Overdiagnosis in Psychiatry

HOW MODERN PSYCHIATRY LOST ITS WAY WHILE CREATING A DIAGNOSIS FOR ALMOST ALL OF LIFE'S MISFORTUNES

JOEL PARIS

OXFORD

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How Modern Psychiatry Lost Its Way While Creating a Diagnosis for Almost All of Life's Misfortunes

JOEL PARIS, MD
Professor of Psychiatry, McGill University

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Kuala Lumpur Madrid Melbourne Mexico City Nairobi
New Delhi Shanghai Taipei Toronto

With offices in
Argentina Austria Brazil Chile Czech Republic France Greece
Guatemala Hungary Italy Japan Poland Portugal Singapore
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Published in the United States of America by
Oxford University Press
198 Madison Avenue, New York, NY 10016

Library of Congress Cataloging-in-Publication Data
Paris, Joel, 1940–, author.
Overdiagnosis in psychiatry: how modern psychiatry lost its way while
creating a diagnosis for almost all of life's misfortunes/Joel Paris.
p. ; cm.
ISBN 978–0–19–935064–3 (alk. paper)
I. Title.
[DNLM: 1. Mental Disorders—diagnosis. 2. Diagnostic Errors.
3. Diagnostic Techniques and Procedures—utilization. WM 141]
RC473.D54
616.89′075—dc23
2014039665

9 8 7 6 5 4 3 2 1
Printed in the United States of America
on acid-free paper

This book is dedicated to my fellow researchers in psychiatry, who have taught me the importance of caution in clinical practice.

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ACKNOWLEDGMENTS

Don Black and Mark Zimmerman read earlier versions of this book and made many helpful suggestions for its improvement.

INTRODUCTION

WHAT HAPPENED TO PSYCHIATRY?

Psychiatry has lost its soul. I am heartsick at what has happened to the profession I love. Overdiagnosis moves lock-step with over-treatment with drugs, ignoring the life circumstances of the patients we treat. Psychiatrists have forgotten the listening skills and careful attention to clinical phenomena that once made their specialty unique. I have written this book for mental health practitioners, for patients, and for the many members of the public who are interested in the fate of psychiatry. They will want to know how and why we got into this kind of trouble.

I always used to say I loved psychiatry because it was about life. I now realize this is not true. Psychopathology does not define the human condition. I worry about the dangers of confusing unhappiness with mental illness. That was the error made by a previous generation of psychodynamic psychiatrists whose theories claimed to account not

only for symptoms, but for all of normal psychology. Now the same mistake is being made again, this time by biological psychiatrists who promote an expansion of the boundaries of diagnosis.

Modern psychiatry has rejected its long-standing psychosocial perspective, and has adopted a narrow version of the medical model. From the National Institute of Mental Health (NIMH) to the National Association for the Mentally Ill (NAMI), the motto has been adopted that mental disorders are brain diseases. This dogma is half-true and half-untrue. Yes, everything we observe clinically also happens in the brain. But you cannot understand the mind on that basis alone.

A landmark event occurred in 1980, when the American Psychiatric Association adopted the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III*), a system that became standard all over the world. Over the next several decades, the *DSM*, including its 1994 revision as *DSM-IV*, was the primary tool used by psychiatrists to classify mental illness, both in the United States and around the world. The *DSM* system is now in its fifth edition (*DSM-5*), and while there have been a few changes, it remains essentially the same. It describes almost any type of psychological symptom using hundreds of categories that include everything from distress and disappointment to disabling illness. The *DSM* makes many of life's misfortunes diagnosable, and implicitly offers psychiatry as a cure for unhappiness.

Paradoxically, one would have thought that psychiatry's move back into the medical mainstream would have encouraged it to focus on severe mental illnesses. That would have been logical, given the many patients who absolutely need

specialist care. But psychiatrists working in outpatient settings, community clinics, or private offices see patients who are much less ill. They want their work to be validated (and made insurable) by the diagnostic system. This is why *DSM-5* encourages clinicians to give every patient a psychiatric diagnosis (for which they can be reimbursed). In this way, economic factors have made the temptation to medicalize the human condition almost irresistible.

The most distressing change in psychiatry is the way it is now being practiced. Patients are often seen for 10–15 minutes, and are given little time to talk about what is happening in their lives. Diagnoses are made rapidly—and often inaccurately. Instead of listening, and asking about current circumstances, psychiatrists focus on a checklist of symptoms, a kind of parody of the criteria listed in the *DSM* manual. Based on the answers to these questions, prescriptions will be written for almost every problem—and "adjusted" every time a patient comes in feeling distressed. It is also worth noting that the practice of psychiatry becomes more lucrative when more patients are seen briefly (and sent off with prescriptions). This way of working meets with approval from psychiatrists and other professionals who believe that mental illness is entirely due to molecules that have gone awry. It is also good news for pharmaceutical companies, whose profits depend on the high volume of drugs prescribed for the most common mental disorders.

For all these reasons, I have become critical of the way many of my colleagues practice psychiatry. But these errors are not based on malignant intent. My colleagues believe they are doing the best for patients, and that talking and listening are old-fashioned practices that belong to an unenlightened past. They want to do *something* for every patient,

even when there is no scientific basis for doing so. They also live in a social environment that strongly reinforces these practices.

