Stewart Justman

The Nocebo Effect

Overdiagnosis and Its Costs

The Nocebo Effect

The Nocebo Effect

Overdiagnosis and Its Costs

Stewart Justman

palgrave
macmillan

THE NOCEBO EFFECT
Copyright © Stewart Justman, 2015.
Softcover reprint of the hardcover 1st edition 2015 978-1-137-52328-0

All rights reserved.

Contains excerpts from *Notes from the Underground* and *The Gambler* by Fyodor Dostoyevsky, translated by Jane Kentish (1991). By permission of Oxford University Press. www.oup.com

First published in 2015 by PALGRAVE MACMILLAN® in the United States—a division of St. Martin's Press LLC, 175 Fifth Avenue, New York, NY 10010.

Where this book is distributed in the UK, Europe and the rest of the world, this is by Palgrave Macmillan, a division of Macmillan Publishers Limited, registered in England, company number 785998, of Houndmills, Basingstoke, Hampshire RG21 6XS.

Palgrave Macmillan is the global academic imprint of the above companies and has companies and representatives throughout the world.

Palgrave® and Macmillan® are registered trademarks in the United States, the United Kingdom, Europe and other countries.

ISBN 978-1-349-57677-7 ISBN 978-1-137-52329-7 (eBook)
DOI 10.1007/978-1-137-52329-7

Library of Congress Cataloging-in-Publication Data

Justman, Stewart.
The nocebo effect : overdiagnosis and its costs / by Stewart Justman.
pages cm
Summary: "The Nocebo Effect documents the transformation of normal problems into medical ones and brings out the risks of this inflationary practice. One notable risk is that people labeled as sick may find themselves living up to their label through the alchemy of the nocebo effect"—Provided by publisher.
Includes bibliographical references and index.

1. Placebos (Medicine) 2. Medicine and psychology. 3. Negativism. I. Title.
RM331.J86 2015
615.5—dc23

2015007677

A catalogue record of the book is available from the British Library.

Design by Amnet.

First edition: August 2015

10 9 8 7 6 5 4 3 2 1

Contents

Acknowledgments vii

Preamble: Indefinite Ailments and Inflammatory Messages ix

1 DSM and the Shaping of Depression 1

2 The Ills of Health 39

3 Searching for Signs 71

Interlude: Medicalization and Magnetism 89

4 Overdiagnosis and Its Harms 93

5 Name Games 121

6 Beware What You Look For: Two Cases of Medical Activism 143

7 The Folly of Systems: The Satiric Tradition and Mental Disorders 169

8 The Malady of Awareness 195

Epilogue: Return to Sources 207

Notes 215

Index 269

Acknowledgments

The author is immeasurably indebted to Frederick Crews, John Haller, Barnett Kramer, John MacKinnon, and Derek Summerfield.

Preamble: Indefinite Ailments and Inflammatory Messages

In the course of Plato's *Republic* Socrates distinguishes two kinds of medicine, one an art worthy of its founder Asclepius, the other a perversion. The true physician, the scion of Asclepius, treats definite ills in definite ways. He cures wounds, for example, his technical skills justifying the analogy of physicians to carpenters, pilots, and musicians elsewhere in the *Republic*. The sham physician flourishes in an unhealthy city by pretending to treat the more or less imaginary ailments cultivated by citizens with nothing better to do. ("With the rich man . . . we do not say that he has any specially appointed work which he must perform, if he would live.") Instead of healing wounds or coming to the aid of those caught in an epidemic—which, while dreadful, is at least not imaginary—the sham physician invents names for the "waters and winds" that seem to fill those who lead empty lives.

Shortly before this discussion of medicine and its corruption, Socrates emphasizes that in a healthy city each citizen plays one and only one part: a shoemaker is a shoemaker "and not a pilot also . . . and a soldier a soldier and not a trader also, and the same throughout." An identical dislike of mixtures appears to inform the Socratic view of health. One is either in health or not. When a sensible man—one who doesn't have the luxury or inclination to devote himself to being sick—falls ill, he either gets well in the natural course of things "or, if his constitution fails, he dies and has no more trouble." The fantasist who consults physicians for his various winds and waters has made illness itself his way of life. If dialectic searches for contradictions, such a life is an enacted contradiction in its own right, an absurdity in the eyes of reason.

While the principle that you're either one thing or another—either sick or healthy—may seem like common sense, in reality it's misleading. Normal health includes ills of many kinds, even ambiguous early forms of cancer, which is why those who seek to expand the domain of medicine are guaranteed to have plenty of material to work with. According to

Socrates, Asclepius concerned himself only with persons who had "a definite ailment." A lot of the ills that disturb us even in health are indefinite, though they can acquire a semblance of specificity by taking on clinical names. It may indeed be unwise, as Socrates suggests, to fixate on one's ills—not, however, because there's nothing there but because there is, and because symptoms can be magnified by the interpretations imposed on them by doctors and patients.

In order to figure in the marketplace, many of the ills troubling our minds and bodies have to lose the ambiguity that seems to belong to them. "Compared with the reality which comes from being seen and heard," wrote Hannah Arendt, "even the greatest forces of intimate life—the passions of the heart, the thoughts of the mind, the delights of the senses—lead an uncertain, shadowy kind of existence unless and until they are transformed, deprivatized and deindividualized, as it were, into a shape to fit them for public appearance."[1] Still more obscure are complaints so potentially indeterminate that we might report them in different ways—as chronic fatigue or fibromyalgia, for example—depending on what diagnosis happens to be in favor, or we might not report them at all. Precisely because such internal events lack the confirmed character of things seen and heard in public, they are highly subject to interpretation and, in fact, distortion. The inside of our being is the ultimate Platonic cave of shadows.

