



DAVID KUPFER WANTS THE *DSM-5*
TO HELP HIS FIELD COME OF AGE
BY ELAINE VITONE

WORKS IN PROGRESS

In the last few years, if you've read anything about the *Diagnostic and Statistical Manual of Mental Disorders*, the psychiatrist's manual (some would say "bible"), it probably hasn't been good. The pharmaceutical industry isn't making new drugs for psychiatric illness, say the blogs, because they can't find targets, and that's the *DSM's* fault. The normal range of human emotion is getting all mushed up with disease and causing overprescription of potentially toxic treatments, say the editorials, and that's the *DSM's* fault. The response around the latest version, *DSM-5*, is even less popular.

"Did you see that one in *The New York Times*? They're blaming [higher rates of ADHD diagnosis] already on *DSM-5*. It hasn't even been published!" says David Kupfer, sitting in his office on the second floor of Western Psychiatric Institute and Clinic on a late afternoon in April 2013, just weeks before the culmination of the massive document-revision effort that he has tended to, round the clock, "like an emergency physician," since 2006.

PHOTOGRAPH | JIM JUDKIS

Kupfer, 72, is tall and wiry with a warm smile, a welcoming presence, and, typically, a sharp suit. It's fitting that, in a 2004 story about the process of applying for competitive federal research funding, *The Wall Street Journal* characterized this MD as a "salesman," even though that's not a word you'd expect to hear when the subject is a professor. But this particular academic's claim to fame is building the once-minuscule research herd of the University of Pittsburgh's Department of Psychiatry into one of the largest and most prominent in the country—a feat that took no small amount of combined persuasive power and business smarts.

Well, his claim to fame until seven years ago, that is.

"So I put in a very brief letter to the editor that came out yesterday," he says. "And I sent it to two of my children who read *The New York Times*. And they said, 'That looks fine, Dad, but why didn't you quote us?'" (He'll use any excuse to talk about his kids.)

It's not that Kupfer is making light of the implications of revising the *DSM*. Weighing heavily on his mind, and on the minds of the 160 members of the task force and work groups whom he led through the revision process, is the fact that the diagnosis criteria listed in the *DSM* are the bases for Medicare and Medicaid reimbursements. There are financial implications, treatment implications, and social implications. Hence, Kupfer made the revision process of the *DSM-5* more transparent than any of its predecessors, putting the draft out to the public three times. Some 13,000 comments were posted online, and the task force and work groups read every one.

There has been tremendous outcry from patient advocacy groups, the pharmaceutical and insurance industries, the media, and the public. Members involved in drafting the previous *DSM* edition have written scathing commentaries and made the rounds of talk shows. At times, it's gotten pretty ugly.

"He listens extremely well," says James Scully Jr., medical director of the American Psychiatric Association, which publishes the *DSM*. "He's calm in the face of everybody lighting their hair on fire.

"He reminds me of General Eisenhower."

Many of the concerns are well intentioned: What of the Asperger's community?

These people have fought hard for acceptance and understanding. Now Asperger's is being stricken from the manual altogether? What of the bereaved, who are no longer explicitly excluded from the criteria for clinical depression? Will we be doling out antidepressants to everyone who loses a loved one, medicalizing a natural reaction to a horrible life event? (For more on these issues, see p. 19.)

It's complicated. But that should be no surprise. The brain is the most complicated organ in the body. It's arguably the most complicated thing on earth.

Psychiatry is still in an adolescent stage. For all the promising research—in genetics, imaging, cognitive neuroscience—scientists are still grasping for biologically based diagnostic measures they can use with sensitivity and specificity.

Kupfer says that when he started this process he honestly thought the *DSM-5* would have a firmer foothold in science. Alas, the science isn't there yet. But he's confident that is coming. His hope is that the new *DSM* will help to nudge psychiatry, finally, into its rightful place—as a branch of medicine

Think of it as "DSM 5.0," he says, because, from here on out, more frequent,

grounded in understanding, in evidence, in measurable outcomes.

This has been an obsession of his for more than 40 years.