The result is a serious overdiagnosis of mental disorders, leading to a serious over-treatment of patients. I have written this book to counter that trend. I want to send out a message that psychiatry is over-stretched. Instead of prescribing treatment for what Freud once called "normal human unhappiness," we need to focus our efforts on patients who are seriously ill, and who need us the most. We do not need to diagnose the human condition.

OVERDIAGNOSIS IN MEDICINE

Psychiatry is not the only field of medicine suffering from a tendency to medicalize life's viccissitudes. One strand is what Moynihan et al. (2002) called "disease mongering," that is, considering normal variations to be pathological and treating them as illnesses. This radical expansion of medicine and the resulting overdiagnosis reflect a number of factors, including the wish of physicians to expand their domain, the wish of patients to find help for suffering, and massive propaganda from the pharmaceutical industry. The danger is that over-zealous diagnosis fails to help the sick while harming the healthy.

Another reason for overdiagnosis is the wish to identify and treat illness in its early stages. This has long been a goal of specialists in cancer, who have supported large public programs to encourage people to be screened, using procedures such as mammography or the measurement of prostate-specific antigen (PSA). Even though these

procedures have had at best mixed results, most physicians think it is better to screen than not to screen. The same idea is held by most patients.

In psychiatry, similar ideas have gained a good deal of traction. The principle has been applied to depression, for which mass screening tests have sometimes been carried out. Unfortunately, such measures pick up distress, not treatable disease, and do not assess severity. By pathologizing episodes that would resolve on their own, screening can do more harm than good (Thombs et al., 2008). Similarly, the movement for the recognition of early psychosis (McGorry et al., 2010) runs against a similar problem: people with subclinical symptoms do not necessarily go on to develop full disorders.

Overdiagnosis in medicine unnecessarily worries people, and often leads to futile and ineffective treatment. Perhaps its greatest problem is that it diverts resources away from the seriously ill, who need our care the most, and directs them to people who are either not ill or who can be expected to recover from their symptoms without treatment. Psychiatrists have enough work to do without expanding the boundaries of the disorders into the world of the "worried well" or of people going through a "bad patch."

Life would be simpler if we could establish a clear definition of mental disorder, and separate it from normal unhappiness. But as Allen Frances (2013) has observed, doing so has proven almost impossible. Each edition of the *DSM* has attempted to provide such a definition, but each definition requires a subjective judgment as to what is illness and what are the vicissitudes of the human condition. This has made it easier to medicalize problems of living.

DON'T BLAME THE *DSM-5*!

To what extent is the *DSM* system responsible for the current plight of psychiatry and the overdiagnosis of mental disorders? With the publication of *DSM-5*, critics of psychiatry had a field day criticizing its diagnostic system. Insiders, such as Allen Frances (2013), focused on retaining the concept of normality, and not expanding psychiatric diagnosis to people who are, like the rest of us, struggling with their lives. Outsiders, such as the psychotherapist Gary Greenberg (2013), have used problems with *DSM-5* as a platform to attack the credibility of psychiatry as a discipline.

My own view, developed in a previous book (Paris, 2013), is that we need to view *DSM-5* in a broader context. It is not fair to hold the latest edition to account for trends that have changed, and continue to change, the very nature of psychiatry. A diagnostic manual is a tool that can be applied in different ways. Used cautiously, it need not lead to overdiagnosis or over-treatment. Nor does the *DSM* force us to focus on symptoms to the exclusion of understanding our patients and their life histories.

Psychiatrists in practice, anxious to be "real doctors," have adopted an ideology based on neuroscience (Paris, 2008a). The belief that mental disorders are "nothing but" brain diseases, strongly influenced by the pharmaceutical industry, is the source of the problem. Psychiatrists do not write most of the prescriptions that patients receive—family doctors and internists do. But as specialists, psychiatrists have great influence on primary care. Family doctors who consult with us are very likely to be told to prescribe more drugs, not less. I sometimes think I am the only one writing consultations

suggesting that patients are being over-medicated and that psychotherapy has not been seriously considered.

When *DSM-III* was introduced in 1980, I was a strong supporter of the new system. I had learned *DSM-I* in medical school and *DSM-II* in residency. Like most psychiatrists, I was unimpressed with the theoretical validity and the sloppy definitions in these early editions. Moreover, psychiatrists couldn't even agree about the most basic diagnoses. With no gold standard, patients might see three psychiatrists and receive three different opinions. To attain scientific credibility, the classification system needed to become more reliable. While disagreements still occur, the reason does not lie with the way the *DSM* editions have been written. Practitioners make diagnoses intuitively, and rarely follow the guidelines in the *DSM* very closely (Zimmerman and Galione, 2010).

Even in *DSM-5*, the reliability of diagnosis remains problematic, as shown by the disappointing results of recent field trials (Regier et al., 2013). Moreover, the categories listed in the manual have uncertain validity, in that all diagnoses are entirely based on signs and symptoms, without confirmation from biomarkers. In that respect, *DSM-5* is no different from its predecessors. This was not a choice, but a necessity. Unlike the rest of medicine, psychiatry has no biological markers to validate *any* of its diagnostic categories.