When problems of mind and body are brought into the public realm, subjected to the shadowless light of the media, and made the topic of campaigning, controversy, and salesmanship, ill-defined events to which there may be no witness but oneself are transformed into a cause célébre. In recent decades, many common problems have been elevated into medical issues in this way, in the process acquiring both evocative names and large constituencies. Ills as well as goods can be shaped from raw materials, packaged, and popularized. But once ambiguous ills inherent in human existence are labeled—branded—as a consequence of medicalization, the experience of having them in the first place can change. Waters and winds cohere into storms.

Once having entered the marketplace, ideas about illness are capable of stirring up illness itself through the power of the nocebo: the neglected twin of the placebo effect.

> A society's ethnomedicine tells societal members what sicknesses there are, how they are acquired, how manifested, how treated. The nocebo phenomenon suggests that the categories of an ethnomedicine may not only describe conditions of sickness, but may also foster those conditions by establishing expectations that they may occur. Thus, a cultural system commonly thought to serve a healing function may also have a contrary outcome, fostering the same pathologies intended to be healed.[2]

I will argue that medicalization promotes harm under the auspices of healing, both by marketing disorders ("fostering the same pathologies intended to be healed") and distorting the calculation of harms and benefits.

The quoted author concludes that in order to avoid triggering nocebo effects, "We must be cautious in both public health communications and in clinical medicine." Ironically, in the same year in which this admonition was issued, direct-to-consumer advertising became legal, and there ensued a flood of suggestive messages urging us to consider the possibility that we might be sick. In addition to such ads, messages that simply violate caution are among the power sources of the medicalization movement. Announcements that populations of staggering magnitude suffer from undiagnosed disorders—that one in twenty may have bipolar disorder (a figure five thousand times the prevalence of what used to be called manic-depressive illness);[3] or that one in eight Americans suffers from social anxiety disorder;[4] or that as much as 24 percent of the population suffers from "depressive symptoms in various combinations";[5] or that a quarter of the population of New York City was in need of psychological treatment following the 9/11 attacks;[6] or that 43 percent of all women suffer from sexual dysfunction;[7] or that half of the US population will at some point meet the requisites of a psychiatric disorder;[8] or that half of American men are "sexually dysfunctional";[9] or that "as many as 72% of people in the workforce are depressed";[10] or that "three-quarters of the general public will experience an event that could cause a traumatic response sometime in their lifetime";[11] or that 82.5 percent of young people will qualify for a psychiatric diagnosis by the age of 21;[12] or that depression will soon be the second leading cause of disability around the world[13]—announcements like these, the very opposite of cautious, provide the themes, banners, and rallying cries of medicalization. Inevitably quoted again and again, their exaggerations building on one another, they are symptoms of an information epidemic that itself defies all limits.

1

DSM and the Shaping of Depression

Chapter and Verse

A received opinion in medical literature holds that Asians are prone to present psychiatric problems as physical complaints—depression as backache. Implying as it does that Asians lack a proper understanding of what ails them or, if they do understand, hesitate to call it by its right name, this dogma enshrines prejudices and misreadings as medical facts. If Asians have trouble speaking the foreign language of psychiatry, the reason may well be that they still possess traditional ways of managing ills like those now bundled into the diagnosis of depression.[1] Cultures with tighter norms of self-restraint, which index stronger social institutions, will struggle to translate the concept of depression arising in a way of life whose theme is the free expression of selfhood.[2] On this showing, psychiatry is the last man standing after the more communal supports of human life, from the family to the church, have been shaken by the rapid advance of Western individualism. Arguably, common problems come to be defined as psychiatric issues in the first place when the institutions in which we live fail us. Psychoanalysis itself arose amid the utter and complete collapse of the credibility of the public world in the twilight years of the Austro-Hungarian empire.[3] So too, it was in the aftermath of the crisis that convulsed all American institutions in the 1960s that the general population, not just the seriously ill, came to be considered as the constituency of psychiatry. Psychiatry emerged from the turbulence of the times with a new authority—the authority codified in the American Psychiatric Association's directory of mental disorders, the Diagnostic and Statistical Manual (DSM). That this volume is colloquially referred to as a bible is itself a reminder of the displacement of traditional institutions by psychiatry.

Not until the publication of its third edition in 1980 did the DSM attain its status as the final arbiter, the bible, of mental disorders; before that it was a little-known, spiral-bound document reflective of the psychoanalytic assumptions then in the ascendant. The gulf between DSM-II and DSM-III might be measured by the difference between "narcissistic personality disorder" and "Major Depression," the former a diagnosis popular in the 1970s but not listed in DSM-II,[4] the latter a diagnosis popular ever since, anchored in the chapter and verse of DSM-III and its successors. It was to abolish obscure theorizing about the origins of psychological problems and to put diagnosis on a solid foundation that DSM-III introduced the system of tabulating symptoms that reigns to this day. According to this scheme, a symptom isn't the manifestation of a problem deeply rooted in the patient's early history, as in Freud, but simply evidence of a disorder—a disorder, not a neurosis. Streamlined by comparison with the cumbersome machinery of Freudianism, the DSM system possessed an appealing straightforwardness and a how-to emphasis that recommends itself to practical minds as Freudian doctrine never could. The product of a zeal for renewal, DSM-III was American psychiatry's Reformation. Said a member of the DSM-III Task Force, "A lot of icons were being smashed."[5]