Kupfer grew up in New York, graduated from his Long Island high school at 17, and was voted "most likely to succeed." Yet a guidance counselor discouraged him from applying to Yale University—he is Jewish and there were still quotas. But he got in. He studied economics, history, and architecture, graduating a year early there, too. And he stayed at Yale for med school.

In the first half of his MD program, he thought he was going to be a urologist. He experimented with kidney-transplantation surgery in the animal lab. (Thomas Starzl, now Distinguished Service Professor of Surgery at Pitt, was just beginning to perform the first successful kidney transplants on humans at the time.) And then, Kupfer discovered something he found even more intellectually challenging: psychiatry.

Here was an area that was utterly bereft of understanding at the biological level. Mental illness was still seen in terms of psychological constructs, and psychoanalysis was very much the rule of the day. Then came the advent of the first psychopharmacological treatment, the bipolar medication lithium. Kupfer was absolutely fascinated. In an age so fixated, to borrow a Freudian term, on the art of caring for the mind through talk therapy, here was the first glint of the science of healing the brain.

He grew curious about the circadian clock and all its quirks that varied from person to person. The overachieving Kupfer realized he himself had always had "gobs" of energy without needing much sleep at all. And neither, he learned, did Yale–New Haven Hospital's psychiatry chief, a quintessential European gentleman by the name of Thomas Detre, who became his mentor. The pair hit it off. Detre was Hungarian. Kupfer's father's family was Hungarian. The two started putting in late nights writing papers together in Kupfer's third year of med school.

Kupfer graduated, and, after his first year of residency with Detre in New Haven, he

accepted an intramural research fellowship at the National Institute of Mental Health.

"I had innocently applied, not realizing only four out of 500 applicants got these positions," he says. (He says "innocently" a lot.) He assumes it was the transplant surgery that set him apart. At the NIMH, Kupfer spent a year running a clinical psychiatry lab, then another year conducting sleep research.

Before neuroimaging, sleep was one of the only things that gave us any real information about what was going on in the brain, Kupfer explains. He examined electroencephalography (EEG) in people with depression and found that certain patterns of activity could be used to separate these patients into subgroups. For example, if a person had an early onset of his first REM period and most of his REM in the first half of the night, that was a bad sign. These findings offered the basis for one of the first biological measures used to understand, classify, and predict long-term outcomes for people with mood disorders. Kupfer landed a paper in *Lancet* in 1972. "I was way ahead of myself in terms of how much undeserved

notoriety I had,” he says.

By the time Kupfer returned to Yale to complete his training, he was convinced his path would be in academia. He won an NIMH career development award and set out to challenge a pervasive notion that distressed him to his core: That psychiatry was different, or even lesser than, the rest of medicine.

For instance, what’s with the intake interview? Before you see a doctor for any other reason, while in the waiting room, you sit with a clipboard, dutifully filling out pages of forms. *Do you exercise? No/Yes, and how much? Do you smoke? No/Yes, and how much? Do you drink? No/Yes, and how much?* And before the physician says so much as, “How are you today?” you’re in the exam room, with your chart filled out by an RN, documenting weight, blood pressure, reason for your visit, and on and on. These metrics are carefully recorded and tracked over time. If your blood pressure spikes dangerously high from one visit to the next, your doctor notices and does something about it.

But when you go to see a psychiatrist, what do you do in the waiting room? Skim *Reader’s*

see him in action now, Kupfer was shy back then, by his own admission.

Kupfer was advisor to two med students that year: Rosenbaum and also Charles Reynolds, an MD, the UPMC Endowed Professor of Geriatric Psychiatry, and director of the Pitt/UPMC Aging Institute. Reynolds recalls, “One of [Detre’s] fundamental critiques of American culture in general was that Americans are often afraid to take appropriate risks to achieve great things. If he weren’t willing to take risks, Detre would have never left the security of Yale.”

But, in the spring of 1973, leave he did, to head to Pittsburgh’s Western Psychiatric Institute and Clinic (WPIC) and chair Pitt’s Department of Psychiatry. His very first recruit was Kupfer, whom he chose to direct research. Kupfer was 31. “It was a very easy job because there was no research here. It was a no brainer.” Ten years later, when Detre became Pitt’s senior vice chancellor for the health sciences and president of UPMC, Kupfer would succeed him as head of the Department of Psychiatry. (Kupfer was also named Thomas Detre Professor of Psychiatry in 1994.)