It is possible to practice effective medicine without biomarkers, particularly in syndromes (such as migraine) that are not well understood. Moreover, psychiatry does as well as most medical specialties in getting its patients better (Leucht et al., 2012). But it is not yet able to ground clinical observations in objectively measured data. Biomarkers could, with time, guide physicians to the mechanisms behind illness. They would not answer all our questions, but if we had them,

overdiagnosis would be a little less likely. Also, at this point, the causes of mental disorder remain largely unknown. That is why clinical diagnosis remains imprecise and uncertain. We cannot blame *DSM-5* for that problem. The manual simply reflects the imperfect state of our knowledge.

DIAGNOSTIC EPIDEMICS

A lack of knowledge should make psychiatrists cautious about their threshold for identifying mental disorders. Yet over recent decades, our field has developed an enthusiasm for making even *more* diagnoses, with an inflated prevalence that leads to *diagnostic epidemics*. Using current definitions (or expanded versions of existing categories), common mental disorders have become ubiquitous.

Frances (2013) has usefully documented how some diagnoses in psychiatry have doubled, tripled, or quadrupled in prevalence over recent years. For example, at least half the population can expect to suffer sometime in their life from what the *DSM* defines as "major depression" (Moffit et al., 2009). But these high numbers may only be an artifact of the way we make this diagnosis. The problem goes back decades, as psychiatry has adopted an overly inclusive definition of depression. It is difficult to say what the real prevalence of depression is when the concept of mood disorder is conflated with unhappiness.

Recently, three disorders traditionally considered to occur rather infrequently (bipolar disorder, attention deficit hyperactivity disorder [ADHD], and post-traumatic stress disorder [PTSD]) are being much more frequently diagnosed. Even disorders once considered quite rare (such as autism) are now being identified in large numbers of patients.

These changes in diagnostic practice tell us more about diagnostic fashion than about scientific progress. Diagnostic fads simply relabel patients that psychiatrists have always seen. The new categories are designed to either suggest a treatment option (as in bipolarity and ADHD), and/or to classify symptoms in the framework of disorders that are either a subject of clinical interest (as in PTSD) or that become eligible to more extensive treatment when identified (as in autism).

There are real dangers to diagnostic epidemics. All too often, they lead to incorrect and unnecessary treatment. Moreover, expansion of diagnosis to subclinical and non-clinical phenomena compromises the validity of the classification system. Finally, enthusiasm for making diagnoses prevents psychiatrists from separating psychopathology from normality. Major depression is the best example: 11% of the general population is currently taking antidepressants (Pratt et al., 2011)—a rate that is much higher than the prevalence of the disorders for which these drugs are usually prescribed. It has also been shown that prescriptions of these agents are often given for "off-label" indications (Mojtabai and Olfson, 2011).

There is no shortcut around these problems. Without a gold standard, screening instruments and scales can only have provisional validity. Psychiatric diagnosis is at best a common language, and current categories should not be treated as "real." This book will underline the difficulties in reaching accurate diagnoses, the dangers of overdiagnosing disorders, and the over-treatment of patients that follows from overdiagnosis, as well as the problems in recognizing what is normal.

PART I

BACKGROUND

1

DIAGNOSIS IN PSYCHIATRY

WHAT DIAGNOSIS IS—AND WHAT IT ISN'T

Medicine is an applied science that requires a classification of the phenomena it studies and treats. The features of illness also need to be described in a logical and scientific way. But the classification of disease does not have the same level of precision as six quarks or 92 natural chemical elements. We can more usefully compare illnesses to species in biology, which tend to be fuzzy at the edges and overlap with each other.

Diagnoses should ideally be based on specific pathological processes related to specific etiological pathways. The term *endophenotype* refers to the mechanisms that underlie disease—as opposed to *phenotypes*, clinical features that can be directly observed. Only some diseases in medicine have identifiable endophenotypes. Even so, diagnoses serve several functions. They guide medical research, allowing for the study of causes, prevalence, outcome, and methods of treatment. They serve as shorthand communication between professionals. Finally, they help patients, by providing an explanation for how and why they are ill.

Symptoms, when they cluster together, form syndromes. But without a specific etiology, syndromes are not diseases.

Since most mental illnesses remain syndromes, psychiatry describes its categories as "disorders." In other words, they do not qualify as diseases in the same way that most medical conditions do. We sometimes forget that mental disorders are convenient labels that lack any ultimate degree of reality.

Moreover, diagnosis in medicine should not be used to describe single symptoms, which can have many different causes. A good example of this mistake was a proposal (not, in the end, adopted) to create a separate category for suicidality in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*). Any symptom can be described using standard scales, but unless symptoms reflect common mechanisms, they don't belong in a diagnostic manual. Finally, diagnosis should not be a political or a social statement. We should not diagnose post-traumatic stress disorder (PTSD) just because we sympathize with suffering in patients.