In the words of its designer, Robert Spitzer, DSM-III gave psychiatry "a fresh start."[6] Animated by this spirit of reform, the framers of the document eliminated the anarchy that allowed clinicians using diverse theories to arrive at conflicting diagnoses, and in its place installed a set of explicit standards written in clear language, without esoteric suppositions, all intended to bring different observers to identical diagnostic conclusions. It bears emphasis that precisely as an exercise of system-building, DSM-III was inspired by a rejection of the confused state of existing psychiatric judgments. A few years before work started on DSM-III, a study was published in which young psychiatrists "were no more likely to agree with an examiner's diagnosis of a patient than would be expected by chance."[7] Reporting to President Carter in 1978, the Commission on Mental Health acknowledged that "opinions vary on how mental health and mental illness should be defined."[8] For a discipline either claiming or aspiring to the status of science, such bedlam was intolerable. At the same time, insurance companies and powerful figures in Washington let it be known that they had no faith in psychiatry's ability to explain and defend its findings. In this state of affairs, DSM-III served to restore and even enhance the credit of psychiatry by acting as a manual for the making of diagnostic judgments. Over the years since 1980 the edition of the DSM that happens to be in force has been the last word on the diagnostic criteria of mental disorders, its influence incalculable and its authority cited in the medical literature, courtrooms, and

elsewhere. And so, from the chaos of conflicting opinions rose the reliable judgments of the DSM system.

The priority of the need to replace capricious judgments with systematic ones is confirmed by Spitzer, who in 1999 wrote:

> An innovation in the third edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-III), carried over into DSM-III-R and DSM-IV, was the presentation of diagnostic criteria for the identification of each of the specific disorders included in the manual. While the immediate goal of including such criteria was to improve reliability by minimizing criterion variance, the ultimate goal was to help clinicians and researchers make valid diagnoses by minimizing both false positives (instances in which individuals who do not have a particular mental disorder are mistakenly diagnosed as having the disorder) and false negatives (instances in which individuals with a particular mental disorder are mistakenly diagnosed as not having the disorder).[9]

The assumption here, the same assumption that seems to have driven the construction of DSM-III, is that systematizing the diagnosis of mental disorders would lead to better outcomes in the form of fewer false positives and negatives. Fewer false positives? Far from reducing false positives, DSM-III so multiplied them that Spitzer's successor Allen Frances, chair of the DSM-IV Task Force, indicts the document he inherited on that very ground: "Diagnostic inflation has been the worst consequence of DSM-III."[10] Indeed, Spitzer himself has commended a book that deplores the overdiagnosis of depression as a direct result of the DSM diagnostic system.[11] Evidently it's possible to systematize the diagnosis of a disorder like depression (first codified in DSM-III, and now the most researched of all psychiatric conditions) while not only failing to rein in, but fueling, bad diagnoses. Even though the DSM-III diagnostic scheme was framed on a medical model in accordance with the desire to return psychiatry to its identity as a medical discipline, somehow the first principle of medicine—avoiding harm—was overshadowed by the imperative of reducing "criterion variance."

What if many doctors arrive at the same inflated diagnosis? (Inflation is a collective event, after all.) The likelihood of inflation was wired into DSM-III if only because its categories were used to determine the prevalence of disorders in the community at large, and those findings were cited in turn by the American Psychiatric Association (APA) in lobbying for "the necessary resources."[12] It's diagnostic inflation that makes possible vast markets for psychoactive drugs addressed to DSM-defined disorders, such as depression, social anxiety disorder, and attention-deficit/hyperactivity disorder (ADHD), the latter two DSM coinages. If diagnoses like these are now spreading around the world "with the speed of contagious diseases,"[13]

this is only because the constituent symptoms, including sleep problems, fatigue, inattention, and, in the case of depression, sadness, are universal as well; they are so much a part of common experience that they can be found anywhere.

A Diagnostic Catch-All

The makers of the DSM may blame the drug industry for overselling disorders, but without the authority of the DSM the disorders couldn't have been diagnosed en masse in the first place.[14] And the DSM's authority is inseparable from its seemingly precise criteria, its itemized specifications. The lawyerly nature of the diagnosis of depression in particular was brought out by one of DSM-III's framers who remarked, not altogether in jest, that "the diagnosis of a depressive episode . . . is a sentence full of subordinate clauses and other grammatical intricacies."[15] In part just because so many elements go into the making of a diagnosis, the text of the DSM allows for more depression than its appearance as a checklist of requirements might suggest. The criteria of a depression diagnosis have changed little over successive editions of the DSM; those in the most recent edition appear in Table 1.1.