Jim Harris, a Johns Hopkins professor of psychiatry and behavioral sciences and a friend of Kupfer’s for some 25 years, says, “[Kupfer] has been uniquely connected in both the psychotherapy side and the neuroscience side of research in mood disorders.”

Jack Barchas, chair of psychiatry at Weill Cornell Medical College, raves breathlessly about both Frank and Kupfer, alternately calling them “incredible,” “brilliant,” and “remarkable” and pointing out that they are one of only two couples ever to have won the prestigious Institute of Medicine’s Rhoda and Bernard Sarnat International Prize in Mental Health. He says, “They are without a doubt one of the greatest couples ever in the field of psychiatry.”

Kupfer (and Detre) didn’t move to Pittsburgh right away. Every two weeks, they’d come work for two days—two *18-hour* days—and this went on for six months. According to Pitt lore, one night, an administrator was leaving WPIC and saw the lights still on in both their offices, and joked to a colleague, *It’s 5:30, and they’re*

partial updates will be released as the science evolves. This may well be the last print edition.

Digest. Your overall mental health, diagnosis, and treatment options are all assessed solely on the basis of one of your conversations with your psychiatrist.

“I think that’s the most ridiculous waste of time,” says Kupfer. “While you’re waiting, you should be filling out a bloody [huge] amount of information, which I will then be able to see before I see you.”

Kupfer put the idea to Detre, and he was game. Through many late nights, they developed a series of forms together—questionnaires for patients to self-report their symptoms—which they called the KDS, for Kupfer Detre System. It was one of the first attempts at evidence-based assessments of mental disorders in the clinic.

He was “quite a research geek back then,” recalls Jerry Rosenbaum, professor of psychiatry at Harvard University, who first knew him in 1972, when Kupfer was his MD thesis advisor. Rosenbaum recalls often finding Kupfer surrounded by reams of computer paper—stacks of KDS data printouts all over his office. And, though you’d never know it to

When the two Yalies first came to Pitt, Detre hired a writer named Ellen Frank, and among the first projects the three of them worked on together was a book about the initial diagnostic interview, *The First Encounter*.

“It was like a seminar in psychiatric diagnosis with two teachers and one student,” says Frank.

The book was never published, but on the bright side, it resulted in Frank going to graduate school and, a couple of years later, in a marriage. Kupfer and Frank, who is now a PhD and Pitt Distinguished Professor of Psychiatry, celebrate their 38th anniversary this summer.

Kupfer pursued his interest in sleep and depression. He then focused on major depression and bipolar disorder and their treatments. Frank and Kupfer became collaborators and went on to make significant contributions to the design of randomized clinical trials for mood disorders. Theirs were among the very first such studies of the treatment of recurrent depression—and not just of one treatment versus another, but also, more importantly, of any drugs at all versus psychotherapy.

still not done with their work? These guys are never gonna make it.

But in the first 10 years, the department shot up to third in NIH funding, and the faculty grew from a few dozen to some 150. The WPIC staff tripled to 1,200.

How did that happen?

Kupfer says he has always been interested in the psychology of motivation: How do you get people to perform beyond what even they believe to be their capacity? “That fits into the rhythm of what I’ve innocently done with my own kids,” he says. “My son told me once, ‘Dad, you’re nothing but a professional coach.’”

He thought of the department as one big laboratory, a place to test out his ideas about motivation. For his test subjects, he used a cadre of faculty he enlisted from what he saw as the most exciting new subfields of psychiatry. When he first arrived in the ’70s, the hot new thing was pharmacology and pharmacokinetics. Over time, he would recruit experts in basic science, neuroscience, neuroimaging, and the translational science of psychiatry.

Kupfer says that the department has been, and continues to be, “a department of kids,” a term he uses often and without condescension. His long-held appreciation for the new and novel has yielded a menagerie of relatively newly minted PhDs.

“They encouraged any warm body,” says Frank, “including a first-year graduate student like me, to apply for research funding.”

