Chapter 1

Introduction: the need for interdisciplinary approaches

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1.1 Introduction

Anxiety research has exploded over the past few decades, yielding a wealth of new information in multiple domains. These domains include underlying neurobiology, risk and protective factors, patterns of expression of normal and pathological anxiety, cultural determinants of this expression, and the delineation of specific anxiety disorders and their evidence-based treatments. As areas of research become increasingly specialized, the need to integrate our understanding across these different domains has become increasingly more important, calling for an interdisciplinary approach. This book brings together research relevant to anxiety disorders from a variety of disciplines into one volume, with the hope that it will encourage readers to bridge these disciplines to further advance our understanding of anxiety and the treatment of anxiety disorders.

Anxiety is a universal human emotion. It alerts us to potential threats and motivates us to prepare for challenges. However, a surprisingly large proportion of the population experiences an excess of anxiety that is counterproductive or even debilitating. This excess often takes the form of prototypical syndromes, which have been termed "anxiety disorders." In the fourth edition of the *Diagnostic and Statistical Manual* (DSM-IV), the anxiety disorders include panic disorder, agoraphobia, social anxiety disorder (SAD, also known as social phobia), specific phobia, posttraumatic stress disorder (PTSD), acute stress disorder, obsessive–compulsive disorder (OCD), and separation anxiety disorder. These disorders are distinguished by their characteristic triggers (e.g., social situations in SAD), distinctive symptoms (e.g., re-experiencing traumas in PTSD), course of illness, and response to treatment.

Typically appearing by young adulthood, the anxiety disorders are the most common class of mental disorders in the United States, with a 29% lifetime prevalence that exceeds that of mood (20%) and substance use disorders (15%) (Kessler *et al.* 2005). As a group, anxiety disorders cost society tens of billions of dollars per year (Greenberg *et al.* 1999). Thus, understanding the causes of these disorders and determining how better to treat them can significantly impact public health.

In 1982, the Anxiety Disorders Clinic, one of the first research clinics in the world to focus on anxiety disorders, was established by Michael Liebowitz and Abby Fyer at Columbia University/New York State Psychiatric Institute (NYSPI). Initial research objectives included improving diagnostic criteria, probing the physiology of panic attacks, examining novel medications, and investigating the presumed genetic basis of these disorders through family studies. At the time, brain functioning was commonly inferred from techniques such as electroencephalographic recordings from the scalp, pharmacologic challenges, or neurotransmitter metabolites accessible in peripheral locations (e.g., platelets, urine and in cerebral spinal fluid). Cognitive–behavioral approaches were available but uncommon in routine clinical practice. Additionally, the US Food and Drug Administration (FDA) had approved no medications for anxiety disorders other than alprazolam for panic disorder in 1981.

Since that time, the scope of anxiety research in general, and in the Anxiety Disorders Clinic in particular, has greatly expanded. Our group, like other research teams around the world, has developed research portfolios that require collaborations with investigators from a wide array of disciplines. We conduct studies in a wide range of fields, including animal models, brain imaging, randomized

Anxiety Disorders: Theory, Research, and Clinical Perspectives, ed. Helen Blair Simpson, Yuval Neria, Roberto Lewis-Fernández, Franklin Schneier. Published by Cambridge University Press.

clinical trials, epidemiology, and treatment dissemination and implementation in the community. Research has transformed how we treat anxiety disorders: evidence-based practices have been developed and are being disseminated not only to mental health settings but also to primary care practices. Cognitive–behavioral approaches reign among psychotherapies, and the FDA has approved several classes of medication for the treatment of anxiety disorders. The focus has shifted away from identifying a treatment that can beat a placebo or usual care to developing better and novel treatments for those who do not fully respond to our first-line treatments. Increasingly, these novel treatments are based on sophisticated theories of the mechanisms underlying the symptoms.

When Cambridge University Press approached us with the idea of writing a treatment manual on the Columbia University/NYSPI approach to the diagnosis and treatment of anxiety disorders, we welcomed the challenge. However, rather than preparing a treatment manual or textbook, of which there are already several excellent examples for anxiety disorders (e.g., Barlow 2004, Antony & Stein 2008, Stein *et al*. 2009), we aimed to do something different. We chose to design a book that would not only provide a critical overview for clinicians but that would also capture the ferment of science as it exists today. For this approach, we turned to our colleagues at Columbia University/NYSPI and asked them to share their perspectives on the most promising new developments and important controversies in their areas of expertise. Our goal was to illustrate what is most novel in the field of anxiety disorders, focusing on areas in which our institution has made a significant contribution, including nosology, assessment, mechanisms, and treatment.

In sum, this book represents a selective review of the work undertaken over the last three decades to advance our understanding of anxiety and of anxiety disorders. Due to the longevity of the Anxiety Disorders Clinic, we have had the opportunity to work with most of the authors over many years. They are our mentors, our colleagues, our collaborators, and our friends. By honoring where we have come from while focusing on where we are going, we hope that this book will communicate the enormous advances that have occurred in the field of anxiety research, and will provide the reader the opportunity to review, in one volume, some of the latest thinking that is shaping the future of this field.