Built into the criteria for Major Depressive Disorder are low thresholds, alternative entry conditions, and many symptoms common in a healthy population, as well as a number of particulars that can easily be forgotten, bent, or waived in practice, as is only fitting for a bible. Requiring just two weeks of symptoms, the DSM criteria will catch the common transient distress that would otherwise resolve spontaneously within four weeks.[16] In the template on which the DSM criteria are based, and which had already been cited perhaps a thousand times in the medical literature—the Feighner criteria—the symptom period for depressed mood is "at least one month."[17] (Note too that depressed mood itself isn't necessary for a DSM diagnosis of depression.) Though the Feighner criteria for depression, for their part, are patterned on others published in 1957, they omit constipation because "it lacked specificity—many constipated people are not depressed."[18] No more specific than constipation are a number of symptoms included in both the Feighner and the DSM criteria for depression, such as fatigue and faulty concentration. In a study conducted by Spitzer and others in 1994, fully 58 percent of 1,000 primary-care patients reported fatigue on a questionnaire.[19] As suggested by frequent reminders in the medical literature that depression disguises itself as common complaints, the diagnostic weight accorded such complaints in the DSM has real implications. In addition to the two-week

Table 1.1 DSM-V Criteria for Major Depressive Disorder

A. Five (or more) of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

   Note: Do not include symptoms that are clearly attributable to another medical condition.

   1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
   2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
   3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
   4. Insomnia or hypersomnia nearly every day.
   5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
   6. Fatigue or loss of energy nearly every day.
   7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
   8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
   9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

   Note: Criteria A–C represent a major depressive episode.
   Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode.

   Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

period, the alternative cardinal criteria, the inclusion of common symptoms, and numerous qualifiers and stipulations that may or may not be observed in practice—all of which enable immense numbers of cases to be diagnosed with an appearance of medical propriety—the DSM interprets distress arising from life itself as evidence of a mental disorder. The result is language that seems impressively specific but actually serves as a catch-all for conditions ranging from ordinary discontents and mild dysphoria to warranted sadness to implacable self-loathing and despair.[20]

In a sense, the story of depression is the story of DSM-III. The disorders codified in DSM-III were supposed to become more definite and distinct over the years, as reliable diagnostic criteria led to the selection of homogeneous populations for research, which in turn would allow for the discovery of identifiers such as the biological correlates of the disorder and the constants of its clinical course. The opposite happened. Instead of becoming more distinct, the disorders of the DSM have run together like watercolors. "Patients do not usually have only mood, somatic, or anxiety symptoms but tend to come with a mix from multiple symptom groups."[21] Even as DSM-IV was in the planning stages, studies repeatedly showed patients meeting the criteria for three, four, or five different DSM diagnoses.[22] Tellingly large percentages of children diagnosed with ADHD, a disorder whose definition mutates from one edition of the DSM to the next, are found to have other disorders, inevitably including depression. (Atomoxetine, better known as the ADHD drug Strattera, was originally studied by Eli Lilly as an antidepressant.[23] The stimulant methylphenidate, commonly prescribed for ADHD, was once used as an antidepressant, and antidepressants themselves are said to be an effective treatment of ADHD in adults.)[24] A study of adults with ADHD found that 87 percent had at least one and 56 percent at least two other psychiatric disorders.[25]

Similarly, though a variety of specific disorders wouldn't be expected to respond to the same drug—in fact, the use of a single remedy for a plethora of ailments traditionally signals the placebo effect—a potpourri of DSM disorders, as well as miscellaneous complaints ranging from nonspecific pain to "abnormal sensations," are treated with selective serotonin reuptake inhibitors (SSRIs), among the banner drugs of our era.[26] (By analogy, aspirin and other NSAIDs are widely used to treat all manner of complaints, including nerves, sleep problems, low mood, and "things in general.")[27] While DSM-III wasn't ghostwritten by the pharmaceutical industry, its officially distinct yet actually blurry categories turned out to be perfectly adapted to the aim of selling drugs to the widest possible market. Drugs have been marketed for premenstrual dysphoric disorder even though its official symptoms are so generic they can be satisfied by depressed men. If diagnostic categories were really as objectively distinct as DSM taxonomy makes them appear—though the framers of DSM-III *hoped* they

would prove distinct rather than knowing them to be so[28]—they wouldn't have presented such good targets for highly promoted drugs that sometimes resemble placebos with side effects.

Because apparently strict DSM criteria lend themselves to inflation, they have enabled the mass marketing of drugs for ambiguous ills like depression even though the full potential of marketing wasn't realized until the advent of direct-to-consumer (DTC) advertising in 1997.[29] Indeed, unless the DSM had established the diagnosis of Major Depression and trained our habits of classification, common side effects of antidepressants, including drowsiness, loss of sexual interest, and "emotional disengagement,"[30] could well have been described as depressing. (The adverse effects of the drugs themselves may have something to do with the negative results of the many antidepressant trials buried in company archives.)[31] The symptom-based taxonomy of the DSM also gave drug companies lists to use both in advertising and awareness campaigns allegedly in the public interest. Twenty years before a Paxil ad showed an anxious woman surrounded by the words FATIGUE, IRRITABILITY, SLEEP PROBLEMS, RESTLESSNESS, ANXIETY, MUSCLE TENSION, and WORRY,[32] DSM-III included each of these symptoms except the second among the diagnostic criteria of Generalized Anxiety Disorder (which required six months of symptoms as opposed to a mere two weeks for Major Depression, despite the kinship of the two disorders and the overlap of their symptoms). Maybe the DSM feeds into advertising because the process of shaping ills into codified disorders is something like a branding operation in the first place.