Investigators who are yet a little “unformed,” Kupfer says, are more willing guinea pigs for the favorite experiment in the Kupfer Laboratory, a.k.a. the Department of Psychiatry (which has been chaired by David Lewis since 2009)—interdisciplinary collaboration.

Kupfer developed his own formula for the proper care and feeding of researchers: Give them the seed money they need to fund their work. Give them credit when their hard work pans out. Promote them, sometimes at a rate

Within a year of their arrival, Kupfer and Detre also started a long-standing policy of issuing rewards to investigators in proportion to the amount of federal-research funding they brought in. It might sound unseemly to some—kind of like corporate culture, says Daniel Buysse, professor of psychiatry and of clinical and translational science, director of the Neuroscience Clinical and Translational Research Center, and codirector of the Sleep Medicine Institute at Pitt. (Buysse is also a Kupfer mentee dating back to 1983.) But he means that as a compliment. “Science is business, and David realized that before a lot of people did. It’s just a reality.” Kupfer operates in a strategic, systematic way, says Buysse. He delegates. He pays attention not only to whether a study is worth doing, but also to whether it can be paid for.

The Research Review Committee makes

something missing.’ It took me two years to find out that he was right.

“He has this ability. He can sense the people who have talents he can elicit. And he can also make the judgment on the other side, which is sometimes harsh. But I think that ability—to actually understand where people are coming from, what their talents are, and how to use them—is really remarkable. And to have it in a person who’s as good a scientist as he is, is really amazing. ... All you have to do is look at the quality of the Pittsburgh faculty. People used to say that if you go to Pittsburgh and David says you have talent, you are gonna stay in Pittsburgh.”

What’s the secret? Kupfer is sure it’s a gift, something that may not be teachable. There are certain attributes Kupfer tends to notice and file away as he gets to know people: birth order, handedness, and the like. (He estimates some

“The profession has got to decide that it needs some measurable outcomes. And it can’t be my saying, ‘Well, I think you’re doing a little better.’ Then somebody else in New York says, ‘Well, hmm. I think you’re doing terribly.’ See? What the heck is that?! It’s not sufficient.”

that might surprise outsiders. But the Pitt lot gets away with this, if history is any indication, because it happens in an environment where people feel safe trying out untested ideas.

But they can’t do that alone.

“David often says we’re like real estate agents,” says Lewis, an MD who is also UPMC Professor of Translational Neuroscience, medical director of Western Psychiatric Institute and Clinic, and among a long list of people who came to Pitt as young pups and grew into research giants. “The three most important things are mentoring, mentoring, and mentoring.”

Very soon after Kupfer arrived at Pitt, he set up the Research Review Committee, which is still active and which he has led since he stepped down as department chair. It’s an internal grant-review process designed to be every bit as stringent as that of the NIMH, if not more. Some 200 faculty now participate, a few of whom are from outside the department and most of whom have served on federal grant-review committees. Grant writers get their feedback within a week. (When the program began, turnaround time was 48 hours. “People dropped everything to read” new proposals, says Frank.)

sense from the standpoint of fostering a collegial, collaborative environment. In reviewing one another’s grant drafts, researchers network with people in their department.

Another way to get people to share new ideas, Kupfer says, is to make them share other things, too. Instead of setting up, say, several different sleep labs for schizophrenia, for depression, for children, and so on, make one big sleep lab and throw all of the researchers together.

Of course, not every excellent scientist is cut out for a place like Pitt. For all their brilliance, some people just aren’t good mentors. And some, if asked to share and share alike, just will not like that *at all*. But Kupfer has a remarkable gift for spotting such people—and for reading people in general—and can do this very quickly. Many of Kupfer’s close friends have stories like this:

“I was working with someone once, and she is quite brilliant,” says Helena Kraemer, professor emerita of biostatistics in psychiatry at Stanford and professor of psychiatry at Pitt. “David met her and talked to her for about 15 minutes. And then he said to me, ‘You know, she’s not going to make it.’ And I said, ‘Why do you say that?’ And he said, ‘There’s just

30 to 40 percent of the department’s faculty are lefties. Kupfer himself is a southpaw, too.)