1.2 Content and structure

We have organized the chapters into four sections.

1.2.1 Section 1: Evolving concepts of anxiety

The first section considers a variety of perspectives on evolving concepts of the nature of anxiety. Comer and Olfson (Chapter 2) set the stage by reviewing the prevalence and distribution of DSM-IV anxiety disorders across the life span, drawing predominantly on large-scale epidemiologic surveys conducted in developed regions of the world. They systematically describe evidence for rates, distributions, correlates, and course of DSM-IV anxiety disorders in the general population. They also describe patterns of comorbidity and service use.

Next, First, Caban, and Lewis-Fernández (Chapter 3) trace the evolution of diagnostic criteria for the anxiety disorders over six decades, from DSM-I in 1952 to the dilemmas facing DSM-5, scheduled for 2013. They discuss the theoretical and empirical findings that led to the refining of these categories, and they detail nosological changes introduced by each successive revision.

Liebowitz (Chapter 4) provides a personal perspective on the evolution of diagnostic approaches to anxiety by describing the development of his research on social anxiety disorder. He discusses initial efforts to classify its phenomenology and relationship to other disorders, such as avoidant personality disorder and atypical depression, and the development of assessment measures. He also documents early steps in developing collaborations between the fields of psychiatry and psychology that have led to state-of-the-art comparative clinical trials of medication and psychotherapy.

Glick and Roose (Chapter 5) provide a concise history of psychoanalytic perspectives on anxiety. They describe the concept of "signal anxiety" and trace changes in this concept from Freudian psychology to ego psychology, object relations, and self psychology. They then describe the emerging integration of psychodynamic concepts with research on temperament, gene–environment interactions, and brain imaging, as well as the relevance of a psychodynamic perspective to general treatment of anxiety disorders.

Finally, Hofer (Chapter 6) applies advances in our understanding of evolution, from Darwin to epigenetics, to consider the origins of adult anxiety and its disorders. He illustrates these concepts with examples from more than three decades of his own research on

early separation-induced anxiety in young rats, and highlights the evolutionary clues that processes of early development provide for understanding the roots of human panic disorder.

1.2.2 Section 2: Challenges in diagnosing pathological anxiety

The second section reviews selected topics in the clinical assessment and classification of anxiety pathologies, focusing on current controversies over the commonalities and differences between different diagnostic constructs. Pinto, Grados, and Simpson (Chapter 7) review efforts to identify clinically meaningful subtypes of OCD and to understand obsessive–compulsive symptoms in terms of a dimensional model. In addition, they discuss methods that may enable a shift from phenotypic classification to characterization of biomarkers or endophenotypes as the "next frontier" in OCD research, and the corresponding implications for improving understanding and treatment.

Schneier and Socha (Chapter 8) assess the relationship of SAD to trait phenomena of shyness, behavioral inhibition, and avoidant personality. They explore the concept that these constructs lie on a spectrum of socially anxious temperaments, are essential and adaptive for group-living species, and influence, to a variable extent, a much broader spectrum of psychopathology.

McGrath and Miller (Chapter 9) review the phenomenology, epidemiology, and neurobiology of co-occurring anxious and depressive symptoms and disorders. They also address the clinical relevance of this comorbidity, including its implications for prognosis, ranging from medication response to risk of suicidality.

Harding, Skritskaya, Doherty, and Fallon (Chapter 10) review the latest research on the classification, epidemiology, etiology, assessment, and treatment of health anxiety (also known as illness worry). Health anxiety is a subtype of anxiety that is not currently identified as a specific anxiety disorder and is seen instead as a component of various DSM-IV categories, including hypochondriasis, OCD, and delusional disorder, among others. The authors suggest that nosological recognition of this anxiety subtype could advance its neurobiological characterization and lead to improved and more focused treatment.

Next, Kaplowitz and Markowitz (Chapter 11) critically examine three decades of research on the interrelationships between anxiety disorders and personality disorders. This work documents high levels of comorbidity, challenges assumptions of the independence of Axis I and II disorders, and raises new questions about assessment of anxious states, related traits, and approaches to understanding their interactions.

Finally, Hinton and Lewis-Fernández (Chapter 12) focus on cultural factors in the diagnosis of anxiety disorders. They describe the critical importance of cultural syndromes in cross-cultural assessment, as these syndromes pattern and even modulate the emergence of various anxiety disorders, such as panic disorder and PTSD. The clinical relevance of cultural syndromes is discussed, illustrating the role of environmental factors in the etiology and course of specific subtypes of anxiety.