The DSM category of depression bundles a number of ills, labels them as one, and gives the entire package instant recognition in the marketplace of ideas and the marketplace per se, and in an era of disease-mongering, as many call it, such techniques have high importance. Not only does an officially specific disorder distinguish itself from generic ills as a branded product sets itself apart from ordinary goods,[33] but the name of the disorder establishes its identity like that of a product. The president of the National Pharmaceutical Council once said that a brand name is simpler and easier to remember and pronounce than a generic one.[34] By the facility standard, "ADHD" is a marketing triumph; and if the most potent brand names are recognized around the globe, the DSM, which underwrites disorders like ADHD, has its own international currency. The branding of products goes along with the expansion of wants and needs that defines a consumer economy, while the popularization of disorders indexes the demand for psychological services—a demand that took off when traditional norms of self-restraint came under general attack in the years leading up to DSM-III.[35] The dizzying increase in diagnosed disorders in the DSM era makes no sense unless we bear in mind the DSM's power to brand categories and

produce belief. In the coming pages I trace in particular some implications of the suggestiveness that surrounds a "specific" disorder much as an associative field surrounds a distinctive, well-established brand.

Now that 10 percent of all Americans over age 6, and 25 percent of American women aged 40–59, take antidepressants like Paxil,[36] one looks back in disbelief to the drive to return psychiatry to clear thinking about the difference between normality and mental disorder that inspired DSM-III. If DSM-III drew the line between normality and illness, it's hard to see why Spitzer's successor should have concluded in 1987, only seven years after DSM-III and just as Prozac was coming to market, that diagnosis was veering out of control—"there were too many categories and too many people being diagnosed."[37] No more than a thin, faint boundary separates the reforming zeal that brought DSM-III into being from the zealous or overzealous application of its categories to the world at large. Even while DSM-III was under construction, efforts were made to apply its categories to the general population.[38] (Indeed, the diagnostic criteria of DSM-III were specifically designed for use by lay interviewers conducting population surveys.)[39] The diagnostic front line is now primary care, where the population presents itself to medicine. Again and again in the medical literature primary-care doctors are reminded that they fail to detect something like half the depression they confront,[40] while the fact is that depression is now more likely to be *over*diagnosed in primary care[41] and that missed cases are least likely to benefit from treatment.[42] Like the addition of new diagnoses by the dozen in DSM-III and its successors, the campaign to make primary-care doctors into officers of the DSM system has contributed to the interpretation of ordinary or "subclinical" conditions as medical issues.

Expanded Eligibility

Because the reformers associated with Spitzer identified themselves as neo-Kraepelinian after the pioneer of psychiatric classification, Emil Kraepelin (1856–1926), we might briefly note both family resemblances and differences between his portrayal of the depressive phase of manic-depressive illness and DSM criteria for Major Depressive Disorder that lend themselves to systematic activism and diagnostic inflation. A generation before the neo-Kraepelinians coalesced into a group, American psychiatrists might have read descriptions like this in the master's textbook:

> In the depressive states of the disease the emotional attitude is regularly that of gloominess, despair, doubt, and anxiety. Patients complain particularly of the loss of interest in things; "everything is the same to them," "they are

> desolate and empty," "they are dead, because they have no feeling," "music does not sound natural," and "the crying of the children no longer creates sympathy." They feel as if they no longer belong to this world . . . The psychomotor field in the depressive form presents a retardation of activity . . . In the mildest degree this retardation appears as a deficiency in the power of resolution. Actions may not only be performed slowly, but even after being started may fail of completion. The simplest movements, such as walking and talking, are performed very slowly and without energy . . . Some patients are so taciturn and monosyllabic that it is impossible to engage them in conversation, and although they are able to count or read aloud as rapidly as ever, they will sit for hours with a letter in front of them, unable to finish writing it.[43]

"Loss of interest in things" becomes the DSM's "markedly diminished interest or pleasure"; the feeling of desolation and hopelessness becomes "depressed mood"; "retardation of activity" becomes "psychomotor retardation"; deficiency of resolution becomes "indecisiveness." Yet the extreme condition sketched by Kraepelin, one in which "'music does not sound natural'" and patients feel as if they "no longer belong to this world," can't be imagined as so common that at any time perhaps 10 percent of the population qualifies. Kraepelin portrays someone more like Melville's Bartleby (taciturn and monosyllabic to perfection) than an ordinary citizen.[44] Unlike Kraepelin's nosology, the operational criteria of the DSM serve as instruments of diagnostic activism. Max Hamilton, the author of a Depression Rating Scale used in trials of antidepressants as well as in clinical practice, once said of the use of checklists, "It may be that we are witnessing a change as revolutionary as was the introduction of standardization and mass production in manufacture."[45] The DSM might be regarded as an elaborate checklist enabling the mass production of diagnoses.

At the center of the movement to formulate diagnostic criteria for mental disorders was the Department of Psychiatry of Washington University, in which a leading figure was Eli Robins, who studied under the brilliant maverick Mandel Cohen. In 1957, well before the popularization of depression, Cohen and coauthors published in *JAMA* an observational study of depressive symptoms that uses the two-tiered criterion system later employed in the DSM; that is, patients qualified for the study if they (a) showed depressed mood, and (b) had six of ten symptoms ranging from constipation and insomnia to suicidal thoughts.[46] (Why six? Years later, the study's first author said, "It sounded about right."[47]) Essentially the same method used in the 1957 paper to delineate depressed patients from healthy controls in the sharpest way has generated depression diagnoses by the million under the reign of the DSM. How can this be?

To begin with, consider the string of options in the crucial first criterion of depression in DSM-III:

> Dysphoric mood or loss of interest or pleasure in all or almost all usual activities and pastimes.

