditions, therapeutic techniques and medications can be structured aggressively around targeted symptom combinations to reduce their effects. Also, being able to predict if patients are at an elevated risk of suicidality can help determine the level of care appropriate to ensure patient safety and to determine the type of safety plans that are needed. Understanding the mechanisms behind suicidal behaviors in advance of completed suicides will provide information that may provide clarity about effective steps in improving outcomes of treatment by stopping suicidal ideation and attempts from escalating to completed suicides. Thus, by utilizing evidence-based research in treatment not only is

patient care improved, but the professional credibility of social workers is enhanced. More importantly, working on reducing human suffering and improving quality of life, which in turn promotes social justice, is in keeping with the National Association of Social Worker's *Code of Ethics* (2008).

CHAPTER II

LITERATURE REVIEW

Previous authors have noted that identifying and determining how certain factors synergistically foster suicidal behaviors and the process that leads from suicidal ideation to completed suicide is complex and still unknown. For example, Goldsmith, Pellmar, Kleinman, and Bunney (2002) reported:

Despite the extensive knowledge that research has provided regarding these [suicidal] risk and protective factors, we are still far from being able to integrate these factors so as to understand how they work in concert to evoke suicidal behavior or to prevent it. (p. 3)

A review of previous research shows that the relationship of suicidality with anxiety disorders is confusing in part because of the many forms of these disorders including posttraumatic stress disorder (PTSD), panic disorder (PD), and generalized anxiety disorder (GAD). Researchers, at present, do not agree on the form(s) of anxiety disorder that is/are most associated with suicidality.

For example, Diaconu and Turecki (2007) conducted a cross-sectional study exploring panic disorder, major depressive disorder, and suicidality among 474 outpatient psychiatric subjects. The authors concluded that panic disorder was associated only with suicidal behavior if the patient had comorbid depression. By comparing suicidal behavior across three groups consisting of a panic disorder with comorbid depression group, a depressive disorders group, and a panic disorders alone group, Diaconu and Turecki concluded that the increase in suicidality was attributed to comorbid depressive disorder.

Because there was little difference in terms of increased risk for suicidal behavior between both the depressive disorders group and the panic disorder with comorbid depression group, they concluded that underlying depressive disorder was the critical indicator for suicidal behaviors. The weakness in this study was a relatively small sample size (78) of patients with panic disorder. A further limit to the study was its inability in allowing the researchers to evaluate a participant's suicidality during an active panic attack or across time. Depending on which comorbid disorders were controlled for, other studies resulted in different conclusions about the relationship between panic disorder and suicidality (Vickers & McNally, 2004; Nock et al., 2009; Beautrais et al., 1996).

Diaconu and Turecki's (2007) evidence that underlying depression and not panic disorder is the key indicator for suicidality, contrasts dramatically with the recent World Health Organization's (Nock et al., 2009) cross-national analysis which involved a much larger sample size. In various nations, the presence (versus absence) of panic disorder was an independent, significant predictor of suicide attempts (ORs = 2.3-3.0) (not just suicidal ideation), after rigorously controlling for various comorbid disorders.

The analysis of the National Comorbidity Survey replication (NCS-R) by Cougle, Keough, Riccardi, and Sachs-Ericsson (2009) had yet different findings that indicated panic disorder was only significantly associated with suicidal ideation and not predictive for suicide attempts. In addition, in this study, findings suggested that anxiety disorders in general, independent of depression and other psychiatric conditions, were significantly correlated with suicidal behavior. This two-step study evaluated English-speaking participants from the contiguous United States, and in the first interview identified those individuals who met the criteria of having a lifetime diagnosis of anxiety disorder and a

comparison group that was representative of those without a diagnosis of anxiety disorder. This subsample included 4,131 participants who completed the second interview providing information regarding lifetime suicidal ideation and suicide attempts. Specifically, after controlling for other psychiatric conditions and demographic variables, the study found that the presence (versus absence) of social anxiety disorder (SAD), posttraumatic stress disorder (PTSD), generalized anxiety disorders (GAD), as well as panic disorder (PD) predicted suicidal ideation, whereas among these anxiety disorders only the presence of SAD, PTSD, and GAD predicted suicide attempts (Cougle et al., 2009). A hypothesis based on the investigators' findings is that anxiety may cause severe distress in patients, especially if the anxiety is severe, so that assessing for suicidality is warranted when patients appear to be severely anxious.

In contrast to Cougle et al.'s (2009) findings, Sareen, Houlahan, Cox, and Asmundson (2009), examining a large nationally representative sample of 5,877 participants ranging in age from 15-54 years (82.4% response rate), found PTSD to be the only anxiety disorder statistically significantly associated with suicidal ideation and attempts. Other anxiety disorders examined included lifetime social phobia, PD, agoraphobia, and GAD. Using multivariate analyses controlling for demographics, PTSD was associated with a nearly three-fold increased risk of ideation and of attempts. The validity of these results is supported by the study's use of a scale to establish diagnoses (the Composite International Diagnostic Interview).

Interpreting the research results about anxiety's role in suicidality discussed above, in light of additional study findings, suggests that symptoms of anxiety are likely to be critical factors in suicidality even in the absence of a specific anxiety diagnosis. Support for this

thesis was found in a study conducted by Diefenback, Woolley, and Goethe (2009) at a major psychiatric facility. A cross-sectional analysis examined 2,778 outpatients' psychiatric diagnoses established by unstructured clinical interviews. Outpatients also self-reported on their symptoms including difficulties with anxiety (defined here as experiencing fear, anxiety or panic) and with suicidal thoughts and behaviors on a standardized self-report questionnaire completed upon admission. Presence (versus absence) of anxiety symptoms was associated with a two-fold increase in the likelihood of suicidality, after controlling for potential confounding by anxiety disorders, depressive disorders, symptoms of depression, and demographics. However, this study may be limited because the psychiatric interviews establishing diagnoses were unstructured and generalizability to other clinic populations might have been limited because the sample consisted only of people receiving outpatient care.

Previous research, including the studies discussed above, considered as a whole strongly suggests an independent role of anxiety disorders (and perhaps of anxiety symptoms alone) in the development of suicidality, although the studies contain methodological limitations including the approaches to measuring psychiatric conditions, cross-sectional study designs, and sampling that may have affected the generalizability of findings. For example, Bongiovi-Garcia et al. (2009) conducted a study assessing how the use of unstructured psychiatric interviews could impact the accuracy of the assessment of patient suicidal ideation. In this study, postgraduate year II physicians (PGYII) supervised by an attending psychiatrist completed unstructured assessments of 201 adult inpatients diagnosed with either major depressive disorder or bipolar disorder (based on the *DSM III-R*, 1987, third edition revised), and the results were compared to assessments by structured interviews

conducted by master's or Ph.D. level clinicians. Bongiovi-Garcia et al. found that 29.7% of patients identified by a structured interview as having suicidal ideation were not diagnosed accurately by the PGYIIs. A potential bias in the study, however, was that clinicians administering both structured and unstructured interviews were not blind to the purposes of the study. Despite this limitation the study demonstrates how suicidal ideation may be underrepresented in clinical diagnosis, which represent the diagnoses in the majority of studies on psychiatric diagnoses and suicidality.

Bongiovi-Garcia et al.'s (2009) study demonstrates one way that methodology can influence the results of a study. As is often a limitation throughout psychiatric research, designing a study to measure the actual state of mind of the patient, i.e., the true nature and severity of psychiatric morbidity, is the most obvious challenge, and it is also difficult to identify the events or circumstances leading to suicidal behaviors. However, this problem can be lessened in research directed toward identifying predictors instead of the causal mechanism for suicidality. In this sense, if what a patient reports, true or false, helps predict suicidality, it is clinically useful. Similarly, if an unstructured approach to establish diagnoses is used, and the diagnoses thus replicate those likely available in clinical settings, such diagnoses could be useful predictors of suicidality. In this way, the true challenge of research is to identify the information that most specifically predicts suicidality.

In an interview with Yan (2009), Nock noted that that future studies are being proposed to examine "symptom clusters" because approximately 52% of the people who had considered suicide seriously (which referred to ideation and not attempts in this study) in developed countries and 43% in undeveloped countries, did not report a prior lifetime DSM-IV diagnosis (Nock et al., 2009). This new focus on symptoms alone requires researchers not

only to identify symptoms that are associated with suicidality, but to consider carefully the potential usefulness of sets of factors not necessarily individually associated with suicidality in future studies.