“There’s some anecdotal stuff that happens to be true, which is that people who don’t share, well, are not likely to share!” he says with a laugh. “In the early days, when we used to recruit people from Yale and take them out for dinner, I would find out whether they would be willing to share their food. Just a little taste.”

When he reviews a CV, Kupfer pays special attention to a candidate’s list of publications. When doctors don’t have a history of sharing authorship, they’re not likely to share other important things. And, perhaps most importantly, he asks, *What has this person done in the way of mentoring?* “Somebody who hasn’t mentored is not a good team player, even if they’re very young. It doesn’t matter who they’ve mentored. It could be a younger sibling.”

In addition to his people-reading skills, he’s famous for his team-building, both at Pitt and beyond. “He is the consummate scientific *shadkhen*” (that’s “matchmaker” in Yiddish), says Laurence Steinberg, PhD, Distinguished University Professor of Psychology at Temple University.

As a result of all this careful people picking and pairing, the Department of Psychiatry’s

research efforts cover just about every aspect of psychiatry and brain science that you can shake a stick at: diagnosis, neurobiology, psychobiology, cognitive neuroscience, biological treatment, policy. From pediatrics to geriatrics. It's all there.

"Very few departments are that broad," says Barchas. "There's almost no area of research that NIH funds that there isn't someone at Pittsburgh working on. It's just plain astounding."

Though the department is welcoming to newbies, a sizeable percentage of its faculty are not "kids," in fact. Many are original Detre/Kupfer recruits from decades ago. You've got to wonder how common that must be.

"I don't know if it's like that at other places, because I've never been anywhere else," Buysse says, laughing.

Posed with the same question, Lewis gives the same answer.

Kraemer says people—even a lot of psychiatrists—tend to use the terms *disorder* and *diagnosis* interchangeably. But the disorder is what's ailing you—the quirk of the organ that is your brain, the fact that your striatum fails to activate in response to a reward stimulus, or whatever. And the diagnosis is someone's *opinion* of what's ailing you.

"From my perspective," she says, "the crucial thing about *DSM-5* is that we're trying to bring diagnosis one step closer to the disorder."

In the absence of biological measures, psychiatrists and others have made their best guesses at diagnosis using the only tools they've had: symptoms. In fact, in previous editions of the *DSM*, symptoms were the only criteria that were *allowed*. This is one of those things that has kept psychiatry out in the wilderness, different from the rest of medicine. As Buysse puts it, you wouldn't lump together any other kind of diseases based on how they look in the clinic, would you? If you put, say, all conditions that cause you to cough up blood into one category, you would be blindly lumping together bronchitis, tuberculosis, and cancer.

"When we say people have depression, it's kind of like the bloody sputum of psychiatry," Buysse says.

Diagnosis has always been challenging, because the scientific community has known so little about disorders. And yet without accurate diagnosis, scientists can't understand the disorder any better, because they can't trust the

reliability of the research.

But if scientists ever want to begin to understand the individual quirks of the organ that is the brain—and to help it heal—they have to start somewhere.

Kupfer's solution: While previous editions have been named with Roman numerals, (*DSM-III*, *DSM-IV*), he decided the fifth edition should be titled with an Arabic number. Think of it as "DSM 5.0," he says, because, from here on out, more frequent, partial updates will be released as the science evolves. This may well be the last print edition. Gone are the days of waiting 15, 20 years to start from scratch. He calls the new *DSM* a "living document."

One aspect of the revision that was utterly ignored by the media in the buildup to the release of the latest edition, but which means a great deal to task force members, is the manual's "meta-structure." Essentially, the book has been reorganized, and the chapters have been reordered. Disorders that now appear to share common biology have been put right next to one another. For example, ADHD, schizophrenia, bipolar disease, anxiety, and depression are now together because they've recently been found to have genes in common.

So how does this help patients?

Alan Schatzberg, professor and former chair of psychiatry at Stanford and former president of the American Psychiatric Association, says, "It helps them in that anxiety and depression seem to be quite related. One seems to presage the other," for example.

And it helps because, if your physician realizes that certain disorders share biology, she might view your family history differently. "We still have distinctions of disorders," Schatzberg says, "but there are commonalities in terms of how they run in families. . . . A schizophrenic kid will have a bipolar father or grandfather."