The word "or" occurs three times, with the effect of expanding eligibility. No longer is depressed mood necessary for depression, and for that matter you can lose either interest or pleasure, and you don't have to lose one or the other in all things, but just most. (Recall too that the DSM halves the symptom period required by the Feighner criteria.) By providing alternative entry criteria for depression—depressed mood *or* loss of interest *or* loss of pleasure—DSM allows three options instead of one, the result being a test so loose that as many as half of screened patients will score positive.[48] The entry criteria therefore need to be supplemented. At this point another change comes into play: The number of secondary symptoms needed for DSM depression is lowered from six to four. It should be noted that symptoms in this category, such as poor concentration, insomnia, and fatigue—and insomnia virtually implies fatigue—are common in the general population and therefore of questionable diagnostic significance. (Thus, in a survey of healthy students conducted a dozen years before the diagnosis of Major Depression was codified in DSM-III, 27 percent reported "inability to concentrate.")[49] Such generic complaints are now the most frequent presenting symptoms of depression, or, rather, presumed depression. Yet while common problems are interpreted as symptoms of depression, the same problems are discounted when produced by the drugs called antidepressants.[50] (Thus, sleep disturbances and fatigue, both DSM symptoms of depression, are listed by Eli Lilly as common side effects of Prozac.)[51] It's as if secondary symptoms lose their significance in the eyes of medicine once they do their job of boosting the diagnosis of depression, even though interpreting "unexplained" symptoms as evidence of a mental disorder conflicts with the principle of avoiding speculation that inspired the diagnostic revolution in psychiatry. Just as the neo-Kraepelinian DSM enables millions to have the depressive disorder portrayed by Kraepelin as far from ordinary, the DSM movement adapts to the entire population diagnostic criteria that were met by "probably the sickest of the whole group" of 248 psychiatric patients in the Cohen study.

Beginning by identifying manic-depressive disease as "a serious cause of disability and even death," the Cohen study later notes that many with this disease are "merely patients who are tired and have insomnia, headache, and nervousness."[52] Spanning a range of conditions,[53] its causal mechanism unknown but the subject of learned speculation, established

by shifting criteria and thresholds, depression defies its own label as a specific disorder. A convincing argument holds that patients who would have identified themselves as anxious a few decades ago, when anxiety ruled the day, now call themselves depressed because depression happens to be in the ascendant for marketing reasons.[54] (If this is so, then the intimate experience of being unwell is much more open to social influences than we may suppose.) In the Cohen study subjects were given over a dozen terms for "depressed," including not just "worried" and "despondent" but "angry" and "disgusted," and counted as depressed if they checked any of them. The only thing all seem to have in common is that they lie off the beaten path of normative cheerfulness. So diagnostically equivocal is the entity reified as depression that nothing jumps out at us in the statement, "Symptoms like anxiety, depression, fatigue, and sleep disturbances seem to be found in many kinds of patient, whatever their physical or psychiatric status."[55] Nothing jumps out even though depression is listed as a symptom and not a specific disorder with symptoms of its own, including all the other symptoms on the same list.[56]

For many patients with a collection of generic symptoms, depression acts as a diagnostic net to gather all together. While DSM-III overthrew the concept of neurosis dear to the Freudians in the name of scientific diagnosis, the fact is that the most common symptoms of neurosis in Freud's time—insomnia, fatigue, dyspepsia, and the like[57]—became the most common symptoms of depression in the age of the DSM. As this may suggest, the makers and inheritors of the DSM revolution reserved the right to interpret physical symptoms as indices of a mental disorder even after the destruction of the Freudian temple.[58] Neurosis as conceived by Freud was a kind of illness continuous with normality, and the same is true of all but severe depression; but the DSM enabled the production of diagnoses on a scale beyond the reach of the Freudians, one as large as the marketplace. This dramatic expansion of diagnosis couldn't have taken place unless the protean neurosis (protean because a symptom can signify anything) had yielded to the codified disorder.

In an intriguing study of the influence of placebos on insomnia conducted a decade before DSM-III, subjects treated with pills with a supposedly arousing effect fell asleep more readily than subjects told the pills were sedating, evidently because being able to attribute their own aroused state to a pill eased their mind. Many people, it seems, are "troubled by their insomnia, taking it as evidence of a major physical or psychological disorder," an inference that sets up "a vicious cycle in which symptoms of insomnia elicit worrisome thoughts that further aggravate the insomnia."[59] The interpretive system installed by DSM-III invites the doctor to construe insomnia as, in fact, evidence of disorders including Major Depression,

though within a few years of DSM-III a new generation of drugs—the SSRIs—arrived on the scene to ease the patient's mind. As it happens, the effect of these compounds, too, is largely placebo.

Skewed Calculations

A half century ago it was recognized that many of the ills that send patients to the doctor "cannot be labeled as 'diseases.' They are patients' problems, concerns, complaints, symptoms, and assorted 'conditions,' including a wide variety of social and psychological problems that are the day-to-day fare of general physicians."[60] Over the intervening decades, many of these ills have been promoted to the category of disorders and given labels that have been taken up by patients themselves.