Overdiagnosis is usually the result of enthusiasm or zealotry, for either a theoretical concept or a treatment method. But expanding illness categories undermines the very purpose of classifying psychopathology. If diagnoses are blended into a spectrum, the differences between them are obscured, and research into their causes will be hobbled. The *DSM-5* system tried to define fewer diagnoses than *DSM-IV*, but still has too many. At this point we know too little to reduce this number by defining meaningful disease "spectra."

THE CURRENT STATE OF PSYCHIATRIC DIAGNOSIS

Medicine works best when accurate diagnosis leads to effective treatment. In contrast, overdiagnosis derives from

inaccuracies that lead to ineffective or harmful treatment. Mistaken therapy is inevitable when we treat people with one problem as if they have another, and when people who are normal or have mild symptoms receive interventions that have been tested on severely ill patients.

In spite of its lack of knowledge of mechanisms, psychiatry has quite a few effective treatments. The effect sizes for our pharmacological interventions compare well to the rest of medicine (Leucht et al., 2012), and clinical trials demonstrate that many forms of psychotherapy are effective (Lambert, 2013). In general, the sickest patients almost always need pharmacotherapy, while mild to moderately ill patients often do as well or better with well-structured forms of psychotherapy. Yet all too often, we treat patients *only* with drugs, even when they don't respond to them and don't need them. This trend, which now dominates clinical practice (Mojtabai and Olfson, 2008), is based on the old saw that when you have a hammer, everything looks like a nail. Ideally, diagnosis should help us to distinguish patients who need pharmacotherapy from those in which its use is either doubtful or optional. But that is not what is happening. Instead, drug treatment for every patient is rationalized by the overuse of existing diagnostic categories.

Ultimately, diagnosis in psychiatry must be based on a better understanding of why people fall ill. We are just not there yet. In the past, psychiatry subscribed to a biopsychosocial model (Engel, 1980), in which multiple factors (biological, psychological, and social) were taken into account, both in etiology and in treatment. This model has been replaced by a reductionistic approach in which mental disorders are "nothing but" brain disorders. Leaders in psychiatric research want to redefine the specialty as a branch of

neurology whose practice consists of "applied neuroscience" (Insel and Quirion, 2005). This model fails to account for the etiology of mental disorders, and is a very poor guide to treatment. We are often told that we only have to wait for further progress in neuroscience—breakthroughs are constantly promised that are supposedly just around the corner. Unfortunately, no matter how many corners we turn, answers remain out of sight.

Biological reductionism has come to dominate academic psychiatry. A neuroscience model has been strongly supported by the National Institute of Mental Health (NIMH), whose director is Thomas Insel, a researcher best known for his work on oxytocin in prairie voles. Although the media have sometimes described Dr. Insel as America's "psychiatrist-in-chief," this is far from the case. The NIMH director actually favors the abolition of psychiatry, which he thinks should reunite with neurology (Insel and Quirion, 2005). As of 2013, to apply for research grants at NIMH, investigators have been advised to eschew *DSM-5* in favor of a new system, the Research Domain Criteria (RDoC; Insel, 2009; Insel et al., 2010). The RDoC system describes a matrix of dimensions of psychopathology, theoretically evolved and assessed across multiple levels. The data supporting this new system are at best sketchy, and mostly absent. To be confident that the blanks will eventually be filled in, one would have to be a "true believer."

In the meantime, psychiatrists continue to practice their craft and treat very difficult patients. They cannot wait 50 years for a brave new world of neuroscience to come to fruition. We don't know the ultimate fate of systems like the RDoC, but similar proposals have been made in the past (Eisenberg, 1986), and they are now remembered only as historical curiosities.

Fortunately, you don't have to understand clinical phenomena on a molecular or cellular level to make a diagnosis. Psychiatry may not be as precise as other branches of medicine, but by using careful clinical observation, we succeed in helping most of our patients. Moreover, some of the most important empirical findings that have made psychiatry effective were based on observation, rather than on laboratory data. We did not need neuroscience to describe bipolar-I disorder and to determine that it responds specifically to lithium. (Moreover, we still don't know how lithium works in the brain.) In the psychotherapies, where the number of evidence-based treatments has steadily increased, we do not need neuroscience to determine that specific psychological interventions are effective in a wide range of conditions, including depression, anxiety, eating disorders, and personality disorders.

Nonetheless, diagnosis in psychiatry would have a more secure grounding if observation of signs and symptoms could be supplemented by biomarkers. These measures could also turn out to be relevant for disorders with psychosocial determinants, since psychological processes have their own effects on the brain. So why doesn't psychiatry have any biomarkers? A look at the history of medical diagnosis may help shed light on that question.

BIOMARKERS IN MEDICINE AND PSYCHIATRY

Until about a hundred years ago, medical diagnosis was as problematic as psychiatric diagnosis is today. Patients were

classified by signs and symptoms such as anemia, swelling, or pain—describing symptoms or syndromes, not diseases with a definite cause or course. Treatment was also symptomatic, and the concept of disease entities only gradually emerged.