Additionally, many previous studies were cross-sectional studies and often involve a retrospective self-report of lifetime occurrences of events, emotions and feelings.

Retrospective self-reports are susceptible to recall bias, particularly as this type of psychiatric research requires that patients self-report about personal, traumatic, and unpleasant events. However, because many traumas are major life events, recall bias may be less of a limitation when patients are asked yes/no questions. Nonetheless, establishing the chronology of events is a necessary factor to support associations as either suggesting cause or as useful for prediction to support interventions. Remembering the sequence of major events in one's life, unless they were perceived to be related, is likely to have biased some past studies.

The study described herein differs from prior research in a variety of ways. The study enables a cross-sectional analysis of the synergistic effects of anxiety and depression diagnoses on the risk of suicidality after controlling for other diagnoses, psychopharmacology treatment, and demographics. Examining anxiety and depressive diagnoses together will advance the literature by estimating anxiety diagnoses' value in predicting suicidality, independent of the effects of a depression diagnosis and controlling for other potential risk factors. In addition, this study serves to inform an upcoming longitudinal research project that will examine the associations between diagnoses, symptoms, and perhaps symptom clusters with subsequent suicidality. The premise we are exploring is that co-occurring anxiety and depressive symptoms versus comorbid anxiety and depression diagnoses will be more predictive of suicidality. Furthermore, interviews with patients during

the upcoming project will allow for comprehensive examination of symptoms and clusters of symptoms. In this way, the current thesis informs the design of the second study by providing an in-depth examination of the anxiety-suicidality association. Such an examination may be useful in planning clinical intervention. Although there have been multiple studies on suicidal behavior, accurately predicting patient risk for suicidal behaviors is still difficult. Demonstrating the need for continued research the WHO (Nock et al., 2009), after conducting a multinational study involving 108,664 participants from 21 countries, recently remarked, "A crucial goal for future research is to better understand how and why such a diverse range of disorders are uniquely associated with suicide attempts" (p.13).

CHAPTER III

METHODOLOGY

Research

The question we are examining is if an anxiety diagnosis is in fact predictive of suicidality in an adult psychiatric inpatient population. If anxiety is predictive of suicidality, does comorbidity with depression have a synergistic effect causing an even greater risk for suicidality than the additive risks of having depression symptoms alone or anxiety symptoms alone? The hypotheses, tested in a cross-sectional sample of psychiatric adult inpatients, included the following:

- Presence of an anxiety diagnosis (any) will be statistically significantly
 associated with suicidality (either suicide ideation or attempts), after
 controlling for confounding by demographics.
- Additionally controlling analytically for the presence of other psychiatric diagnoses will not explain the expected association between anxiety diagnosis and suicidality.
- 3. The presence of both an anxiety disorder and a depressive disorder will have a synergistic effect on the risk of suicidality, as demonstrated by an increase in risk of suicidality among patients with both an anxiety diagnosis and a depression diagnosis compared to patients with neither diagnosis being greater than the sum of the increases of risk for patients with an anxiety diagnosis

alone and patients with a depression diagnosis alone, each compared to patients without either diagnosis.

Additional research questions that were examined but not formally statistically tested included the following,

- 4. Crude analysis will suggest that anxiety symptoms are statistically significantly associated with suicidality (either suicide ideation or attempts).
- 5. Crude analysis will suggest that depressive symptoms are statistically significantly associated with suicidality (either suicide ideation or attempts).
- 6. Crude analysis will suggest that the relative risk of suicidality for anxiety symptoms (presence versus absence) will be greater than the relative risk of suicidality for a diagnosis of an anxiety disorder (any yes/no).
- 7. Crude analysis will suggest that the relative risk of suicidality for depressive symptoms (presence versus absence) will be greater than the relative risk of suicidality for a diagnosis of a unipolar affective disorder (any yes/no). These crude analyses will inform the design of a subsequent, longitudinal study.
- 8. In an examination of two-way interactions, the presence of both anxiety symptoms and depressive symptoms will have a synergistic effect on the risk of suicidality, as demonstrated by an increase in risk of suicidality among patients with both anxiety symptoms and depression symptoms compared to patients with no symptoms being greater than the sum of the increases of risk for patients with anxiety symptoms alone and patients with depression symptoms alone, each compared to patients without any symptoms.

Research Methods

This study was completed in collaboration with, and advice from, Dr. Stephen Woolley, Senior Scientist at the Burlingame Center for Psychiatric Research and Education at the Institute of Living (IOL) in Hartford, CT, who also served as thesis advisor. The study was a quantitative, cross-sectional study drawing analytic goals from previous studies at the IOL. The study was completed under the previous Hartford Hospital protocol (HH #2118) and examined data routinely collected at the IOL. This cross-sectional analysis examined the association between anxiety and suicidality after controlling for diagnoses, psychopharmacology treatment and demographics. The Institute of Living/Hartford Hospital's Institutional Review Board (IRB) (protocol HH #2118 as referenced above) previously approved the research conducted for the purposes of this thesis in compliance with hospital and Federal research regulations for the protection of human subjects.

Sampling and Recruitment

Study subjects were drawn from the target population of adult (defined as greater than or equal to 18 years of age) psychiatric inpatients admitted for care during the 10-year period from January 2000-March 2009 at the IOL. This time period was selected in order to ensure adequate statistical power but to avoid possible changes in diagnostic practice that might occur over a longer time period. Participants were recruited using the IOL's on-going database of all admitted inpatients. The cross-sectional study sample consisted of 20,823 adults for whom data were collected upon admission to the IOL by the hospital's Outcome Assessment Program (OAP). In addition to the cross-sectional analysis, a substudy of patients who completed OAP follow-up post-discharge questionnaires during the final five

years of the ten-year period was examined to assess patients over time. The subsample included all 948 adult patients who voluntarily completed OAP questionnaires at 1 month follow-up and all 202 patients who voluntarily completed OAP questionnaires at 6 month follow-up. At no point did the research restrict or impact receiving appropriate mental health care as the IRB assured that the continuity and unfettered delivery of patient care and confidentiality was maintained.

Data Collection

The IOL routinely administers these self-reported OAP questionnaires upon hospital admission. Post-discharge, the IOL then mails OAP questionnaires to all previous inpatients at 1 month and 6 month follow-up. In addition, data recorded in the hospital's clinical database included inpatient diagnoses, demographics (such as age, race, sex, and ethnicity), and psychopharmacologic agents utilized in treatment. Symptom information recorded from post-discharge returned OAP responses and entered into the OAP database included anxiety and depression symptoms. The OAP questionnaires, developed by Dr. John Goethe at the IOL, which include symptom questions (see Appendix B) adapted from the McLean Hospital Basis-32 (Eisen, Grob, & Klein, 1989), is used in evaluating treatment outcome/improvement.

The two primary <u>independent variables</u> included diagnoses of anxiety and of depression. A diagnosis of anxiety consisted of PTSD, SAD, GAD, obsessive-compulsive disorder (OCD), and/or PD. A diagnosis of depression consisted of having any of the following disorders: major depressive disorder, mood disorder not otherwise specified, dysthymic disorder, or depressive disorder not otherwise specified. Bipolar disorder and its

variants were excluded from the study because mixed and manic states, which can involve symptoms relating to both depression and anxiety, would have rendered results uninterpretable. Anxiety symptoms were defined as having fear, anxiety, or panic with a response of "none" or "little" representing the absence of symptoms and "moderate," "quite a bit," or "extreme" representing the presences of symptoms. Similarly, the presence versus absence of depressive symptoms was rated on the same dichotomous scale.

During the study, factors targeted for control analytically included age, race, sex, ethnicity, psychopharmalogical agents, other mental illness diagnoses, and personal difficulty in the previous month with problems or areas of daily life (e.g., managing day-to-day, relationship with family, self-confidence, disturbing thoughts). These covariates were assessed for possible confounding of the analysis of risk of suicidality associated with anxiety or depression diagnoses. We collapsed categories of responses about difficulties to compare patients having "none," "little," or "moderate" difficulty with those having "quite a bit" or "extreme" difficulty. In addition, we examined these variables dichotomized with other cut-points.