Not just the DSM but what has come to be known as medicalization—the framing of normal conditions as medical issues—now reaches into all corners of private and public life, and those who execute its mandate can be confident that their hunt for ills to treat will be successful, simply because what they're searching for is everywhere. If you're looking for symptoms of postconcussive syndrome, for example, you'll find them even in a population of healthy college students who have never suffered a head injury.[61] In the pages to come I document the crusade against normality, arguing that human life abounds with raw material for medicalization to mold into disorders, and that the shaping process produces harm in violation of medicine's first principle. Much as the DSM system has defeated its own goal of curtailing bad diagnostic practices, medicalization in general has disordered the calculation of risks and benefits. To begin with, the benefits of drugs decline as they are prescribed to populations less unwell than those on whom they are first tested, which is exactly the pattern seen in practice over recent years. "New medical interventions tend to be studied in severely ill patients where significant benefits can be expected. After a therapy is established, physicians tend to broaden its use and prescribe it to a wide range of patients, including a high number of less sick patients."[62] Medicalization targets the vast market of the less sick, straining the ratio of risks and benefits precisely by treating those who don't stand to enjoy "significant benefits."

However, medicine has extended its writ not only over the less sick but many not sick at all, such as patients suffering from normal distress. Consider the case of a woman whose diagnosis of depression appears not to be based on DSM-IV, which was in effect at the time.

> Ms. A is a 32-year-old mental health services worker who consulted with her family physician following the sudden death of her mother 2 weeks

> earlier. She had hoped that her physician would either offer her time in the consultation to process her sense of shock and validate her feelings or refer her to a therapist attached to the practice. Instead, her physician suggested that she should start a course of antidepressants. She accepted the antidepressant prescription without expressing her preference for psychological therapy, but left the consulting room having already decided that she would not redeem the prescription. She did not understand how antidepressants could help her to come to terms with her unexpected bereavement. From her observation of clients on long-term treatment for severe depression, she perceived that one of the adverse effects of antidepressants was reduced energy and motivation to deal with problems.[63]

One has the impression that the doctor in this instance didn't weigh pros and cons but came to an automatic conclusion, leaving the drawbacks of antidepressants to the patient. Yet the patient wasn't depressed but "in shock," and for a good reason. Maybe the doctor thought the dulling effect of an antidepressant would be a balm for someone in shock, but that isn't what the patient was looking for; in fact, if she had presented with "reduced energy and motivation to deal with problems" she might well have been diagnosed as depressed. The study from which I've taken this case (actually a composite) never questions the diagnostic fashions that lead to the overprescription of antidepressants, though it does comment that giving antidepressants to the mildly depressed results in a poor risk/benefit ratio.[64] Inasmuch as SSRIs are negligibly superior to placebo in treating depression in most cases, determining the ratio of risks to benefits for an overdiagnosed disorder like depression comes to resemble dividing by zero. As if the benefits of SSRIs and similar drugs did in fact compute to nothing, a comparison of large surveys conducted in Britain in 1993 and 2000 showed that "widespread increased prescribing of psychotropic medication"—led by SSRIs—"has not improved the mental health of the nation."[65]

In addition to treating milder forms of disease and even conditions indistinguishable from normality, medicalization seeks out disease in its incipient stages, before it has had time to manifest itself. As a result of the early-detection imperative, "common problems will be identified in many individuals who would not be harmed by the disease and, therefore, would not benefit from treatment."[66]

One such problem is prostate cancer. Early in the era of prostate-cancer screening, proponents "dismissed concerns about harms"[67] and argued that there was no time to wait for evidence of benefits to emerge from clinical trials, as if the principle of weighing harms and benefits simply didn't apply to the practice of screening millions for a highly ambiguous cancer.[68] Around the same time, proponents of mass screening for coronary risk factors made the assumption that such a program could benefit

but could not harm.[69] The drive to screen for depression shows the same one-sidedness; thus, the US Preventive Services Task Force found no data on the harms of screening adults despite the patent risk of labeling normal distress as a mental disorder,[70] among the many pitfalls and shortfalls of depression screening. (I will propose an analogy between the crusade against prostate cancer and that against the "psychological cancer," depression.) Clearly, unless the costs of medicalization were somehow effaced, it would be difficult to get people to buy into the broadening of medical definitions and boundaries. Yet those costs may also escape the notice of those who impose them. "Downstream harms from overtesting and overtreatment may be completely invisible to clinicians," because of their belief in their own beneficence, the delayed onset of the harms, or both.[71]

A measure of the inattention to harm in a climate of medicalization is the scant information about adverse effects of drugs in published papers. In 2001, four years after DTC advertising revolutionized the marketing of drugs, an analysis of safety-reporting in a broad array of drug trials assessed the provided information as "largely inadequate," with approximately the same amount of print space devoted to the authors' names and affiliations as to the adverse effects of the drugs under study.[72] Trials of drugs used to treat mental illness follow the same pattern. "Even with lenient criteria, very few . . . have adequate reporting of clinical adverse events."[73] How to balance risks and benefits without good information about the risks? So it is that doctors routinely strain risk/benefit calculation by prescribing highly promoted drugs whose utility profile remains unknown in the absence of good information (and prescribing them in decreasingly severe cases). "Only when more adequate types and numbers of patients are studied for sufficiently long periods can a more accurate profile of their risks and benefits emerge."[74] Given, too, that the prescription of psychoactive drugs is "always a fine balancing act"[75] owing to individual differences, the sometimes paradoxical character of drug effects, and our ignorance of the actual (in contrast to presumed) causes of mental disorders, the mass prescription of these drugs in and of itself violates the balancing of risks and benefits. A searching critique of the use of psychoactive drugs as putatively specific agents concludes that belief in them "has led to their indiscriminate prescription to millions of people often for decades on end. It is likely that many people exposed to the harmful physical and psychological effects of these drugs derive no benefit from them."[76] However, if their prescription really is indiscriminate—as the evidence suggests—then it's not just likely but very likely that for most, not just many, of those who take psychoactive drugs there are no benefits to set against harms.