1.2.3 Section 3: Understanding the causes of anxiety

The third section presents diverse approaches to understanding what causes anxiety and anxiety disorders. These chapters draw on both human and animal studies, and they encompass biological and psychosocial domains. Nugent, Weissman, Fyer, and Koenen (Chapter 13) begin this section by reviewing current evidence for genetic factors in the etiology of human anxiety disorders. They address whether anxiety disorders share heritability, consider intermediate phenotypes and candidate genes that might account for the shared risk, and discuss how emerging technological advances in the field of genetics will affect future research.

Richardson-Jones, Leonardo, Hen, and Ahmari (Chapter 14) review recent strategies for developing animal models of anxiety, focusing on genetic manipulation in mice. They illustrate how state-of-the-art genetic methods have been used to probe the role of a specific serotonin receptor (the 5-HT_{1A} receptor) in anxiety-related behaviors.

In the next chapter, Weisstaub, McOmish, Hanks, and Gingrich (Chapter 15) also discuss how mouse models can help elucidate the causes of anxiety. They review the cortical systems that modulate the expression of anxiety and illustrate how genetic strategies have been used to elucidate the role that different aspects of the serotonin system, including the serotonin transporter, 5-HT_{1A} receptors, and 5-HT_{2A} receptors, play in the generation and modulation of anxiety.

Gordon and Adhikari (Chapter 16) summarize research that has mapped the brain circuits underlying learned fear, bringing the amygdala to the forefront of our understanding of fear responses and suggesting neurobiological underpinnings of cognitive–behavioral therapy (CBT) techniques. They also discuss

new animal models of innate anxiety, and consider the relevance of both conditioned and innate fear models to understanding the pathophysiology of human anxiety disorders.

Etkin and Wager (Chapter 17) review the burgeoning literature using functional human neuroimaging to clarify what is known about the neural basis of anxiety in healthy and clinical populations. They present evidence for a neurocircuitry model of anxiety that includes a core limbic–prefrontal circuit for affective reactivity (identified in animal and human studies of fear conditioning) and that is modulated by executive working memory and affect appraisal systems.

Hambrick, Comer, and Albano (Chapter 18) present the cognitive–behavioral model of anxiety, focusing on the core feature of anxious apprehension and how it can lead – through a combination of biological vulnerability, developmental experiences, and life events – to the generation of anxiety disorders. They illustrate how this model informs cognitive–behavioral treatments and continues to evolve over time.

Dohrenwend (Chapter 19) focuses on the controversy over the relative importance of the traumatic stressor versus vulnerability factors in the etiology of PTSD. He reviews the historical broadening of the definition of traumatic stressor (Criterion A) as well as the accumulating evidence for the appearance of PTSD after subthreshold stressors.

Mulhare, Ghesquiere, and Shear (Chapter 20) consider the fundamental role of attachment and separation in the generation of anxiety. They also review recent data on the role of attachment security and anxiety sensitivity in the development of a number of anxiety disorders.

Last, Natarajan, Shrestha, and Coplan (Chapter 21) present findings from studies of non-human primates that inform our understanding of the development of human anxiety disorders. They review primate data on neurobiological mechanisms by which genetic predisposition can interact with early deprivation to generate anxious behavior. They also discuss how some types of stress may promote resilience.

1.2.4 Section 4: Treatment of anxiety: current status and controversial issues

The final section describes evidence-based and novel treatment approaches for anxiety disorders. Rodriguez and Simpson (Chapter 22) review evidence-based treatment strategies for OCD, including both medications and cognitive–behavioral therapy, as well as first-line and augmentation strategies. They also discuss novel treatment approaches that are based on increasingly sophisticated theories about the brain mechanisms underlying obsessions and compulsions.

Schneier, Pontoski, and Heimberg (Chapter 23) review the evidence for first-line and alternative medication and psychotherapeutic treatments for social anxiety disorder. They also probe what is understood and what remains unknown about widely used but little-studied approaches to combining medication and cognitive–behavioral treatments, such as the relative efficacy of concurrent versus sequential treatments.

Sullivan, Suh, and Neria (Chapter 24) review data from randomized controlled trials to address the optimal treatment of PTSD. In particular, they consider the evidence for the efficacy of established medication and psychosocial treatments (e.g., serotonin reuptake inhibitors and prolonged exposure), experimental approaches (e.g., pharmacological strategies to prevent the disorder), and widely used but controversial treatments (e.g., benzodiazepines, eye movement desensitization reprocessing).

Sinha and Klein (Chapter 25) evaluate findings on medication and cognitive–behavioral treatment of panic disorder. They raise methodological concerns about this literature and challenge some prevailing views on the efficacy of treatments for panic disorder, while also addressing practical issues such as appropriate dosing and duration of treatments.

Papp, Gorenstein, and Mohlman (Chapter 26) review evidence-based treatments for generalized anxiety disorder (GAD) and focus on the specific challenges of treating the growing population of older patients. They discuss the importance of modifying approaches to both pharmacotherapy and psychosocial therapy in the elderly, and propose treatment guidelines that emphasize flexibility and multimodal approaches.