The <u>dependent variable</u> for all analyses was suicidality coded dichotomously by collapsing categories of responses to a question asking about difficulty in their every day lives during the past month with "suicidal feelings or behavior (thinking about or attempting suicide by any means)." Absence of suicidality was indicated if patients indicated that they had "none" or "little" difficulty, and presence of suicidality if they had "moderate," "quite a bit," or "extreme" difficulty.

Data Analysis

The following analytical approach was based on approaches utilized in the Burlingame Center (Woolley, Fredman, Goethe, Lincoln, & Heeren, 2008; Diefenbach, Woolley, & Goethe, 2009) and executed under the direction of Dr. Woolley. Descriptive statistics were utilized to examine the properties of the population with implications for generalizability. Bivariate analyses were examined to further describe the study population, to assess the crude hypothesized associations, and to investigate the crude associations between potential confounders (identified in the literature or selected by the authors based on theories of the progression of suicidality) that might affect the results of hypothesis testing. Estimates of effects calculated in all analyses were odds ratios (ORs), and indications of the precision of these estimates were expressed as 95% confidence intervals (CIs) calculated by the approximate method. For these and stratified analyses, variables were dichotomous.

In addition, we examined the significance of pairwise associations of variables using t-tests, one-way analysis of variance (ANOVA) or Pearson correlation coefficients to assess associations involving continuous measures, and chi-square analysis for paired dichotomous variables. Following bivariate analysis, we stratified the analysis of the associations between primary exposures and outcomes by strata of covariates that appeared to be associated with these exposures and outcomes. These analyses allowed us to estimate the adjusted ORs while controlling for confounding by individual covariates. The ORs were estimated by calculating the Mantel-Haenszel pooled estimator of the ORs (Rothman & Greenland, 1998). Stratified analysis also allowed us to examine for modification of the effects of exposures on outcomes, and to characterize the effect on risk of suicidality of dual exposures to anxiety or depression and a covariate. In this way, we assessed interaction reflecting possible synergy or

antagonism of primary exposures with additional patient characteristics. We judged evidence of synergism or antagonism by applying the criteria that deviations of the combined effects from additivity of the individual effects were \pm 25% among the doubly exposed. Finally, we constructed binary logistic regression models of the risk of suicidality by controlling for demographics and other identified potential confounders, and selecting additional covariates using a stepwise selection algorithm (p = 0.10 inclusion/removal criterion).

CHAPTER IV

RESULTS

Univariate/Descriptive Analyses

From univariate analysis, it was determined that the population consisted of 10,767 females and 10,056 males for a total target population of 20,823 patients. The mean age was 43.0 years of age with patients ranging from age 18 to 102. Race was collapsed into a dichotomous variable with 13,020 patients who identified as White and 7,803 who identified as Black, Asian, Native American Indian, Hispanic, or Other, all of whom we categorized as Non-White. There were 8,821 inpatients carrying depression diagnoses and 2,967 patients carrying anxiety diagnoses. Expressing moderate to extreme suicidality, there were 12,126 individuals. A complete list of variables that we assessed is included below in Table 2A.

	Table 2A. Univariate Analysis (n = 20,823)							
		At admission						
Potential Confound	lers		N		%			
Demographics	gender	female	10,767		51.7			
		male	10,056		48.3			
	race/ethnicity	White	13,020		62.5			
		Black, Asian, Native American Indian, Hispanic, Other	7,803		37.5			
	age (years)		43.0	17.5	18-102			

Key Variables	<u> </u>						
Anxiety (Includes PTSD, SAD, GAD, OCD, and PD)		2,967	14.2				
	PTSD	1,866	9.0				
	anxiety disorder not PTSD	1,218	5.8				
Depression (Includes MDD, mood disorder NOS, dysthymic disorder, or depressive disorder NOS)		8,821	42.4				
	major depressive disorder	7,252	34.8				
	dysthymic disorder	163	0.8				
	depressive disorder NOS	1,328	6.4				
	mood disorder NOS	146	0.7				
Suicidality	greater than (but not including) little	12,126	58.2				

Potential Confou	nders	N	%	
Diagnoses	bipolar (BP) disorder	3,137	15.1	
	substance use disorder	10,134	48.7	
	Schizophrenia	2,565	12.3	
	schizoaffective disorder	3,103	14.9	
	other psychotic disorder	827	4.0	
	eating disorder	340	1.6	
	adjustment disorder	284	1.4	
	impulse control disorder	351	1.7	
	oppositional defiant disorder	5	0.0	
	attention deficit disorder	202	1.0	
	Paraphilia	34	0.2	
	conduct disorder NOS	28	0.1	
	Delirium	97	0.5	
	personality change d/t medical condition	14	0.1	
	pervasive developmental disorder	32	0.2	
	Dementia	1,669	8.0	
	cognitive disorder NOS	83	0.4	
	personality disorder (any)	6,862	33.0	
	borderline personality disorder	2,284	11.0	
		Mean	SD Range	
	Number of psychiatric diagnoses	2.0	1.4 0 - 10	
		N	%	
Medications	antidepressant anytime	14,901	71.6	
	SSRI anytime	9,909	47.6	
	TCA (tricyclics) anytime	672	3.2	
	MAOI anytime	24	0.1	
	other antidepressant anytime	8,622	41.4	
	antipsychotic anytime	14,497	72.0	
	anticonvulsant anytime	8,060	38.7	
	(mood stabilizers)			
	lithium anytime	1,643	7.9	
	stimulant anytime	140	0.7	
	benzodiazepine anytime	7,962	38.2	
	polypharm anytime	2,171	10.4	

Potential Confour	Potential Confounders				
ECT		975		4.7	
Symptoms	Difficulty managing day-to-day life (greater than moderate)	18,232	2 87.6		
	Difficulty managing day-to-day life (greater than little)	20,790		99.8	
Length of stay (days)		Mean	SD	Range	
, ,		7.0	10.0	1-224	

Univariate analyses for the 1 month and 6 month data subsets were then examined (Tables 2B and 2C). Although anxiety and depression symptom information was not available at admission, symptom information was collected at the 1 month and 6 month follow-ups.

	Table 2B. Univariate Analysis (n = 948) At one month follow-up								
Key variables	Variables	n	%						
Symptoms	anxiety symptoms (fear, anxiety or panic)	432	44.8						
	depressive symptoms (depression, hopelessness)	496	51.5						
	suicidal feelings or behaviors (moderate to extreme)	215	22.7						
	difficulty managing day to day	326	33.7						

Table 2C. Univariate Analysis (n = 202) At six month follow-up								
Key variables	Variables	n	%					
Symptoms	anxiety symptoms (fear, anxiety or panic)	81	39.3					
	depressive symptoms (depression, hopelessness)	99	47.8					
	suicidal feelings or behaviors (moderate to extreme)	45	22.3					
	difficulty managing day to day	55	26.6					

Bivariate Crude Analyses

By utilizing bivariate analysis, crude odds ratios (ORs) were determined in order to evaluate any possible associations between variables that suggest these variables might confound the anxiety diagnosis-suicidality or the depression diagnosis-suicidality association. A diagnosis of anxiety or depression was associated with an increased risk of having both anxiety and depression (OR = 3.13; CI = 2.88, 3.39). Furthermore, when looking

at the crude analysis, depression was associated with an increased risk for suicidality (OR = 3.53; CI = 3.33, 3.75) and anxiety was associated with an increased risk for suicidality (OR = 2.80; CI = 2.56, 3.07). Impulse control disorder, oppositional defiant disorder, and paraphelia were not associated with anxiety, depression or suicidality. Numerous diagnoses were associated with risk for suicidality as shown below in Table 3A.

Male gender was associated with a lower risk of having anxiety and depression (OR = 0.39; CI = 0.36, 0.43 and OR = 0.56; CI = 0.53, 0.59 respectively), and was associated with a slightly lower risk for suicidality (OR = 0.91; CI = 0.86, 0.97). Being Non-White was associated with a decrease in the odds of having anxiety and depression but an increase in the risk for suicidality. Also, antidepressants, including selective serotonin reuptake inhibitors (SSRIs), stimulants, and polypharmacology (in this case, the use of more than one psychopharmacological agent) were associated with an increase in risk for suicidality. Lithium and antipsychotics were the only medications associated with a decreased risk for suicidality from the crude analysis. Difficulty managing day-to-day life, both greater than a little and greater than moderate, was associated with a significant elevation in the odds ratio for suicidality (greater than a little OR = 3.16; CI =2.89, 3.44; greater than moderate OR = 9.04; CI = 7.33, 11.15).