Within the chapters, the diagnostic criteria will be very different. In *DSM IV*, physicians were presented with checklists—if the patient has five of these seven psychiatric symptoms, he has disorder X. But the science is telling us that it doesn't always work that way.

Which is what has led to what are often called "wastebasket" diagnoses, not otherwise specified (NOS). That's where people just outside of the criteria end up. Previous *DSMs* have led to overflowing waste bins—in autism spectrum disorders, famously, among others.

So, in 5.0, diagnosis is not so all-or-nothing, you-have-it-or-you-don't. Now, it's about severity of symptoms. A continuum. A spectrum. The evolving understanding of the underlying biology of disorders is teaching psychiatrists to focus more on the similarities between disorders than their differences—or, rather, what is *perceived* as their differences.

Because they've found that often they've been wrong.

Disorders psychiatrists thought *weren't* related really *are*. Like autism. In *DSM-IV* there were four distinct diagnoses thereof (Asperger's and so on). But the science to justify all this hairsplitting just isn't there. So in 5.0, it's one big autism spectrum.

Alternatively, disorders that people think *are* related really *aren't*, says Kupfer. To illustrate, he points his finger at each of the swiveling, black-leather Eames chairs around the low, white marble table in his office.

"Let's say we have [several] people sitting here," he says. "All of them have clinical depression. The person next to you, you know, that person is suicidal but also has clinical depression. This person over here also meets the criteria for clinical depression, but he's psychotic—he has delusions. And what about this person? This person's had all kinds of panic attacks. The person next to me has a drug problem. And this person on the other side of you? It's his first episode, and he may never have another episode. All right? They all meet the diagnosis of clinical depression, but we treat them differently."

Nobody here is suffering from just depression, Kupfer says, and that's where the term *comorbidity* comes from. But the evidence is showing scientists that that comorbidity is the rule rather than the exception—and 5.0 says as much, for the first time in *DSM* history.

"Comorbidity may simply mean that we've got the wrong diagnosis." That is, maybe, for each of the imaginary patients at the table, there is a different disorder that cuts across several different clusters of symptoms. But psychiatrists will never recognize these cross-cutting clusters unless they start measuring and tracking symptoms in a systematic way.

In the new *DSM's* Section III—an appendix of sorts where the task force has included items that are in need of further investigation—is a return to the Kupfer Detre System. (Remember those reams of papers that surrounded Kupfer in his office in 1969?) It's a

computer-based questionnaire patients can fill out in less than 15 minutes, an inventory of general measures of mental health status: level of depression, anxiety, sleep, substance abuse, and so on—mental health counterparts of blood pressure and heart rate.

Kupfer hopes professionals in the field of psychiatry will take this tool and run with it. Perhaps it will stimulate new ways of thinking about disorders. “Maybe you can begin to divide your subgroups differently, like we do with the rest of medicine.” In other words, maybe psychiatrists can start to get past the bloody-sputum kind of thinking. “And once we get *there*, we can start making some progress.”

Such an inventory could be helpful in the clinic, Kupfer says. “I’d sit down with you and go over these things as part of my getting to know you. You get into things a lot quicker, and I think you do a much more accurate evaluation.

“The profession has got to decide that it needs some measurable outcomes. And it can’t be my saying, ‘Well, I think you’re doing a little better.’ Then somebody else in New York says, ‘Well, hmm. I think you’re doing terribly.’ See? What the heck is that?! It’s not sufficient.”

Also in Section III is a tool clinicians can use for something the task-force folk call “dimensional diagnosis.” It’s a way to assess symptoms along a spectrum—not whether or not a patient has depression, but how much?

Reynolds says this new emphasis on dimensionality could lead to better prospects for patients diagnosed as NOS—not only in terms of getting them out of the wastebasket diagnoses, but also to improving their outcomes.

“Many people live with subsyndromal, sub-threshold symptoms, for example, of depression,” he says. “It’s important to recognize that. Because many such persons are at risk of going on to develop frankly clinical expressions, for example, of depression or schizophrenia.

“I think the *DSM-5* will also assist with the further development of prevention science within psychiatry. This is a very important aspect of *DSM-5*.”