Next, Vidair and Rynn (Chapter 27) address how to assess and treat anxiety disorders in children. They provide a comprehensive review of the literature supporting the use of both CBT and medications in children with anxiety disorders, discuss the controversial issue of whether medication treatment is associated with increased risk of suicidal behavior in children, and highlight future research questions.

Mantovani and Lisanby (Chapter 28) review current data on electromagnetic modalities in the treatment of

anxiety disorders. The approaches range from one of the oldest (electroconvulsive therapy) to some of the newest modalities (vagal nerve stimulation and transcranial magnetic stimulation).

Patel, Tranguch, and Muskin (Chapter 29) review a spectrum of complementary and alternative treatments of anxiety disorders, including mind–body medicine (e.g., meditation), biologically based practices (e.g., dietary supplements), manipulative and body-based practices (e.g., massage), and energy medicine (e.g., acupuncture). Focusing on the most rigorous studies, their critical review lays out the current state of knowledge in these areas, as well as directions for future research.

Finally, Okuda, Khan, De La Cruz, and Blanco (Chapter 30) review current evidence on the treatment of anxiety disorders in primary care settings, including effectiveness of medication and psychosocial therapies. They describe studies of organizational and educational interventions aimed at improving quality of care for anxiety disorders in primary care, such as the collaborative care model, and critically discuss gaps and future directions.

1.3 Conclusion

In the final chapter (Chapter 31), we summarize some of the key observations from the variety of approaches to anxiety and anxiety disorders presented in this book, highlight the potential and limitations of current research, and offer recommendations for future research directions. We believe that an interdisciplinary approach to anxiety will lead to the greatest progress in this field, and the multiple perspectives brought together, integrated, and assembled in this book are intended as a step in that direction. The ultimate goal is to generate an ongoing and productive dialogue between researchers and clinicians with these different perspectives in order to transform how we understand anxiety and treat anxiety disorders.

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Section 1 Chapter 2

Evolving concepts of anxiety
The epidemiology of anxiety disorders

Jonathan S. Comer, Mark Olfson

2.1 Introduction

Psychiatric epidemiology uses population-based survey methods to inform understanding of the prevalence, course, and correlates of mental disorders. Whereas the focus of clinical practice is on the individual patient, psychiatric epidemiology studies the manifestation and distribution of mental disorders in the general population in order to evaluate the public health burden and economic impact of psychiatric conditions, and to provide clues to etiology.

Over the past three decades, advances in psychiatric epidemiology and population-based sampling methodology have enhanced our understanding of the public health burden of psychiatric disorders. Measurement in epidemiology has progressed from reliance on unsystematic reports from hospitals and other service facilities to employment of highly structured interviews that reliably assess well-defined diagnostic entities in representative household samples (Dohrenwend & Dohrenwend 1982). In the United States, almost three decades ago the Epidemiological Catchment Area (ECA) study documented rates of DSM-III conditions in five US communities in household and institutional settings (Robins & Regier 1991). Since this landmark study, a number of large-scale US surveys have expanded on the ECA findings to provide nationally representative data using broad structured diagnostic interviews that reflect evolving iterations of the DSM (e.g., Kessler *et al.* 1994, 2005a, Grant *et al.* 2004a). During this period, there have also been rigorous epidemiologic surveys documenting distributions of disorders throughout Europe, Australia, South America, parts of Asia, Africa, and the Middle East (e.g., ESEMeD/MHEDEA 2000 Investigators 2004a, Kessler & Ustun 2008, Stein *et al.* 2008). Advances have also occurred in evaluating the prevalence and associated public health burden of psychiatric disorders in youth, although these surveys have been limited to narrower geographical regions (Costello *et al.* 2005). Progress in household survey methods – including improvements in diagnostic nomenclature, the advent and availability of reliable structured diagnostic instruments, and developments in probability sampling – has enhanced our understanding of the prevalence, distribution, correlates, and course of anxiety disorders across the life span.

Anxiety disorders are the most prevalent class of mental disorders (Kessler *et al.* 2005b), and collectively they impose a substantial public health burden on society. This burden is reflected among persons with anxiety disorders in elevated rates of general medical disorders (Kessler & Greenberg 2002), high healthcare utilization and costs (Rice & Miller 1998, Greenberg *et al.* 1999, Wittchen 2002), loss of worker productivity (Kessler & Frank 1997), increased risk of suicide attempts and suicidal ideation (Kessler *et al.* 1999, Pilowsky *et al.* 2006), and poor health-related quality of life (Mendlowicz & Stein 2000, Comer, Blanco, Hasin, *et al.* in press).