In the late nineteenth century, physicians learned how to identify specific etiologies for conditions such as infectious diseases, caused by microorganisms that could be cultured and observed under a microscope. Physicians also learned to validate clinical diagnoses by conducting autopsies and biopsies, allowing for direct observation of pathological changes in organs. These methods proved invaluable in many diseases. Even so, much of medicine remained in a muddle about classifying disease—until technologies were developed to assess markers in living patients. These blood tests and imaging techniques are the backbone of modern diagnosis.

Thus medicine becomes more scientific when biomarkers provide objective measures of disease processes, even if they are not yet available for all diagnoses that physicians treat. (Some conditions remain syndromes, much as in psychiatry.) Biochemical measurements can assess the physiological changes associated with illness. Imaging allows observation of the organs of the body in situ, and can pinpoint abnormalities that previously could only be guessed at. In recent years, a few diseases have also been linked to changes in the genome. All these methods will continue to shape medical diagnosis in the twenty-first century.

Psychiatry has not yet found similar ways to validate its diagnoses, and it entirely lacks biomarkers. In spite of all the progress in neuroscience over the last 20 years, we are still waiting for findings that can be applied to clinical practice.

At this point, there are none (Hyman, 2011). Unfortunately, the hype around neuroscience, with its beautifully colored pictures of brain activity, has deluded many into believing that it has all the answers (Satel and Lilienfeld, 2013). No patient has yet benefited from any of these scientific advances.

Over the years there have been a number of false starts. Blood tests are not helpful in psychiatry: due to the blood-brain barrier, peripheral levels do not necessarily reflect CNS neurochemistry; we can only indirectly measure the activity of neurotransmitters, or of brain hormones. And while these measures are sometimes used in research, they have thus far had no clinical application. Similarly, a large number of studies have applied imaging technologies, usually functional magnetic resonance imaging (fMRI), to mental disorders. But the results are almost always suggestive but nonspecific. While imaging procedures will eventually be refined, they have thus far failed to identify patterns that can be specifically and sensitively correlated with any category of mental illness. Diseases in which a brain lesion can be identified have often become the province of neurology rather than psychiatry. Uher and Rutter (2012) described the impact of neuroimaging on the major mental disorders that psychiatrists treat as essentially "non-informative." There is no way of looking at a brain scan and coming up with any diagnosis.

Genetic studies in medicine have some practical value in oncology, but have been disappointing for psychiatry (Hyman, 2011). None of the genetic markers studied thus far is specific to any diagnosis, and none explains more than 1% of the outcome variance for any disorder. This could be because we don't have the right categories, and have to await

the discovery of endophenotypes. Even in disorders in which it is established (from behavior genetics) that heritability is high, we do not know the mechanisms. The main problems derive from complex interactions between multiple genes, from gene-environment interactions, or from epigenetics (the mechanisms determining whether genes are switched on or switched off). This is why expecting to find "genes for" schizophrenia (or any other illness) is naïve (Kendler, 2005). Genetic research could eventually help to identify vulnerabilities, but that development is not likely in the foreseeable future (Uher and Rutter, 2012).

In summary, psychiatry is more or less where the rest of medicine was a hundred years ago—at the very beginning of a long quest for valid diagnostic procedures. This situation should not come as a surprise. If you are studying the liver or the kidney, most cells (or groups of cells) do more or less the same thing. But every neuron in the brain is more or less unique, and there are 100 billion of them, connected in networks that can be counted in the trillions. While research on neural networking might eventually help to sort out this mind-boggling complexity (Zorumski and Rubin, 2011), we are unlikely to find consistent links between psychiatric symptoms and specific regions of the brain. That is because each neural system makes only a small and partial contribution to clinical outcomes. If we do discover biomarkers of this kind, they will probably not look like brain scans, but will reflect a complexity that only some future technology will be able to handle. In summary, the expectation that the kind of breakthrough that created molecular genetics will happen to brain science is attractive to scientists, politicians, and the public at large. But the problem is much too complex for a short-term solution.

Several obstacles interfere with the incremental levels of progress that could be possible in the coming decades. One is that research methods on biomarkers are very expensive, and are often used in small (and inevitably unrepresentative) samples. In neuroimaging, researchers often report differences in samples that rarely exceed 20 subjects. In genetic research, single genes hardly ever have strong effects on their own. One needs very large samples to obtain sufficient power to pick up even the weakest differences, each of which are subject to modulation by other genes, and by the environment.

The story of the search for biomarkers that could validate psychiatric diagnoses is one of short-term frustration but long-term hope. For clinicians, keeping this lack of basic knowledge in mind might help to encourage caution about overdiagnosis.

Finally, biomarkers, even if we were to discover them, would not provide all the data needed to understand how the mind works. Some observers (Fulford et al., 2006) have questioned whether they are either necessary or sufficient to justify a medical diagnosis, and whether relying on them excessively downgrades the psychosocial factors in illness. I would say they are potentially highly useful but conceptually and practically incomplete.

In the past, medicine advanced when new technologies were developed. It could be that yet-to be-developed technologies could change psychiatry within the lifetime of some readers of this book. Even so, it is more realistic to expect incremental change than dramatic breakthroughs. When you are talking about something as complex as the mind, you cannot succeed in reducing thought, emotion, and behavior to cellular mechanisms.