	Table 3A. Bivariate Analysis At Admission									
	(n = 20,823)									
OR = o	dds ratio						Suggests dec	reased risk	of suicda	ality 🔲
CI = co	nfidence interval, 95%						Suggests inc	reased risk	of suicid	ality
A				nxiety Diagnoses $(n_1 = 2,967)$ $(n_2 = 8,821)$ $(Includes MDD, mood disorder NOS, dysthymic disorder, or depressive disorder NOS)$			21) d disorder order, or	Suicidality $(n_3 = 12,126)$ (greater than little)		
	Variable	% of n ₁	OR	CI	% of n ₂	OR	CI	% of n ₃	OR	CI
	Gender: male	29.46	0.39	0.36, 0.43	40.02	0.56	0.53, 0.59	47.34	0.91	0.86, .97
Demographics	Race: Other (Black, Asian, Native American Indian, Hispanic, Other)	32.82	0.79	0.73, 0.86	36.40	0.92	0.87, 0.98	40.63	1.39	1.31, 1.47
ph			Yes	No		Yes	No		Yes	No
ics	Age		40.19	46.01		44.45	45.71		40.67	51.46
				.91, $p < 0.05$			17, p < 0.05			6.14, p < 0.05
	Anxiety	XXXX	XXXX	XXXX	22.23	3.13	2.88, 3.39	18.94	2.80	2.56, 3.07
Key Variables	Depression (Includes MDD, mood disorder NOS, dysthymic disorder, or depressive disorder NOS)	66.09	3.13	2.88, 3.39	XXXX	XXX	XXXX	54.55	3.53	3.33, 3.75
Symptoms	Difficulty managing day- to-day life (greater than moderate)	90.76	1.44	1.27, 1.65	87.56	1.00	0.92, 1.09	92.77	3.16	2.89, 3.44
otoms	Difficulty managing day- to-day life (greater than little)	97.60	1.58	1.23, 2.02	96.12	0.90	0.77, 1.04	99.04	9.04	7.33, 11.15

			Anxie	ty Diagnoses		Depress	sion Diagnoses		,	Suicidality
	Variable	% of n ₁	OR	CI	% of n ₂	OR	CI	% of n ₃	OR	CI
	Dementia	1.35	0.14	0.10, 0.19	3.78	0.31	0.28, 0.35	2.44	0.13	0.12, 0.15
	Schizophrenia	2.53	0.16	0.13, 0.20	0.49	0.02	0.01, 0.03	6.70	0.28	0.26, 0.31
	Schizoaffective	9.44	0.56	0.49, 0.63	1.07	0.03	0.03, 0.04	14.12	0.86	0.80, 0.93
	Major depressive disorder	60.47	3.46	3.19, 3.75	82.21	N/A	N/A	45.56	3.37	3.17, 3.60
	Other psychotic disorder	1.42	0.31	0.23, 0.43	1.45	0.24	0.20, 0.29	2.64	0.44	0.38, 0.51
	PTSD	62.89	N/A	N/A	13.50	2.62	2.37, 2.89	12.63	3.61	3.19, 4.07
	Anxiety disorder not PTSD	41.05	N/A	N/A	9.64	3.37	2.97, 3.82	7.03	1.73	1.52, 1.96
D	Substance use disorder	48.50	0.99	0.92, 1.07	50.11	1.11	1.05, 1.17	56.39	2.12	2.00, 2.24
iag	Eating disorder	3.71	2.95	2.34, 3.72	2.68	3.15	2.49, 3.97	2.19	2.57	1.99, 3.32
Diagnoses	Adjustment disorder	0.91	0.63	0.42, 0.94	1.00	0.61	0.47, 0.78	1.68	1.84	1.42, 2.39
ses	Attention deficit disorder	1.79	2.16	1.58, 2.96	1.13	1.34	1.01, 1.77	1.12	1.48	1.10, 1.99
	Bipolar disorder	15.00	0.99	0.89, 1.11	0.67	0.02	0.02, 0.03	15.11	1.01	0.93, 1.09
	Conduct disorder	0.00	N/A	N/A	0.02	0.10	0.03, 0.44	0.03	0.12	0.04, 0.34
	Delirium	0.17	0.33	0.13, 0.80	0.40	0.77	0.51, 1.16	0.22	0.28	0.18, 0.43
	Pervasive developmental disorder	0.27	2.01	0.90, 4.48	0.11	0.62	0.29, 1.31	0.08	0.33	0.15, 0.69
	Cognitive disorder NOS	0.27	0.64	0.31, 1.33	0.57	2.07	1.33, 3.21	0.35	0.77	0.50, 1.19
	Personality disorder	53.05	2.69	2.48, 2.91	41.06	1.88	1.78, 2.00	43.54	3.47	3.25, 3.70
	Borderline Personality disorder	27.00	4.08	3.71, 4.50	14.37	1.82	1.66, 1.98	15.99	4.61	4.10, 5.19
	Antipsychotic anytime	69.87	0.89	0.81, 0.96	56.15	0.25	0.23, 0.27	68.12	0.62	0.58, 0.66
	Antidepressant anytime	90.63	4.47	3.94, 5.08	94.38	13.85	12.56, 15.27	83.37	4.09	3.84, 4.36
M_{ϵ}	SSRI anytime	62.89	2.07	1.91, 2.24	67.03	4.07	3.84, 4.32	56.92	2.50	2.36, 2.65
edic	Anticonvulsant anytime	41.15	1.13	1.04, 1.22	25.46	0.36	0.34, 0.39	38.28	0.96	0.91, 1.01
ati	Lithium	6.07	0.72	0.62, 0.85	2.22	0.17	0.14, 0.19	7.22	0.81	0.73, 0.89
Medications	Benzodiazepine anytime	50.29	1.78	1.65, 1.93	39.69	1.11	1.05, 1.18	37.29	0.91	0.86, 0.96
	Polypharm anytime	14.80	1.62	1.44, 1.81	7.38	0.55	0.50, 0.61	12.10	1.56	1.42, 1.72
	Stimulant anytime	0.71	1.06	0.67, 1.69	1.10	3.09	2.16, 4.43	0.83	1.87	1.29, 2.70
ECT	ECT	5.29	1.17	0.98, 1.39	7.63	3.20	2.79, 3.68	4.64	0.98	0.86, 1.11

We then turned to bivariate analyses comparing admission data with 1 month and 6 month data. Whereas the anxiety diagnoses examined in crude bivariate analysis at follow-up were associated with a decrease in suicidality, anxiety symptoms were associated with an increased risk of suicidality at 1 month post-discharge (OR = 8.30, CI = 5.70, 12.09) and at 6 months post-discharge (OR = 18.69, CI = 7.36, 45.45). Additional crude analyses for depression symptoms and difficulty managing from day-to-day at 1 month and 6 month follow-up are described in Table 3C and 3D.

Table 3B. Subsample: Bivariate at Admission For Comparison $(n = 2,040)$									
	Anxiety Diagnoses (n ₁ =276)			Depressive Diagnoses (any except bipolar) (n ₂ =869)			Suicidality (n ₃ =942) (moderate to extreme)		
Variable	% of n ₁	OR	CI	% of n ₂	OR	CI	% of n ₃	OR	CI
Anxiety Diagnoses	XX	XX	XXXX	21.63	3.40	2.59, 4.45	13.69	.93	0.68, 1.28
Depressive Diagnoses	68.12	3.40	2.59, 4.45	XX	XX	XXXX	44.06	1.10	0.88, 1.37
Difficulty Managing Day to Day	68.48	0.97	0.47, 2.00	67.78	1.17	0.70, 1.96	99.04	13.08	6.39, 26.77