In this chapter, we review the prevalence and distribution of DSM-IV anxiety disorders across the life span, drawing predominantly on large-scale epidemiologic surveys conducted in developed regions of the world, where the most rigorous work has been conducted. We refer to relevant DSM-III and DSM-III-R literatures only where DSM-IV research is lacking, or to assess temporal trends. Our review is organized around (a) rates, distributions, correlates, and course of the DSM-IV anxiety disorders in the general population; (b) comorbidity patterns; (c) anxiety disorders in primary care; and (d) service use patterns associated with the anxiety disorders. We conclude by highlighting areas in need of empirical attention and laying out an agenda for future epidemiologic research in this area.

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2.2 Anxiety disorders in the general population

Epidemiologic surveys consistently document that anxiety disorders are the most prevalent class of mental disorders. In the USA, almost 30% of Americans meet diagnostic criteria for at least one anxiety disorder in their lifetime (Kessler *et al.* 2005a), with 11–18% of adults meeting criteria for an anxiety disorder within the past year (Grant *et al.* 2004a, Kessler *et al.* 2005b). Prevalence rates of anxiety disorders are roughly equivalent across major US racial/ethnic groups (Breslau *et al.* 2004).

Lifetime prevalence rates of anxiety disorders appear to be somewhat lower outside of the USA, ranging roughly from 9% to 16% across Europe and throughout parts of Africa and Asia (ESEMeD/MHEDEA 2000 Investigators 2004a, Cho *et al.* 2007, Stein *et al.* 2008). Similarly, 12-month prevalence rates of anxiety disorders are notably lower in Mexico, Nigeria, Korea, and across Europe, than in the USA, ranging roughly from 4% to 7% (ESEMeD/MHEDEA 2000 Investigators 2004a, Medina-Mora *et al.* 2005, Gureje *et al.* 2006, Cho *et al.* 2007). At present, it is not clear whether such geographic differences reflect true differences in the prevalence of anxiety disorders, differences across cultures in willingness to endorse emotion-related symptoms, or methodological differences across surveys.

Interestingly, research in the USA shows lower lifetime rates of anxiety disorders among immigrants than among US-born natives of the same national origins (Vega *et al.* 1998, Grant *et al.* 2004b). Early age at immigration and longer duration residing in the USA are both associated with increased risk for mental disorders among immigrants relative to natives (Breslau *et al.* 2007), perhaps highlighting the important roles of early socialization and acculturation in conferring increased risk.

Sex differences in the prevalence of anxiety disorders are consistent across cultures and survey methods. Lifetime and 12-month prevalence rates of anxiety disorders among women are roughly twice the rates found among men (ESEMeD/MHEDEA 2000 Investigators 2004a, Jacobi *et al.* 2004, Kessler *et al.* 2005a, Pirkola *et al.* 2005). In children, girls generally report higher rates of anxiety disorders than boys (Costello *et al.* 2003).

Onset of anxiety disorders typically occurs in early adolescence and young adulthood, and they usually manifest before mood or substance use disorders (Kessler *et al.* 2005a). Approximately 2–4% of youth between the ages of 5 and 15 currently meet criteria for an anxiety disorder (Costello *et al.* 2003). Substantial rates of anxiety disorders have also been reported in preschool children (Egger & Angold 2006), although such findings should be met with caution given the lack of consensus in distinguishing normal and abnormal preschool behavior, sole reliance on parent report, and absence of data on the predictive validity of early childhood diagnoses.

Although anxiety disorders on average have an earlier onset than most other classes of mental disorders, the age-of-onset distribution varies across individual anxiety disorders. Based on recall of community-dwelling adults, specific phobias and separation anxiety disorder have the earliest median age of onset (at about 7 years of age), followed by social anxiety disorder (about 13 years), panic disorder and agoraphobia (about 21 years), and generalized anxiety disorder (early thirties) (Kessler *et al.* 2005a).

Cross-sectional work supports a decline in lifetime prevalence of anxiety disorders in older adulthood. Whereas roughly one-third of US adults between the ages of 18 and 59 report meeting lifetime criteria for an anxiety disorder, only one-sixth of US adults over the age of 60 similarly report the presence of a lifetime anxiety disorder (Kessler *et al.* 2005a). It is not clear whether this pattern reflects a true cohort effect, a methodological artifact, or a combination of the two. Lower lifetime prevalence of anxiety disorders among older adults may also reflect earlier mortality associated with psychiatric disorders. That is, those who live into the upper reaches of human life expectancy are less likely to suffer from mental disorders.

When left untreated, anxiety disorders are typically unremitting and persist as chronic conditions associated with reduced quality of life, including decrements in social functioning, role functioning, educational attainment, financial independence, and mental health (see Mendlowicz & Stein 2000). Many of the DSM-IV anxiety disorders are associated with poorer overall mental well-being than cancer, heart disease, arthritis, hypertension, and a host of other chronic general medical conditions (Comer, Blanco, Hasin, *et al.* in press). Anxiety disorders are also associated with decrements in educational achievement. Anxiety disorders are significant predictors of failure to complete high school, failure to enter college among high-school completers, and failure to complete college among college entrants (Kessler *et al.* 1995a).