SCREENING AND PSYCHOLOGICAL TESTING

In the absence of biomarkers, psychiatry and clinical psychology have had to focus on *phenomenology*—what can be directly observed by professionals or reported by patients. The art of the clinician lies in asking the right questions, and in observing phenomena accurately. Mental states are measured either by asking patients themselves to describe them, or by having clinicians rate and score them.

These methods can be made more reliable using *psychometrics* (literally, measuring the mind). The most common method in psychology is the use of self-report questionnaires. These instruments are developed using special techniques (item analysis to make sure questions are relevant, and factor analysis to create specific sub-scales). These measures are the backbone of psychological research and have been used to measure everything from personality traits to quality of life. While one might question whether people are always the best judges of their own problems, self-report is usually more reliable than clinical observation.

Since psychologists are interested in normal variation, self-report methods have been widely used in community populations. The question is whether questionnaires are equally useful for clinical diagnosis, or only give the impression of science by providing quantitative scores. In practice, they can only be used as screening measures to identify patients who need to be examined in more detail. As we will see, diagnosing bipolar disorder or attention deficit hyperactivity disorder (ADHD) on the basis of self-report questionnaires has been one of the leading causes of overdiagnosis of these conditions.

The other method of measurement depends on clinical ratings that are scored by practitioners. These "semi-structured" interviews present a list of standard questions to guide the rater, who can then ask them in his or her own words. This is the method that underlies *DSM* diagnosis, but formal interviews elaborate the criteria to ensure that nothing important is missed. However, making valid judgments of this kind requires training, since all answers to questions are subject to a degree of interpretation. The advantage of a semi-structured interview is that clinicians cannot skip criteria, or jump to conclusions based on just one of them.

Even so, since there is no "gold standard" for semi-structured interviews, and since many are directly based on *DSM* criteria, they can be no more valid than the categories they are designed to measure. These instruments are valuable in research, in that they ensure that patients in a sample have more or less the same psychopathology. But they do not necessarily increase the validity of diagnoses, or prevent overdiagnosis.

One good example is the problems that emerge when similar interviews are used in epidemiological research (Akiskal et al., 2006; Grant et al., 2004). If research assistants, who often administer them, carry out the ratings, the frequency of disorders may not reflect the clinical experience of a better-trained observer. And the most likely problem is not underestimation, but overestimation.

Finally, psychometric data, whether rated by patients or by clinicians, are entirely based on signs and symptoms. They are not necessarily linked to the unknown mechanisms that underlie clinical symptoms, or to biological pathways that could eventually be discovered. No matter how accurate clinical assessment is, diagnostic categories can only

be considered provisionally valid, while waiting for a better understanding of mental disorders.

While biomarkers may not provide a complete answer to these questions, they could, at least in principle, be closer to the underlying causes of illnesses. Without them, diagnoses in psychiatry cannot be more than syndromes: convenient ways of communicating about patients with common signs and symptoms. The study of the mind and its maladies remains an enormously complex challenge, full of problems and questions. An honest psychiatrist must accept that answers will require many decades of research. This is where psychiatry is today, and we need to accept these limitations.

OVERDIAGNOSIS AND UNDERDIAGNOSIS

Life is full of decisions that carry potential benefits and risks. These choices can change in the presence of psychopathology. Anxious mood is associated with an overestimation of risk, preventing necessary decisions from being made. Impulsivity produces an underestimation of risk, leading to poorly considered actions that can have negative consequences.

The same dilemmas about risks and benefits apply to clinical assessment. If we underdiagnose patients, we may fail to identify treatable disorders. If we overdiagnose patients, we may treat them for disorders they do not have. Finding the right balance is not easy.

Technically, the consequences of these choices are quantified using the concepts of *sensitivity* and *specificity* (Altman and Bland, 1994). For any disease, there are, at least in

principle, true positives, false positives, true negatives, and false negatives. Sensitivity is the proportion of true positives correctly identified, and specificity the proportion of true negatives correctly identified. (The ratio of true positives to true to false positives is the *positive predictive value*.)

Sensitivity and specificity are a trade-off. The right choice depends on whether there is a greater risk in underdiagnosis or in overdiagnosis. When sensitivity is too low, underdiagnosis is likely. But when sensitivity is too high, overdiagnosis is a danger. If you have too many false negatives, you may be missing treatable illness. But when you have too many false positives, your decision-making system has an alarm system that goes off when it shouldn't.

There is a very good reason that overdiagnosis is more likely than underdiagnosis. A bias toward false positives is part of the culture of medicine. Every medical student is taught, above all, not to "miss anything." Yet most conditions that physicians see are, by definition, common. Medicine has an old saw: "when you hear hoofbeats, think horses, not zebras." You can be a good doctor by recognizing the most common clinical presentations, and with experience, it can take only 5 or 10 minutes to identify most of them.