Table 3C. Bivariate at 1 Month Follow-up (n = 948)										
	Anxiety Symptoms (n ₁ =432) (fear, anxiety or panic)				Depressive Symptoms (n ₂ =496) (depression, hopelessness)			Suicidality (n ₃ =215) Suicidal feelings or behaviors (moderate to extreme)		
Variable	% of n ₁	OR	CI	% of n ₂	OR	CI	% of n ₃	OR	CI	
Anxiety Symptoms	XX	XX	XXXX	70.56	11.78	8.64, 16.05	80.93	8.30	5.70, 12.09	
Depressive Symptoms	81.02	11.78	8.64, 16.05	XX	XX	XXXX	92.56	26.29	14.41,47.96	
Difficulty Managing Day to Day	56.71	7.60	5.59, 10.33	53.63	8.22	5.93, 11.41	66.05	6.00	4.32, 8.34	
Anxiety Diagnoses	11.11	0.87	0.59, 1.29	12.10	1.06	0.71, 1.56	10.70	0.89	0.54, 1.43	
Depressive Diagnoses (any except bipolar)	45.60	1.09	0.85, 1.41	46.37	1.21	0.94, 1.56	46.05	1.10	0.81, 1.50	

Table 3D. Bivariate at 6 Month Follow-up (n=202)									
	Anxiety Symptoms			Depressive Symptoms			Suicidality		
	$(\mathbf{n_1} = 81)$			(n ₂ =99)			(n ₃ =45)		
	(fear, anxiety or panic)			(depr	ession, h	opelessness)	Suicidal feelings or behaviors (moderate to extreme)		
Variable	% of	OR	CI	% of	OR	CI	% of	OR	CI
	\mathbf{n}_1			n ₂			n_3		
Anxiety Symptoms	XX	XX	XXXX	73.74	36.50	15.58, 85.52	86.67	18.69	7.36, 47.45
Depressive	90.12	36.50	15.58, 85.52	XX	XX	XXXX	97.78	88.00	11.79, 656.69
Symptoms									
Difficulty	55.56	16.57	7.38, 37.23	47.47	13.30	5.61, 31.50	64.44	9.06	4.32, 19.02
Managing									
Day to Day									
Anxiety	14.81	1.11	0.50, 2.46	18.18	1.96	0.88, 4.39	11.11	0.77	0.27, 2.16
Diagnoses									
Depressive	51.85	1.29	0.73, 2.25	51.52	1.33	0.77, 2.30	53.33	1.35	0.69, 2.62
Diagnoses									
(any except									
bipolar)									

Stratified analysis was then used to assess for evidence that demographics, diagnoses, or pharmacological agents confounded the anxiety diagnosis - suicidality association. These analyses suggest that antidepressant use and having greater than little difficulty (includes "moderate," "quite a bit," or "extreme") managing day-do-day variables confound but do not modify the anxiety diagnosis – suicidality association. We found no evidence that the variables examined confounded the depression diagnosis – suicidality association.

Two-way interactions were then used to assess for synergism and antagonism. As described in the Methods section, if we found that excess risk in the doubly exposed category was greater than the sum of the two singly exposed categories by a margin of \pm 25%, synergism was suspected.

Analysis of anxiety and depression diagnoses provided no evidence of synergism in the risk of suicidality. Evidence of synergism was found between an anxiety diagnosis and,

• gender

- difficulty managing day-to-day greater than a little
- difficulty managing day-to-day greater than moderate
- antipsychotics
- antidepressants (not the subcategory of SSRI's)
- polypharmacological agents
- stimulants
- borderline personality disorder.

A depression diagnosis and the following variables met our criterion for synergism,

- difficulty managing from day-to-day greater than a little
- difficulty managing from day-to-day greater than moderate
- substance use disorder
- antidepressants (slight)
- lithium

If the doubly exposed category was <u>less than</u> the sum of the two singly exposed by a margin of \pm 25%, antagonism was suspected. The only variable that appeared to act antagonistically on the effect of anxiety (diagnoses) on suicidality was eating disorder. Variables that appeared to act antagonisit ally on the effect of depression (diagnoses) on suicidality included race, benzodiazepines, and ECT.

Through analysis of two-way interactions at 1 month, findings suggested that anxiety symptoms and depressive symptoms acted synergistically to increase the risk of suicidality (see Table 4 below). Evaluating two-way interactions at 6 month was not possible due to devisors of 0 in the denominators.

Table 4. Example of assessing interaction on an additive scale for two dichotomous exposures and a dichotomous outcome

ONE MONTH FOLLOW-UP										
	Exp	oosure 1			Non-exposure 1					
	Exposure 2	Non-exposure 2			Exposure 2	Non-exposure 2				
Cases	163	35		Cases	9	3				
Non-Cases	180	101		Non-cases	70	374				
Total	343	136		•	79	377				

Exposure 1= Difficulty with depression, hopelessness at 1 month follow-up Exposure 2 = Difficulty with fear, anxiety, panic at 1 month follow-up

Cases = Difficulty with suicidal feelings or behaviors at 1 month follow-up

Additivity criteria => If the equality holds, no interaction

$$\frac{R(AB)}{R(\overline{A}\overline{B})} = \frac{R(\overline{A}B)}{R(\overline{A}\overline{B})} + \frac{R(A\overline{B})}{R(\overline{A}\overline{B})} - 1$$

112.89 \neq 58.23 => Interaction or synergism as equality does not hold by a margin > 25%

Binary Logistic Regression

The next analysis we performed was binary logistic regression (results shown in Table 5). The model fit was assessed for the regression model of risk of suicidality at admission, and the Nagelkerke R Square was 0.35. Variables that were forced into the equation included anxiety, depression, age, race, and gender. The remainder of the variables were entered as covariates and selected for retention in the model by forward stepwise conditional method. Anxiety diagnoses was associated with an increased risk for suicidality. After controlling for demographics, diagnoses and medications, the OR for anxiety diagnosis was 1.38 (CI = 1.24, 1.35) indicating that an anxiety diagnosis was statistically significantly associated with a 38% increased risk of suicidality. Many mental illnesses including axis II diagnoses were associated with an increase in suicidality including schizoaffective, borderline personality disorder, substance abuse disorder, adjustment disorder, and bipolar disorder. Certain diagnoses such as schizophrenia decreased the risk for suicidality (OR =

0.60, CI = 0.53, 0.68). Some medications decreased the risk for suicidality while antidepressants, for example, increased the odds ratio for sucidality. Again, difficulty managing day-to-day significantly increased suicidal risk more than 7 fold (OR = 7.86, 6.24, 9.90). The following variables were eliminated during stepwise regression: eating disorder, impulse control disorder, oppositional defiant disorder, paraphilia, conduct disorder, delirium, personality change due to a medical condition, antipsychotic (any), anticonvulsant (any), stimulant (any), and ECT.

In subanalyses, we then analyzed suicidality at 1 and 6 month follow-ups, forcing the variables that were maintained in the above model into a new binary logistic regression analysis. The results were not statistically significant as demonstrated in Table 5. In these analyses, for some variables scant data resulted in variables included in the cross-sectional analysis being dropped.

Table 5. Regressio	n Analyses:	: Variables Remaining	In the Equa	ation, OR and 95% CI			
	(n = 20, 8)	At admission 823; missing 55across ious data points)	At on	e month follow-up $n = 530$	At six month follow-up $n = 115$		
	OR	CI	OR	CI	OR	CI	
Anxiety	1.38	1.24, 1.53	0.89	0.46, 1.74	0.42	0.09, 1.88	
Depression	2.64	2.38, 2.94	0.88	0.43, 1.76	0.98	0.22, 4.27	
Gender (Males)	1.25	1.17, 1.35	0.86	0.54, 1.38	0.46	0.15, 1.37	
Race (Non-White)	1.35	1.26, 1.46	1.02	0.64, 1.63	0.92	0.32, 2.66	
Age	0.97	0.97, 0.98	1.01	0.99, 1.03	1.02	0.98, 1.06	
Dementia	0.49	0.42, 0.57	1.01	0.38, 2.67	0.17	0.01, 3.52	
Schizophrenia	0.60	0.53, 0.68	0.71	0.30, 1.67	0.22	0.02, 2.19	
Schizoaffective	1.24	1.10, 1.40	0.99	0.44, 2.27	0.46	0.06, 3.36	
Other psychotic disorder	0.67	0.56, 0.80	0.75	0.19, 2.93	0.33	0.02, 4.99	
Substance use disorder	1.42	1.32, 1.53	1.21	0.73, 2.00	0.73	0.23, 2.30	
Adjustment disorder	1.85	1.38, 2.48	1.40	0.26, 7.62	0.62	0.05, 8.06	
Attention deficit disorder	0.67	0.48, 0.92	4.05	0.51, 32.01	N/A	N/A	
Bipolar disorder	1.53	1.35, 1.73	0.73	0.32, 1.69	0.42	0.07, 2.62	
Pervasive developmental disorder	0.18	0.08, 0.39	0.00	N/A	N/A	N/A	
Borderline Personality disorder	2.78	2.43, 3.18	1.33	0.65, 2.71	2.37	0.49,11.62	
Antidepressants (any)	2.97	2.75, 3.22	1.35	0.80, 2.29	0.96	0.23, 3.98	
Lithium (any)	0.90	0.79, 1.01	1.02	0.43, 2.42	0.60	0.31, 2.42	
Benzodiazepine (any)	0.85	0.79, 0.91	0.71	0.45, 1.10	0.87	0.31, 2.42	
Difficulty managing day-to-day greater than a little	7.86	6.24, 9.90	0.87	0.31, 2.46	0.00	N/A	