Reynolds, who chaired the work group on sleep-wake disorders for *DSM-5*—a work group Kupfer chaired for *DSM-IV*—is proud to point out that this section includes, for the first time in *DSM* history, biological measures with proven diagnostic use, as well as epidemiologic studies, all written right into the

official diagnostic criteria.

“We had not been allowed to include biological measures in *DSM-IV*,” Reynolds says. “That was just not part of the spirit of the times. It has been a long journey, a journey not without quite a bit of controversy along the way. David was never afraid of the controversy, never afraid to take risks and to try to push the field forward.”

On a chilly morning in April 2013, Kupfer welcomes this *Pitt Med* writer who has come to crash his party. “Have some breakfast—you’re too skinny anyway,” he says, channeling my mom.

It’s the start of an intensive, five-day course for bipolar-disorder-research “kids” from around the world—this year, from Poland, Chile, and Colombia, as well as across the United States. Kupfer started this semiannual course eight years ago, bothered by the stagnation in bipolar disorder research. (“Lithium was something that was being used . . . in the late ’60s,” he says. “We don’t have a better drug to treat bipolar disorder 45 years later. There’s something wrong. Radically wrong.”)

More than a decade ago, Kupfer and Schatzberg founded the Career Development Institute for Psychiatry, a similar mentoring program for physician-scientists in all areas of psychiatry. A collaboration between Pitt and Stanford, the institute has since been revised and expanded as a long-distance mentoring program, offered year-round. The idea is to try to figure out how to change the nature of mentoring, or lack thereof, in other places and “influence or pollute their own environment back home—not in an antagonistic way, but to help them on their home turf,” Kupfer says. “Because not everybody is gonna move to the six or seven places where we would say there’s good mentoring.”

Two years ago, the American College of Neuropsychopharmacology presented Kupfer with the Julius Axelrod Mentorship Award. (Kupfer knows its namesake as “Julie,” who consulted for Pitt’s department many years ago.) The morning of the award ceremony, he looked around the room and realized that among the 200-some people there, he’d probably mentored a quarter of them. When he came home, Pitt gave him a T-shirt emblazoned with “Mentor of All Mentors.”

These are the kinds of things Kupfer does to keep himself “off the street,” he says. Another

is an international conference on bipolar disorder. The first one, which took place 15 years ago, was a small affair in Pitt’s student union. The last couple have drawn more than a thousand attendees from 25 countries.

“His energy is frightening,” jokes Frank, of her partner the night owl.

As the participants take their seats at this spring’s crash course, Kupfer encourages them to relax. Here, he lives up to his reputation as a “consummate schmoozer,” as *The Wall Street Journal* called him. “The dress mode is as casual as you are comfortable with,” he says—he’s dressed business-casual today. “We want you to enjoy yourself and work with the faculty colleagues”—many of whom are alums of this program, he notes, and all of whom have come here, pro bono. (Mentoring, mentoring, and mentoring.)

And it does seem cozy, or as cozy as it can be for a group of young investigators in the presence of one of the most influential academic psychiatrists in the world.

Kupfer has the mentees go around the room, introduce themselves, and talk about what challenges they face in doing what they want to do. The mentor faculty then do the same. They commiserate over many shared frustrations: work/life balance, clinical-work/research-work balance, departmental politics, getting published. Kupfer interjects often with advice. (“When my children ask me what they need to get ahead in life, I say, ‘There are only, really, two or three things, and one of them is that you’ve really got to learn how to write.’”)

And then it’s Kupfer’s turn. He says his biggest challenge, now that the *DSM-5* is coming out, will be to gradually extricate himself from those efforts, which have kept him on call 24/7 for seven years, and get back to his real passion, mood-disorder research—bipolar-disorder research in particular. “The real problem for me is the question of how many of these involvements should be where I commit myself as principal investigator—which is something like five years, 10 years—versus helping other people attain their PI status. . . . That’s something I’ve always been comfortable doing.”

Then, a faculty member asks, “If you knew then what you know now, would you have done the *DSM-5*?” and a chuckle spreads through the room.

“Absolutely,” he says. “No question about it.” ■