Beyond these general trends in the epidemiology of *any* anxiety disorder, in this chapter we next consider patterns associated with several specific anxiety disorders: social anxiety disorder (SAD), generalized anxiety disorder (GAD), panic disorder/agoraphobia (PD/AG), obsessive–compulsive disorder (OCD), posttraumatic stress disorder (PTSD), separation anxiety disorder (SepAD), and specific phobia (SP).

2.2.1 Social anxiety disorder (SAD)

Social fears are relatively common. Roughly one-quarter of US residents report at least one lifetime social fear. The most common of these fears are public speaking (21.2% lifetime prevalence) and speaking up in meetings (19.5%) (Ruscio *et al.* 2008). A diagnosis of social anxiety disorder (SAD), also referred to as social phobia, is appropriate when such social fear is excessive and persistent and accompanied by situational avoidance or substantial distress, as well as functional impairment. Lifetime prevalence estimates of SAD range from 5% to 12%, with 1–7% of adults reporting SAD in the past year (Lampe *et al.* 2003, Grant *et al.* 2004a, 2005a, Kessler *et al.* 2005b, Medina-Mora *et al.* 2005, Ruscio *et al.* 2008). Within the USA, 12-month prevalence of SAD is somewhat lower among Hispanic, Asian, and African Americans than among non-Hispanic White Americans (Smith *et al.* 2006).

Prevalence estimates of DSM-IV SAD are slightly lower than those for earlier DSM criteria, in which the disorder was conceptualized as more akin to a simple phobia. In addition, 12-month SAD prevalence estimates appear to be somewhat higher in the USA (about 7%) (Kessler *et al.* 2005b, Ruscio *et al.* 2008) than in Mexico (1.7%) (Medina-Mora *et al.* 2005), Australia (2.3%) (Lampe *et al.* 2003), South Africa (2.8%) (Stein *et al.* 2008), and across Europe (1.2%) (ESEMeD/MHEDEA 2000 Investigators 2004a).

Across cultures, epidemiologic work typically finds women to be at greater risk for SAD than men (Wittchen *et al.* 1998, ESEMeD/MHEDEA 2000 Investigators 2004a, Grant *et al.* 2005a), although in an exception, Stein and colleagues (2000) did not identify a gender effect. In a nuanced set of gender analyses accounting for the number of reported social fears, Ruscio and colleagues (2008) found that women are at higher risk for more generalized forms of SAD (five or more social fears), whereas men are at higher risk for less generalized forms (four or fewer social fears).

Developmental patterns suggest that the average onset of SAD is in adolescence or young adulthood. Retrospective data find that the onset of social fears (median onset 10–13 years of age) typically precedes the systematic avoidance of social situations (median onset 12–14 years of age) by about 1–2 years (Ruscio *et al.* 2008), with the mean age of full SAD onset at roughly 15 years of age (Grant *et al.* 2005a). Earlier onset is associated with more pervasive social anxiety in adulthood. For example, those with more generalized forms of SAD (i.e., five or more social fears) typically report onset between early childhood and mid-adolescence, whereas those with less generalized SAD (i.e., four or fewer social fears) are more likely to report cases of onset well into the mid-twenties (Ruscio *et al.* 2008). Although social fears are fairly common in youth, the presence of four or more social fears in childhood or adolescence seems to distinguish SAD youth from their non-anxious counterparts (Puliafico *et al.* 2007).

SAD typically displays a persistent course, with only 20–40% of cases remitting within 20 years of onset, and only 40–60% remitting within 40 years. Compared with matched unaffected controls, individuals with SAD report impaired social functioning, diminished social support (Hambrick *et al.* 2003, Eng *et al.* 2005), lower levels of educational attainment, poorer occupational function (Schneier *et al.* 1994, Wittchen *et al.* 1999, Stein & Kean 2000), and decreased rates of marriage (Schneier *et al.* 1992). Merikangas and colleagues (2007) found that after controlling for comorbid conditions, SAD is associated with an average of 14.9 yearly disability days in the USA.

2.2.2 Generalized anxiety disorder (GAD)

Across several DSM iterations, generalized anxiety disorder (GAD) has evolved from a non-specific residual anxiety category to its current status as a primary anxiety disorder. It is characterized by excessive and uncontrollable worry together with associated somatic symptoms. The shifts in GAD criteria have likely resulted in considerable heterogeneity in studies examining the epidemiology of GAD, and have hampered long-term investigations of the course of the disorder (Kessler *et al.* 2004, Holaway *et al.* 2006).