In that the overprescription of psychoactive drugs has taken place under the auspices of the DSM, the ascendancy of the DSM system has

distorted the calculation of risks and benefits. Consider the case of the DSM-authorized disorder ADHD (originally ADD). In that the safety and efficacy of the medications used to treat ADHD are established in brief clinical trials while the drugs are actually used for years on end, the mass prescription of stimulants represents an experiment in itself. Of course, it could be said of many other drugs that their long-term use is underwritten by short-term trials. In this instance, though, the drugs are administered to children as young as two, unlikely to be represented in any trial population.[77] An investigator of the prescription of psychoactive drugs to preschoolers reports that while 55 percent more of these children were diagnosed with behavioral disorders in 2009 than in 1994, only 29 percent of those diagnosed were given drugs (as against 43 percent in 1994). "We were very pleased to see that the rate of psychotropic drug use in this age group isn't going steadily up each year," said the investigator. "But we are still giving these drugs to young children, so we need more research into if and how they influence the developing brain."[78] Virtually by definition, it defies medical prudence to prescribe psychoactive drugs to two-year-olds even while their effect on the brain remains unknown.[79] Medical prudence involves not just totaling pros and cons in some fashion but weighing risks and benefits in the light of the particular duty to avoid harm incumbent on a doctor as a doctor.[80]

And in the case of ADHD, the balance of the evidence is particularly disturbing. Though the DSM-II precursor of ADHD (Hyperkinetic Reaction of Childhood) was thought to subside by adolescence,[81] and though nearly 90 percent of ADHD cases appear to be mild to moderate, long-term outcomes of ADHD are dismal, with diagnosees at markedly higher risk of dropping out of school, early pregnancy, drug abuse, auto accidents, being fired, incarceration, even death.[82] (In a study that followed an ADHD population for 33 years, diagnosees died at a rate 2.5 times higher than controls. Subjects exhibiting aggression or antisocial behavior were excluded from the study.)[83] If a drug showed results like these it would be pulled from the market; if a trial yielded such results, it would be stopped. How do outcomes so alarming follow from a disorder whose symptoms can be as trivial as fidgeting[84] and whose cases fall overwhelmingly into the mild-to-moderate range?[85] Either a disorder questionably distinct from normality[86] is inherently fraught with great risk or it becomes so as a result of a process set in motion by diagnosis itself. The latter possibility—that diagnosing ADHD can harm, if only by cuing the behavior of the child and the expectations of others[87]—doesn't seem to enter into the judgments that support the diagnosis. As a result of what has been called "diagnosis threat," people whose attention is called to cognitive deficits supposedly associated with mild head injury perform

worse on various tests than people with the same history not cued to do poorly.[88] The ADHD label has all the automatic associations and evocative power of a stereotype, with the authority of medicine to boot, and it would be strange if such a potent influence had, in fact, no influence on the labeled child.[89] Children are not notably invulnerable to the power of suggestive messages. A diagnosis that tells children there's something radically wrong with their wiring, such that they need a drug to regulate themselves, can leave them "less well-equipped to draw upon their own resources to solve their problems."[90] That the neurological cause of the child's theorized defect of self-regulation is also theoretical doesn't keep the notion of such a cause from being powerful. People caught up in mass psychogenic outbreaks experience illnesses whose causes, such as a toxic gas, they are fully convinced of even if they can't be found.

In laying out the hazards of the DSM system, and DSM-V in particular, the architect of DSM-IV (which broadened the criteria for ADHD) reminds both primary-care doctors and psychiatrists to "conduct a risk-benefit analysis" before making a diagnosis. "In toss-up situations, weigh the pluses and minuses of giving the diagnosis," writes Allen Frances. "The basic question boils down to, 'Is this diagnosis more likely to help or more likely to hurt?'"[91] Only if clinicians under the influence of the DSM system had somehow forgotten such elementary principles would they need to be reminded of them. Frances concludes that the best that can be said of DSM-IV is that it didn't make the DSM system even worse than it already was.[92]

Writing in 2009, the chair of the DSM-V Task Force held out the hope that "Mental disorder syndromes will eventually be redefined to reflect more useful diagnostic categories ('to carve nature at its joints') as well as . . . clear thresholds between pathology and normality."[93] It's a sobering thought that after 30 years of DSM hegemony and the writing of billions of prescriptions, the boundary between normality and disease remains so nebulous to psychiatry that its clarification is postponed into the indefinite future, as something that will "eventually" come about. If medicalization means the definition and treatment of normal conditions as medical problems, this statement of hope amounts to a confession that the DSM has contributed in a large way to exactly that. But in addition to the overprescription of drugs with questionable harm/benefit profiles, medicalization poses a subtler risk: the risk that the suggestiveness of the diagnoses given to common problems will color people's understanding of themselves and even mold their experience.

Suppose a team of psychologists wants to test the theory that people receiving a high blood-pressure reading will notice more of the symptoms they associate with high blood pressure. Doing what experimenters do,