Even so, physicians love to tell stories about missed diagnoses of rare diseases. These incidents often become the subject of clinical-pathological conferences. I remember one from my own student days where the treating physicians failed to recognize an (extremely rare) diagnosis of hyperparathyroidism. But looking harder for that condition in patients you see in normal practice would be neither practical nor helpful. Fewer medical stories focus on overdiagnoses that lead to useless or harmful treatments. This bias reflects a "can-do" philosophy, in which every effort is made

to carry out active interventions, and to search for the diagnostic categories that support doing so.

Psychiatric diagnosis faces a larger hurdle. We can never say that a category is a true positive if we have no "gold standard" on which to base our conclusion. For this reason, specificity and sensitivity often refer to how well observable criteria support a *DSM* diagnosis—which is not the same thing. At best, current diagnoses, based on phenomenology alone, can only be considered to be rough versions of true illnesses that are yet to be discovered.

SCHIZOPHRENIA: OVERDIAGNOSIS AND UNDERDIAGNOSIS

Underdiagnosis is more likely when a disorder is unappealing. That is most likely to happen when the course of the illness is highly chronic, or when effective treatment is complex or inaccessible. A good example is one of the most important conditions in our clinical practice: schizophrenia.

It is difficult to determine whether any mental disorder is underdiagnosed or overdiagnosed. Without a gold standard, one cannot be sure. There are also few empirical studies that can shed light on this issue. But in my professional lifetime I have seen an increasing reluctance on the part of psychiatrists to diagnose schizophrenia.

One might think that a diagnosis so central to psychiatry would not suffer from underdiagnosis. After all, we have powerful tools to manage the psychotic symptoms that mark this illness. But the long-term prognosis of the disorder varies from uncertain to grim. For this reason, psychiatrists may hesitate to diagnose schizophrenia—even when it is obvious.

Yet 50 years ago, American psychiatrists diagnosed *most* psychotic patients with schizophrenia. There was even a category of "pseudo-neurotic schizophrenia" (Hoch et al., 1962), which describes patients who today would be seen as suffering from severe anxiety disorders or personality disorders. The main reason for this diagnosis was the wish to prescribe antipsychotic drugs, which were in their early days of glory, and whose problematic side effects were not yet well known.

Moreover, schizophrenia was too broadly defined 50 years ago, allowing for expansion of the diagnosis. And since lithium was not yet being used, there was little value in differentiating schizophrenia from bipolar disorder. If both types of patients were prescribed antipsychotics, then diagnosis had no effect on treatment. Still another problem was that schizophrenia was (and still is) a heterogeneous syndrome without biological markers; even the course of the disorder is not consistent (Craddock and Owen, 2005).

A research project helped to change the situation. The "New York–London study" (Cooper et al., 1972) showed how fashion in diagnosis can be more important than facts. In the 1960s, researchers interested in differential diagnosis presented filmed interviews of psychotic patients to American psychiatrists (who usually diagnosed them with schizophrenia) and to British psychiatrists (who usually diagnosed them with mania).

In 1970, lithium became widely available. Now differential diagnosis was crucial, since lithium was specific in preventing relapse of manic-depression, which had not been possible when patients were maintained on antipsychotics alone. Then research by Abrams and Taylor (1981) on the differential diagnosis of schizophrenia and bipolar disorder clarified the clinical features of both disorders. It had

been widely believed that a set of "first-order" symptoms described by the German psychiatrist Kurt Schneider (1959) were specific to schizophrenia. (That is what I was taught as a resident, and we all dutifully memorized Schneider's list.) But Abrams and Taylor showed that these symptoms are as common in mania as in schizophrenia, and are not specific indicators for either diagnosis.

Younger psychiatrists may not realize that lithium was once a miracle drug—one of the greatest breakthroughs in the history of medical therapeutics. It is understandable that psychiatrists in that era wanted their patients to benefit from it, and were tempted to rediagnose difficult cases as "manic-depressive." Whereas schizophrenia had been overdiagnosed in the past, it now became much less common. Diagnostic fashions can shift from one extreme to another.

Even today, schizophrenia can suffer from under diagnosis. Faced with managing intractable cases, clinicians sometimes look for ways to avoid making this diagnosis. Although some patients show a partial recovery, long-term studies show that its relatively poor prognosis has not changed since the time of Emil Kraepelin, the German psychiatrist who first made the distinction between this type of psychosis and manic-depression (Jobe and Harrow, 2005). This explains a certain preference for diagnoses that focus on mood symptoms.

However, there is also a reason for the reluctance to diagnose schizophrenia to recede. This is due to recent interest in early intervention, with the idea that the disease can be treated more effectively in its early stages (McGorry et al., 2010). However, while identifying schizophrenia in adolescence would have advantages, it has not been shown that early treatment actually improves long-term prognosis.

We have also seen a trend to early diagnosis in other areas of medicine. But this development, however well intentioned, has problems of its own. It is, for example, not clear that everyone with abnormal lipid levels really needs to be on a statin, given that more readily preventable risks, such as hypertension, obesity, smoking, and blood glucose, are the strongest predictors of cardiac disease (Danaei et al., 2009). Practice that focuses more on blood levels than on clinical outcomes reflects a naïve belief in pharmacological intervention that characterizes our medical culture.