Despite the changing focus of GAD across DSM refinements, a coherent portrait of DSM-IV GAD is now beginning to emerge. It is a highly prevalent anxiety disorder associated with an unremitting course and considerable life impairment. Lifetime prevalence estimates of DSM-IV GAD range from 3% to 6%, with 1–4% of adults reporting DSM-IV GAD in

the past year (Carter *et al.* 2001, ESEMeD/MHEDEA 2000 Investigators 2004a, Jacobi *et al.* 2004, Grant *et al.* 2005b, 2005c, Kessler *et al.* 2005a, 2005b, Lieb *et al.* 2005, Cho *et al.* 2007). Lifetime prevalence rates in the USA (about 4–6%) (Grant *et al.* 2005c, Kessler *et al.* 2005a) are somewhat higher than those reported outside the USA (about 2–3%) (ESEMeD/MHEDEA 2000 Investigators 2004a, Cho *et al.* 2007, Stein *et al.* 2008). Within the USA, 12-month prevalence of GAD is somewhat lower among Hispanic and Asian Americans than among non-Hispanic White Americans (Smith *et al.* 2006). Across cultures, GAD is roughly twice as common among women as among men (Wittchen *et al.* 1994, ESEMeD/MHEDEA 2000 Investigators 2004a, Jacobi *et al.* 2004). However, there is some evidence that gender differences attenuate in middle and older adult cohorts (Hunt *et al.* 2002).

Among the anxiety disorders, GAD has the latest mean and median age at onset (early thirties) (Grant *et al.* 2005c, Kessler *et al.* 2005a, Lieb *et al.* 2005), although substantial numbers of children and adolescents do meet full criteria (Albano & Hack 2004, Comer *et al.* 2004, Robin *et al.* 2005, Alyahri & Goodman 2008). Early GAD onset is associated with greater excessiveness and uncontrollability of worry, as well as a more chronic course with more severe life impairment (Ruscio *et al.* 2005). Although the 12-month prevalence of GAD is significantly lower among older adults than among middle-aged adults (1.6% versus 4–5%) (Hunt *et al.* 2002), GAD may nonetheless be the most common anxiety disorder in the elderly (Beekman *et al.* 2000).

Across the anxiety disorders, GAD may be the most profound and have the most deleterious effect on functioning and health-related quality of life (Grant *et al.* 2005c, Comer, Blanco, Hasin, *et al.* in press). Individuals with GAD are at significantly increased risk of impaired social and role functioning, mental health, and overall physical and mental well-being (Mendlowicz & Stein 2000, Stein & Heimberg 2004, Henning *et al.* 2007). In the National Survey of Functional Health Status, overall mental well-being for individuals with 12-month GAD was almost two standard deviations below that identified for "healthy" individuals (i.e., those with no chronic conditions) (Comer, Blanco, Hasin, *et al.* in press). GAD is also associated with poor marriage stability, as afflicted individuals are almost twice as likely to have their first marriage end in divorce (Kessler *et al.* 1998). Occupational impairment is also common (Merikangas *et al.* 2007).

2.2.3 Panic disorder (PD) with and without agoraphobia

Panic attacks are discrete periods of intense fear or discomfort accompanied by at least four DSM-IV specified symptoms (e.g., palpitations, sweating, shortness of breath, nausea, derealization, paresthesias), reaching peak intensity within 10 minutes. Roughly one-fifth of the general US population has experienced an isolated panic attack (Kessler *et al.* 2006). When panic attacks recur and are accompanied by persistent concern over future attacks, worry about attack implications, or significant behavioral changes to prevent future attacks, a diagnosis of panic disorder (PD) is warranted. When PD is accompanied by intense anxiety about being in places or situations from which escape may be difficult or in which help may not be available in the event of an unexpected panic attack, and such situations are avoided or else endured with marked distress, a diagnosis of PD with agoraphobia is applied.

Across cultures, lifetime PD rates range roughly from 2% to 4%, and 1–3% report the presence of PD within the past year (ESEMeD/MHEDEA 2000 Investigators 2004a, Grant *et al.* 2004a, Jacobi *et al.* 2004, Goodwin *et al.* 2005, Medina-Mora *et al.* 2005, Kessler *et al.* 2006). PD with agoraphobia appears to be somewhat less frequent, with 12-month and lifetime prevalence rates both at roughly 1% (Grant *et al.* 2004a, Kessler *et al.* 2006). Rates for PD and PD with agoraphobia are twice as high in females as in males (Goodwin *et al.* 2005, Jacobi *et al.* 2004, Kessler *et al.* 2006). Within the USA, 12-month prevalence of PD is somewhat lower among Hispanic and Asian Americans than among non-Hispanic White and African Americans (Smith *et al.* 2006).

PD and agoraphobia typically begin in young adulthood (at about 21 years) (Kessler *et al.* 2005a) and only rarely before adolescence. Cross-sectional work suggests that the mean onset of PD is roughly one year following the mean onset of an initial panic attack (Kessler *et al.* 2006), although this has yet to be confirmed by prospective, longitudinal work. A vast majority of initial panic attacks are reported as occurring outside of the home – while on a bus, plane, or subway, or while walking, driving, or at school or work (Craske *et al.* 1990, Shulman *et al.* 1994).