CHAPTER V

DISCUSSION

Our study found that, in a sample of adult psychiatric hospitalized inpatients, anxiety and depression diagnoses were associated with approximately 40% and 160% increased risk of suicidality, after controlling for demographic and clinical confounders. Furthermore, our analysis provided evidence that the effects on risk of suicidality of these two diagnostic groups were independent, neither synergistic nor antagonistic. However, our analysis provided evidence that many other personal and clinical factors did interact with either anxiety or depression diagnosis to modify these diagnoses' association with suicidality.

We have already established that the role of anxiety in suicidality is complicated. In the passage below, noted author William Styron provides a glimpse at the damaging effects of anxiety:

But it is my conviction now that alcohol played a perverse trick on me when we said farewell to each other: although, as everyone should know, it is a major depressant, it had never truly depressed me during my drinking career, acting instead as a shield against anxiety. Suddenly vanished, the great ally which for so long had kept my demons at bay was no longer there to prevent those demons from beginning to swarm through the subconscious, and I was emotionally naked, vulnerable as I had never been before. (Styron, 1990, p. 43).

In William Styron's memoir, *Darkness Visible*, he described how anxiety played a significant role in the progression and development of his depression, resulting in suicidal ideation. In fact, Styron believed alcoholism is what dampened his anxiety and staved off his depression. Despite such vivid accounts detailing how anxiety can prompt suicidality, there is still much disagreement about the anxiety – suicidality association. For example, one study not only

suggested that comorbid panic disorder and depression in psychiatric inpatients (each patient had at least one major depressive episode with or without a suicide attempt history) did not increase lifetime suicide attempts but instead that higher levels of anxiety and agitation offered protection against suicidality in the target population of 272 patients (Placidi et al., 2000). However, as already described in the results, our study within the inpatient adult population demonstrated that anxiety was statistically significantly associated with suicidality after controlling for confounders including other psychiatric diagnoses (such as depression). Even though our research did not delineate ideation from attempts or completed suicide, our results suggest that clinicians need to be aware of the significant role that anxiety may play in the development of suicidal behaviors. This conclusion is reinforced by the WHO's cross-national analysis, examining the association of mental disorders and suicidal behavior, which suggested that clinicians should be mindful that anxiety may be an important risk factor influencing whether a patient transitions from suicidal thoughts to attempts or even to completed suicide (Nock et al., 2009). Although we did not find synergism or antagonism when an anxiety diagnosis was coupled with a unipolar depression diagnosis, both diagnoses were statistically significantly associated with increased suicidality, providing evidence that an anxiety disorder should be considered a risk factor, independent of depression, for suicidal behaviors.

Further suggesting an association between anxiety and suicidality, benzodiazepines which are used in the treatment of anxiety disorders, were associated with a reduced risk of suicidality in both the bivariate and regression analyses. Therefore, the administration of benzodiazepines in a patient who presents with an anxiety diagnosis could potentially be therapeutic in preventing suicidal behaviors. Antipsychotics, anticonvulsants, and stimulants

were not retained for inclusion in the regression model, indicating that these psychopharmacological agents were not statistically significantly associated with suicidality after controlling for other factors' effects. However, antidepressants were associated with increased risk of suicidality, suggesting that care should be taken when administering this medication and that patients should be carefully monitored for signs of developing suicidality. In fact, one commonly listed side effect of certain antidepressants is anxiety (Mayo Foundation for Education and Research, 2008) which perhaps may account for the increased suicidal risk found in our sample, despite these medications' presumed alleviation of depressive symptoms. Joiner (2010) described that antidepressants might be "activating" and that too much activation might result in anxiety, agitation, and restlessness, which he notes as indicators for high risk of suicidality. In this author's (MT) personal communication with T. Joiner, he remarked:

I often say in trainings "I've never heard anyone about to die or almost die by suicide described as sluggish... agitated, on edge, can't sleep, hyped up, nervous energy, yes - but never sluggish." This state is key to understanding suicidal behavior, and it is underappreciated. (March 14, 2010)

Fawcett (Jancin, 2003) made similar references regarding suicidality at the Annual Conference of the American Association of Suicidology (Santa Fe, 2003). Fawcett even indicated that it was his professional goal to have the severity of a patient's anxiety assessed as part of routine clinical suicidal assessments. In a study, Busch and Fawcett (2003) examined the suicide risk of inpatients. Chart reviews were completed on 76 patients between the ages of 15-76 who committed suicide while they were in inpatient treatment. Items from the Schedule for Affective Disorders and Schizophrenia (SADS) and traditional risk factors (including previous suicide attempt and suicidal ideation) had been evaluated

during the week before the patient committed suicide. Surprisingly, 78% denied any suicidal ideation during their "last communication" and the researchers concluded that the standard risk predictors were in fact "not predictive" for acute risk (Busch & Fawcett, 2003).

However, in the last week of their lives, 79% of inpatients had met the SADS criteria for severe anxiety or agitation. This raises the point that suicide assessments that only focus on questions regarding ideation, intent, plan and lethality of method may have limited utility as predictors of completed suicides. Furthermore, due to the tremendous stigma of suicide (Joiner, 2005), people may feel reluctant to admit suicidality; however, one could surmise that patients would more readily admit to severe anxiety (as the above study suggests) giving credence to Fawcett's professional goal.

Obviously not everyone with symptoms of anxiousness meets criteria for a *DSM-IV-TR* (2000) anxiety diagnosis. Logically, because our research indicated that an anxiety diagnosis was associated with increased suicidality (after controlling for numerous covariates), the next step was to discern if the presence of the symptoms of anxiety (without an anxiety diagnosis or by controlling for various anxiety diagnoses) was predictive of suicidality. In our preliminary analysis of the presence versus absence of anxiety symptoms in adult inpatients (who did not necessarily have an anxiety diagnosis) at 1 month post discharge, the presence of anxiety symptoms was associated with an 8-fold increased suicidal risk. One possible explanation is that anxiety may in fact be one of the underlying commonalities across mental illnesses that accounts for the risk of suicidality. One could argue that the presence of mental illness, and perhaps any type of illness that is not completely curable, is indeed anxiety provoking. Although our findings were not conclusive

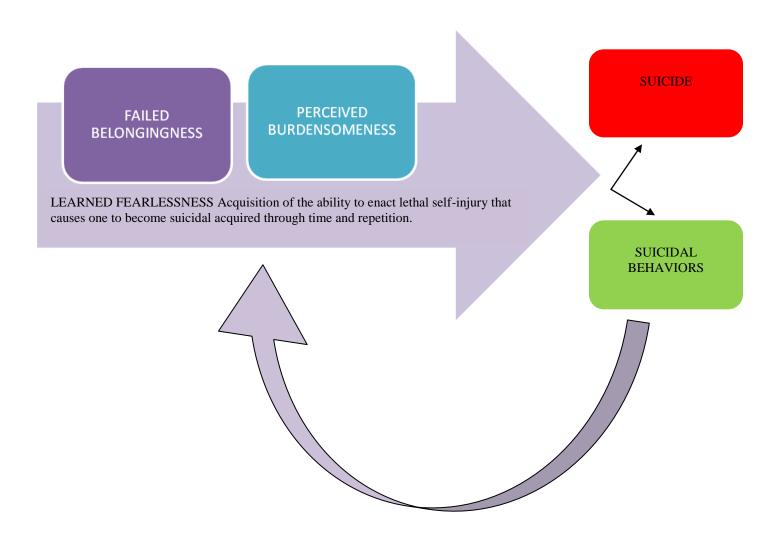
of this point, these preliminary data suggest that an analysis of symptoms or symptom clusters may better predict suicidal risk than a *DSM-IV* diagnosis.