Enthusiasm for early treatment of schizophrenia led to a proposal for including a category of "risk psychosis" in *DSM-5* (Addington et al., 2008). This idea was eventually shelved when it became clear that among young people with symptoms that seem to suggest an early onset of schizophrenia, only 30% actually go on to develop psychosis (Bosanac et al., 2010). Thus, including risk psychosis would have led to unnecessary antipsychotic prescriptions in people who do not need them. This example illustrates how the wish to treat, even before a disease develops, can be an important driver of overdiagnosis.

Because of a reluctance to diagnose schizophrenia, as well as the unclear boundary between schizophrenia and bipolarity, a diagnosis of *schizo-affective disorder* is sometimes made, particularly when patients do not have what clinicians believe to be classical symptoms of the disorder (Pope and Lipinski, 1978). But what are the "classical" features of schizophrenia? The image of a chronic patient with limited emotional range ("flat affect") may not be as common as clinicians believe. Schizophrenia patients can become depressed, and about 5% will eventually commit suicide (Palmer et al., 2005).

Schizo-affective disorder is a final twist to the story of the problems that clinicians have in putting patients in valid categories. It is a "fudge" diagnosis, applied to bipolar patients who are more psychotic than clinicians expect them to be. Yet with careful study of clinical features and family history, most patients can be slated either into schizophrenia or bipolar disorder (Lake and Hurwitz, 2006). It is only appealing because it is seen as having a more favorable prognosis.

The reluctance to recognize a serious illness like schizophrenia reflects a universal human tendency to resist bad news. However, psychiatrists cannot make difficult patients go away by failing to diagnose them.

WHY OVERDIAGNOSIS IS THE GREATER PROBLEM

Just as underdiagnosis derives from therapeutic pessimism, overdiagnosis emerges from outbreaks of optimism. Also, the loose use of terms to describe drugs is seriously misleading. Antipsychotics do much more than control psychosis, effects of antidepressants are not specific to depression, and mood stabilizers do not necessarily stabilize mood.

Yet given the enthusiasm about developments in psychopharmacology, after the introduction of antipsychotics, even schizophrenia became a more popular category. At around the same time, as tricylic antidepressants were found to be efficacious, clinicians were attracted by a concept of "masked depression" (Razali, 2000), which suggested that patients without depressive symptoms could respond to antidepressant drugs. Actually, these agents do have a much wider range of indications, and are often effective in anxiety disorders

(Casacalenda and Boulanger, 1998). Pharmacological agents often have broad spectrum effects that go beyond any single category. One cannot conclude from that observation that every clinical picture that responds to an antidepressant is "really" depression.

With the popularity of second-generation antidepressants, primary care physicians became less reluctant to prescribe medication. Patients who respond to serotonin reuptake inhibitors benefited from this development. Unfortunately, a large number of patients do not respond, or have only a placebo response, to these agents (Kirsch et al., 2008). Ironically, optimism about the effects of antidepressants has greatly fueled placebo responses in patients.

In the mental disorders that have vastly increased in prevalence in recent decades, optimism about pharmacological treatment lay behind what proponents call "increased recognition" of a diagnostic category. The first is major depression (Patten, 2008), in which diagnosis has been associated with the wish to prescribe antidepressants. The second is bipolar disorder, now often diagnosed in a broad "spectrum" (Paris, 2012), in which the wish is to prescribe mood stabilizers (and/or antipsychotics). The third is ADHD, driven by a wish to prescribe stimulants (Frances, 2013). In all three cases, optimism has also spread to epidemiological research, and we have seen a dramatic increase in prevalence, both in community studies and in clinical populations. This could represent increased recognition of diagnostic entities, but it could also be a fad for giving patients diagnoses that suggest a specific form of treatment.

Two other conditions have dramatically increased in prevalence for rather different reasons. The first is posttraumatic stress disorder (PTSD), a diagnosis that entered the

DSM manual only in 1980 (McNally, 2003). While there are evidence-based treatments for PTSD, there is no quick fix. Social and political forces, such as the widespread sympathy for victims, not radical optimism about treatment, drive the increased use of this diagnosis. Patients with this condition have always existed, but what has changed is an attribution of their symptoms to the effects of traumatic experiences. In addition, making the diagnosis allows patients to obtain fairly generous disability benefits.

Another diagnosis that has been increasing rapidly in prevalence is autism (and autism spectrum disorders). In this case, there is little reason for therapeutic optimism, since no existing treatment has been found to be more than marginally effective (McPheeters et al., 2011). Yet autism describes a set of serious symptoms for which both families and professionals have sought a diagnostic home. By placing a disparate group of developmental disorders in one category, research is encouraged, and hopes for an eventual cure are raised. Another reason for the popularity of this diagnosis may be the availability of benefits for long-term disability.

ORDER AND CHAOS

The world is full of chaotic events. In psychiatry, since clinical phenomena are complex and difficult to classify, psychiatrists are still searching for a Linnaeus or Mendeleev to put order into chaos. Minds crave meaning, which helps explain the continued influence of traditional religious beliefs, in which unpredictable events reflect supernatural intent. The American psychologist Paul Bloom (2004) has shown that a search for order begins early in infancy, and that young