PD with and without agoraphobia tends to persist and interfere with family and occupational functioning (Kessler *et al.* 1998). In the workplace, PD and agoraphobia are associated with approximately 18–21 yearly

disability days (Merikangas *et al.* 2007). Quality of life is poor among individuals with PD (Mendlowicz & Stein 2000), and recent analyses of the National Survey of Functional Health Status find that individuals with PD exhibit considerably poorer overall mental well-being compared to individuals with a number of chronic general medical conditions (Comer, Blanco, Hasin, *et al.* in press).

2.2.4 Obsessive–compulsive disorder (OCD)

Few large-scale epidemiologic surveys have assessed obsessive–compulsive disorder (OCD). Consequently, our understanding of the distribution, course, and correlates of OCD in the general population lags behind our understanding of community patterns associated with SAD, GAD, and PD. Lifetime prevalence estimates across household surveys that have assessed OCD range from 1.6% to 2.5% (Canino *et al.* 1987, Weissman *et al.* 1994, Kessler *et al.* 2005a). Twelve-month prevalence rates have been documented at 0.7–2.0% (Jacobi, *et al.* 2004, Kessler *et al.* 2005b, Torres *et al.* 2006, Cho *et al.* 2007). In contrast with several other anxiety disorders, there do not appear to be significant cohort effects in the prevalence of OCD (Kessler *et al.* 2005a).

As with other anxiety disorders, OCD prevalence rates are generally higher among women than among men (Horwath & Weissman 2000), although the pattern may be reversed among youth (Comer *et al.* 2004). At the symptom level, there is evidence that females with OCD are more likely to present with obsessions regarding contamination and aggression, whereas males with OCD are more likely to present with sexual obsessions, checking/repeating compulsions, and needs for symmetry (Lensi *et al.* 1996, Bogetto *et al.* 1999, de Mathis *et al.* 2008). In youth, boys appear to be at greater risk for earlier onset of OCD (Hanna 1995, Gellar *et al.* 1998, de Mathis *et al.* 2008).

OCD typically develops in mid to late adolescence (Riddle 1998, Comer *et al.* 2004) with a median age at onset of 19 years (Kessler *et al.* 2005a). Earlier onset is associated with a more complex and intractable course in adulthood (de Mathis *et al.* 2008). Individuals with OCD report markedly reduced quality of life and general well-being (Mendlowicz & Stein 2000), diminished occupational attainment, impaired family functioning (Koran 2000), and higher rates of suicidal thoughts and attempts (Torres *et al.* 2006). Severity of OCD is inversely correlated with social functioning (Koran *et al.* 1996).

2.2.5 Posttraumatic stress disorder (PTSD)

Since its formal introduction as an anxiety disorder in 1980 (DSM-III), PTSD remains one of only a handful of diagnostic entities in the DSM taxonomy that directly and causally links symptoms to a preceding event/experience. Field trials document three reliable symptom clusters among individuals exposed to diverse traumatic events: (a) re-experiencing symptoms, which are the most common, (b) avoidance/numbing symptoms, and (c) physiological hyperarousal.

Lifetime and 12-month prevalence estimates for PTSD are substantial in the general population, though much lower than the prevalence of exposure to potentially traumatic events. Whereas surveys find that lifetime prevalence of traumatic exposure in the USA falls between 50% and 60%, lifetime and 12-month prevalence estimates for PTSD are roughly 7% and 4%, respectively (Kessler *et al.* 2005a, 2005b). Intriguingly, prevalence rates of traumatic exposure are somewhat higher outside of the USA, whereas rates of PTSD tend to be somewhat lower (Creamer *et al.* 2001, Zlotnick *et al.* 2006, Cho *et al.* 2007, Stein *et al.* 2008). Reported rates of PTSD following traumatic exposure are considerably lower in youth than in adults (Copeland *et al.* 2007; see also Egger & Angold 2006, Alyahri & Goodman 2008). This latter finding may reflect true age-related differences in PTSD rates following traumatic exposure or delayed onset of PTSD following traumatic exposure in youth. Alternatively, this finding may call into question the developmental appropriateness of DSM-IV PTSD criteria for capturing maladaptive child reactions to trauma.

Rates of PTSD are higher among women than men, despite the higher prevalence of exposure to traumatic events reported among men (Kessler *et al.* 1995b, Creamer *et al.* 2001). Women are at greater risk for developing PTSD following exposure to all forms of potentially traumatic events except sexual assault, for which conditional risks are equivalent across gender (Kessler *et al.* 1995b, Stein *et al.* 1997). Across men and women reporting traumatic exposure, approximately 75% report exposure to more than one traumatic event. Among potentially traumatic events, sexual assault, which is more commonly reported by women, is the most highly linked to subsequent development of PTSD (Creamer *et al.* 2001, Zlotnick *et al.* 2006). Similar gender patterns are found in children (Copeland *et al.* 2007).

A substantial number of individuals exposed to traumatic events initially endure remarkably well,