For example, in this study difficulty managing from day-to-day (greater than a little), an indicator of stress that might be expected to increase anxiety, was strongly associated with a 7-fold increased risk for suicidality. However, *The Columbia Suicide Severity Rating Scale*, (Posner et al., 2008) and *The Reasons for Living Inventory* (Linehan, Goodstein, Nielsen, & Chiles, 1983) do not directly assess client anxiety or difficulty managing from day-to-day. Nonetheless, our data suggest that instruments such as these might be complemented by asking about anxiety and difficulty managing from day-to-day and that asking these clinical questions may be important because suicidal patients may be reluctant to admit they are at risk (Busch & Fawcett, 2003).

In addition, when analyzing two-way interactions in a preliminary analysis, we found that the risks associated with anxiety symptoms and depression symptoms were synergistic; i.e., the risk in patients having both symptoms exceeded the risk expected from the additive effects of suicide risk due to depression symptoms alone plus suicide risk due to anxiety symptoms alone. Further research is warranted to examine the effects of symptom clusters on suicidal risk. Intimating that there is not just one factor responsible for suicidality, in Joiner's personal correspondence (personal communication, March 14, 2010) he indicated that depression, anxiety and numerous other factors exert influence on suicidality. However, Joiner stated that he believed that these biological, social, or environmental risk factors exert influence through a common pathway that ties together dozens of risk factors. The theoretical model that he proposes, which outlines his idea of the common pathway, is that suicidality occurs when there is a combination of learned fearlessness ("a type of habituation to suicidal

behaviors which impedes the fear and pain associated with self-harm"), and two simultaneously occurring long-term mind-states (Joiner, 2005, p. 59). The first mind state is perceived burdensomeness where a person perceives that he (she) is a burden and his (her) death is worth more than his (her) life to others. The second mind-which is termed failed belongingness is the person's perception that he (she) is completely alienated from others (see Figure 1 below).

FIGURE 1. ADAPTED FROM JOINER: WHY PEOPLE DIE BY SUICIDE



Adapted with permission from T. Joiner, personal communication, May 14, 2010

The relevance of Joiner's theory to the current study's findings are that multiple factors might act in concert to overcome the will to live, indicating that more research about the effects of symptoms and symptom clusters is needed to assess the independent and combined roles they may play in the risk of suicidality, and the need to further qualify the nature of the anxiety. Additional analysis of anxiety and the risk of suicidality may indicate that the symptom of anxiety is truly part of the "common pathway" and not an ancillary contributing factor. In this case, anxiety associated with suicidality might be examined for evidence that it has specific qualities that produce so much discomfort that the patient inherently can no longer cope with the pain and needs an immediate change. Fawcett and Harris (2001) described it as a "ruminative form of anxiety," eloquently stating "the constant repetition of this increasingly fearful idea becomes inescapable torture for the patient, true psychic pane, from which the idea that the only escape is death seems a logical conclusion" (p. 480). In an examination of Joiner's theoretical model, one might ask what came first, the habituation/learned fearlessness to risk bodily harm or the ruminative anxiety about continuing to cope in the world? This author (MT) suggests that a person's inability to tolerate this frenetic form of anxiety may be the common pathway to suicidality and that an acquired ability to enact lethal self-injury through time and repetition, although certainly a risk factor, is not necessarily part of "the common pathway."

If learned fearlessness was in fact the common pathway for completed suicide, one would potentially expect that with each additional trauma [as Joiner (2005) indicates that repetitive exposure to trauma could be a contributing factor to learning fearlessness] there would be an additive or supra-additive effect of each trauma increasing the risk for suicidal ideation and attempt. However, in a study recently conducted with data from the WHO

World Mental Health Surveys (Stein et al., 2010), findings suggested that although there was a dose-effect of an increase in suicidal ideation and attempt as the number of trauma exposures increases, there is a subadditive effect in the strength of the association with suicidal ideation and attempt. In other words, the magnitude of the effect of each additional trauma on suicidality, decreases with each exposure (Stein et al., 2010). Again, future research on anxiety symptoms in relationship to suicidality is warranted.

Limitations

Measurement errors may have occurred because data were obtained from clinical records and via patient self-reports, and because of retrospective reports and any limitations in scales. For example, when measuring suicidality (an ordinal variable) we cannot assume that the magnitude of the change in morbidity between "no" and "little" suicidality is equal to the magnitude between "quite a bit" and "extreme." This limitation was addressed by dichotomizing suicidality while assuming the ordinal nature of the original Likert scale. For the substudy analysis, there is the possibility that selection bias was introduced if only certain categories of patients were willing to respond to the questionnaires mailed at 1 and 6 month follow-up.

An additional limitation involves the lack of symptom (in contrast to diagnoses) information recorded at admission and discharge into the hospital database during the designated study period. As a result, we were unable to draw comparisons between admission and post-discharge anxiety symptoms, and thus we could not establish that independent variables preceded suicidality. Also, because the population consisted only of psychiatric inpatients, there is a question about generalizability to a broader clinical population or to the general population at-large.

Although there are limitations in this study, the potential benefit to clinical practice from a large study including examination of combinations of potential risk factors not thoroughly examined in previous research has merit. This study provides additional understanding about the associations of anxiety and depression with suicidality which has obvious important implications for patient safety.

Conclusions

In conclusion, we found that anxiety diagnoses were associated with increased suicidal risk when controlling for confounding in an inpatient adult population. As anticipated, depression diagnosis was also associated with suicidality, but this diagnosis did not explain the statistically significant association between anxiety diagnosis and suicidality. We did not find a synergistic effect on suicidality when comorbid anxiety and depression were present. Preliminary analyses suggest that anxiety symptom information may be a better predictor of suicidality than the presence of a *DSM-IV* diagnosis. Additional research is warranted to examine the nature of anxiety symptoms that precede suicidal behaviors and to examine if symptom clusters work synergistically to increase suicidal risk as well as what symptom clusters present the greatest suicidal risk.

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APPENDIX A

HARTFORD HOSPITAL

OFFICE OF RESEARCH ADMINISTRATION. 80 SEYMOUR STREET P () HCX 60.97 HARTHOR 1 CT 00102 5037 369044-2961 FAX 960/545 5112

October 5, 2009

Dr John Goeth⊜ c/a Stephen Woolley, PhD Burlingame Center - IOL

Re: #2118 "Psychiatric Treatment Practices and Patient Outcomes"

Dear Dr. Goethe:

We have reviewed your request to allow Monica Tronsky to collect data under the above referenced protoco in fulfillment of her master's thesis in Smith College's School of Social Work. The understanding is that she will be accessing IOL patient data stored in the Hartford. Hospital medial database and the IQL's Outcome Assessment Program database to examine "The Association between Unipolar Depressive Disorder, Anxiety and Suicidality." The HRPP office has confirmed that she has properly registered through the Volunteer Services Department and has completed the required human subjects protection training through the CITI Program.

This request has been given expedited review by the Institutional Review Board (Assurance #FWA00000801) and was approved as submitted. It will be presented as information to the full board at the next meeting

Sincerely yours,

Robert b. Siegel, M.D., Chairman

Institutional Review Board

clb

APPENDIX B

	The Institute of Living's Outcome Assessment Program Questionnaire Version 3.0 Follow - Up Assessment (Adult)														
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	O None					•			-			•			
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	 Seven to Fifteen to 				s				O Do no O Not ap						
3. W	hen was you			-		ıt adn	nissio	n to		-	ital?				
	Less thatOne to th								ears ago ars ago						
	O Four to e	eleven n	nonths	ago		Not:	appli	cable	, because			l to a ps	ychiatric	hospital	
4.0	One to tv	•	_				-		italized a			had?			
4. 0	ver your who				-				-		•	nad?			
5. Si	nce the abov	e disch	arge, h	ave	you	been a	dmitt	ted to	any part	ial hospita	l or day tr	eatment	progran	ı (including	
tl	he IOL)? ○ None = 0	3.Om	O.T.		O.T.	hma	0.0	lour	○ Eine	0.6 or m					
6. If	you were ad											vour dis	charge.	what was th	e
	tal amount o	f time y	ou we	•					II the hosp	italization	s together)?	ciaige,	what was th	
	Less thatSeven to			s					O Twen		ys or more	,			
	O Fifteen to		_		/S				O Not ap	pplicable					
7. W	hen was you				nissio		_		_		ay treatm	e nt prog	ram?		
	O Less that One to the								five years ore years a						
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The Institute of Living's Outcome Assessment Program Questionnaire Version 3.0										
	Follow - Up Assessment	(Adult)	_							
Episode										
Please answer each question by filling in the item which best represents the treatment services you have										
received during the last 30 days. Please ch	oose only one response	for each question	z.							
Attending Individual Psychotherapy										
Once a week	O More than once a we		O Every 2 or 3 weeks							
O About once a month O Not at all	O Less often than every	y three months	O About every three months							
10. Attending family or couples therapy										
Once a week	○ More than once a we	ek	O Every 2 or 3 weeks							
 About once a month 	O Less often than every		O About every three months							
○ Not at all										
Attending Group Psychotherapy										
Once a week	More than once a we		© Every 2 or 3 weeks							
O About once a month O Not at all	O Less often than every	y three months	O About every three months							
12. Attending AA or NA meetings or oth	er support groups									
Once a week	○ More than once a we	æk	O Every 2 or 3 weeks							
O About once a month O Not at all	 Less often than every 	y three months	O About every three months							
13. Attending a medication group	○ M th		0 F 2 3							
 ○ Once a week ○ About once a month 	 More than once a we Less often than every 		O Every 2 or 3 weeks O About every three months							
O Not at all		,								
 Individual physician visit for psychi 	atric medication only									
 Once a week About once a month 	O More than once a we		O Every 2 or 3 weeks							
O Not at all	Less often than every	y three months	About every three months							
15. Other medical or physician visits (not	included above)									
Once a week		æk	© Every 2 or 3 weeks							
O About once a month	 Less often than every 	y three months	O About every three months							
O Not at all 16. Participating in vocational rehabilita	tion:									
O Yes	□ No									
17. What was your current employment:		s?								
			dia-kitisa damakan da							
O Employed full-time, more than 35			disability through work							
O Employed part-time, less than 35		O Homemaker								
 Not employed but looking for wo 		O Student, full-t	ime							
 Not employed and NOT looking f 	or work	○ Retired								
○ Not employed and on Social Security disability										
18 How estisfied are you with your own	ent amployment etatue!	,								
 How satisfied are you with your currence Not at all satisfied Slightly sa 			satisfied O Extremely satisfied							
Cristal an Salanica Congility at			•							
Page 2/5	fupadult-c.frm		30649							
This questionnaire is adopted from the BAS	IS-32 ©1985 by Evaluative	Service Unit, McLe	an Hospital.							

	The Institute of Living's Outcome Assessment Progra Follow - Up Assessment (A		tionnaire	Version	3.0							
	Episode	iddit)										
Using durin	Instructions: Below is a list of problems and areas of daily activities in which some people experience difficulties. Using the scale below, please fill in the bubble that best describes how much difficulty you have had in this area during the past month. Please respond to each item. If you feel that an area is not applicable for you, please indicate "No difficulty" by filling in the bubble in that column.											
	1	<u>No</u> Difficulty	A Little Difficulty	Moderate Difficulty	Ouite a Bit of Difficulty	Extreme Difficulty						
	Managing day to day life (getting places on time, making everyday decisions).	0	0	0	0	0						
20.	Adjusting to major life stresses (divorce, moving, the death of friend or family member).	^а О	0	٥	٥	0						
21.	Work (<u>If employed</u> : completing tasks, performance standards, <u>I</u> unemployed: looking for work).	<u>f</u> 0	0	0	0	0						
22.	Relationships with your family members (getting along with your partner or family).	٥	0	0	0	0						
23.	Lack of self-confidence (feeling bad about yourself, feeling that you are stupid or not worthwhile).	٥	0	0	٥	О						
24.	Depression (feeling sad, hopeless or down in the dumps).	0	D	0	0	D						
25.	Suicidal feelings or behavior (thinking about or attempting suicide by any means).	0	0	0	0	0						
26.	Physical symptoms (headaches, aches and pains, sleep problems stomach aches, dizziness).	· 0	0	0	0	0						
27.	Fear, anxiety or panic (nervousness, jitters, fear of open spaces, heights, darkness etc.).	0	0	0	0	0						
28.	Confusion, concentration, memory (trouble understanding things or thinking clearly).	0	0	o	0	0						
29.	Disturbing or unreal thoughts or beliefs (feeling that others ar watching or can read one's mind, feeling that one can fly or the TV is speaking to one personally).	e •	0	0	0	D						
	Hearing voices or seeing things (hearing messages or commands from a voice inside one's head, seeing things no one else can see).	0	0	o	0	0						
	Manic behavior (racing thoughts, a decreased need for sleep, increased talking or other behavior which other people would consider very unusual or inappropriate).	0	0	0	0	0						
32.	Mood swings, unstable moods (feeling happy one minute and sad the next).	٥	٥	٥	٥	٥						
	Hard to control behavior (feeling the need to frequently repeat some behavior such as: hand-washing, hurting self, checking lights or appliances).	0	0	О	0	0						
34.	Sexual activity or preoccupation (any sexual issue that is a problem such as: sexual addiction, fear of sex, out of control sexual feelings or behavior, feeling confused about your sexual identity).	٥	0	0	0	0						

Page 3/5 fupadult-c.frm

This questionnaire is adopted from the BASIS-32 $_{\odot}1985$ by Evaluative Service Unit, McLean Hospital.



The Institute of Living's Outcome Assessment Program Questionnaire Version 3.0												
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Episode												
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								No Difficulty	A Little Difficulty	Moderate Difficulty	Bit of	Extreme Difficulty
											Difficulty	
35. Trying to control	_	-						0	0	0	0	0
 Drinking alcoholi school or work du 								_	_	_	_	_
intoxicated).	e to nai	igovi	ers, Dia	CKOU	ns, c	IIIVI	ing writte	0	0	0	0	0
37. Taking illegal dru	gs or m	isus	ing pre	scri	ptio	n d	rugs.	0	0	0	0	0
38. Trying to control												_
using laxatives, di								0	0	0	0	0
39. Controlling temp			ts of ar	nger,	, vio	len	ce (screaming,	0	0	0	0	0
throwing things, hi					c			Ü	0	0	0	· ·
 Impulsive, illegal driving, vandalism, 							npie, reckless	0	0	0	0	0
41. Feeling satisfactio							with what yo					
are doing, general					8	PPJ		0	0	0	0	0
 Stress (feeling stre 				of y	our	life.	For example:	0	_	^	^	^
work, finances, rel		•						Ų.	0	0	0	0
43. If you have side ef						dica	itions, do	0	0	0	0	0
they interfere with 44. During the past mo						rout	d vou emoko			~		
44. During the past inc							u you sinoke (оп а турк	ai uay i			
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□ Spouse/Partne			1dren		Do		•					
Other Family	Membe	rs			Dic							
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47. If so, do you take	•			_	•			Yes O	NO ON	ot Applic	able (N/A))
48-52 Please list belo	ow any	psyc	cinatri	e me	uica	tu(O)	us you take:					
			_									
Page 4/5					1	fupa	adult-c.frm				306	149
This questionnaire is	adopted	from	the BA	SIS-3	2 © <i>1</i>	985	by Evaluative S	ervice Un	it, McLean	Hospital		

The Institute of Living's Outcome Assessment Program Questionnaire Version 3.0 Follow - Up Assessment (Adult)									
Episode									
For office use only: Med 1	Med 2	Med 3	Med 4	Med 5					
53. Do you experience O Yes	any side effects from t		○ Not App	plicable (N/A)					
O Drowsiness Sleep difficult Sexual difficult Anxiety/Tensi Dizziness/Fair	ties O dities O ion/Restlessness O ntness O	ou are experiencing (plea Tremors/Shakiness Blurred vision Weight loss of more than Nausea/Vomiting Dry mouth Weight gain of more than	O Tardiv O Headac I 4 lbs O Low bl O Urinar O Consti I 4 lbs O High b	e dyskinesia					
	-	atment you received at 7 Moderately satisfied	_	extremely satisfied					
Page 5/5	ou wish to add?	Smadule - Sm		30649					
	adopted from the BASIS-32	fupadult-c.frm ©1985 by Evaluative Servio	ce Unit, McLean Hospital.						