Alan Hu Foundation Mental Health Lecture Series

Positive Psychology: A Dimensional Approach to Well-Being Webinar by UCLA Professor Robert Bilder, PhD

Tennenbaum Family Distinguished Professor of Psychiatry and Psychology, Chief of Psychology at UCLA Health and Director of the Center for the Biology of Creativity. May 10, 2022

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CHIH-CHING HU: Hello everyone, good evening, good afternoon, and good morning, depending on where you are coming from. Welcome to the Alan Hu Foundation Mental Health Lecture Series. I am Chih-Ching Hu, Co-Founder of Alan Hu Foundation, and host for your webinar.

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Today, Dr. Robert Bilder will present "Positive Neuropsychology: A Dimensional Approach to Well-being." First off, I would like to thank you all for joining us across the country and around the world. I would also like to thank the Mental Health Association for Chinese Communities for providing simultaneous Chinese interpretation. Thank you, MHACC Founder and President, Elaine Peng, and thank you, Ida Shaw, for Chinese interpretation.

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The Alan Hu Foundation Mental Health Lecture Series aims to make mental health knowledge common knowledge. Alan Hu Foundation's mission is to promote mental health, raise awareness, and remove stigma surrounding psychiatric disorders, and support fundamental research for cures. Please consider making a gift to Alan Hu Foundation. Your gift will be 100% invested into the foundation's mission to support mental health.

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Today, it is my great honor and privilege to introduce Dr. Robert Bilder. Dr. Bilder is Tennenbaum Family Distinguished Professor of Psychiatry and Psychology, Chief of Psychology at UCLA Health, and Director of the Center for the Biology of Creativity. He's a board-certified clinical neuropsychologist and directs the UCLA post-doctoral fellowship program in neuropsychology.

His research on brain and behavior aims to eliminate boundaries between mental health and illness and between everyday and exceptional creativity. Over the last decade, he has been a leader within the Semel Healthy Campus Initiative. He is currently co-leader of the Mind Well pod, which aims to enhance psychological well-being among UCLA students, staff, and faculty through both curricular and extracurricular programming.

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In today's talk, Dr. Bilder will explain how current theories suggest there are not clear lines separating different psychiatric conditions or boundaries between health and illness. Instead, interactions among dimensions of brain function determine how resilient we are when confronted with stressors. He will focus on how we can use strategies from positive psychology to enhance well-being and increase resilience to stress. The global application of these practices could reduce the incidence of common psychiatric disorders, including anxiety, mood, and substance use syndromes, by more than 50%.

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Following the presentation, there will be a Q&A session. Please submit your questions using the Zoom Q&A function. The presentation is for educational purposes only and is not intended for medical diagnosis. If you have any persistent symptoms, please seek professional help.

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With that, I'm going to return to Dr. Bilder. Welcome, Dr. Bilder.

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DR. BILDER: Thank you so much. Thank you for that kind introduction, and thank you. Let me see if I can actually pull up my slides. There we go. So, thank you so much for inviting me. It's a great honor to be able to present here, and thank you in the audience for coming and joining us at whatever hour it may be for you to learn a little bit about positive neuropsychology and dimensional approaches to well-being. I'm very excited to share these things with you.

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It's been said that there are two kinds of people in this world. There's the kind of people who breaks the world into two kinds of people, and then those who don't. And I think that one of the key points that I'll share with you is, I'm one of the kinds of people that does not break the world into two kinds of people. Rather, I think that there's pretty much infinite diversity of people. And I'm reminded that there was a great clinician named Sir William Osler that once said, "I've never seen two patients with the same disease." And I think that that's something that we should recognize all the time when working with mental illness, is that no two patients have the same problem, and when diagnostic classifications are made, that these are not good descriptions of any of us. We're all unique, and each of us is different.

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And what I want to share with you is some information that very few people are aware of today, and it goes back, interestingly enough, just about a hundred years when, believe it or not, there was a global pandemic, the influenza pandemic. It had spread through the world, and one of the great psychiatrists of history, Karl Menninger, decided to study what happened to people when they were afflicted by influenza. Influenza, as you may know, is a diffuse systemic illness. In other words, it infects various organs in the body and has no preferential impact on the brain or any particular brain system. Yet, Karl Menninger had noticed that people had various mental changes after they were affected by this virus. And he went about trying to characterize these changes, and what he found was really quite astonishing.

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What he found is that, in the early stages of illness when things were not that severe, people became more nervous. They showed what used to be called neurotic phenomena. But if they became sicker, then they showed other kinds of changes, including more episodic and explosive discharges, the kind of manic symptoms that we hear about. And then if they got sicker than that, they began to show more persistent and severe patterns of disorganization. And now, amazingly enough, at the same time that Karl Menninger was doing this work, another doctor in Spain, Llopis, was studying the victims of pellagra, vitamin B deficiency, that similarly had no predilection to infect any particular part of the brain. Yet still, as people became sicker with this systemic illness, they also showed signs of mental changes from neurosis to depression, to mania, to the so-called positive symptoms of schizophrenia and psychosis like delusions and hallucinations. If they got worse, they showed negative symptoms that we see in schizophrenia, like flattening of affect and lack of volition, apathy. If patients got sicker, they went into a coma. And if they got sicker than that, they died. But if they did not die and if they recovered, what they saw is that they would regress back through the same pattern. So as they got well, they went back through coma to negative symptoms, to positive symptoms, to mania, to depression, to neurotic symptoms—all due to a systemic illness.

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The remarkable thing about both of these studies, in different continents, due to diffuse systemic illnesses, is that one single dimension of illness severity seems to underlie all of the different kinds of expressions of mental and emotional distress. And so here we have evidence for more than 100 years that the boundaries between these different symptom presentations—neurotic symptoms, depressive symptoms, manic symptoms, all the

symptoms that we see in schizophrenia—were all produced and caused by a diffuse systemic illness that was not due to infection of any particular brain organ. It had to do with mass action on the brain and impact on the overall severity of brain dysfunction.

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So you may wonder, well, we have now been using modern diagnostic systems like the Diagnostic and Statistical Manual for Mental Disorders, which is now in its fifth edition with a text revision even as of last month, so isn't that got it right in terms of the different dimensions? Well, what I'd like to tell you is that I think that's not true. There are not clear boundaries between many of these disorders, and we can see it in many, many different ways. And I'm trained as a neuropsychologist, so one of the factors that we look at carefully are cognitive deficits, which provide an index of brain function and dysfunction.

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Interestingly enough, if we look at just the overall magnitude of neuropsychological deficit across the different disorders, there's not a clear separation where some disorders have mental or cognitive deficits and others don't. Instead, there's a mild or relatively small effect in unipolar depression that's similar to that you see in a syndrome like ADHD. But as you go into illnesses like bipolar disorder or manic-depressive disorder, there's a greater severity of illness and then a mild cognitive impairment that we see in older adults is a little bit more severe. The cognitive deficits associated with schizophrenia are a little bit more severe, and the problems in dementia are even more severe. But here again, we're talking about an overall dimension of severity that shows no discrete pattern affecting the particular disorder.

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When we look at brain structure, early in the 1980s, it was found for the first time that people with schizophrenia tended to have enlarged ventricles, a reduction in the gray matter on the cortex of the brain, and decreases in the size of the hippocampus, a critical structure in the brain long thought to be involved in learning and memory. And what was found shortly after the discovery that these changes occurred in schizophrenia, which, of course, had previously been called a functional disorder, but now we had evidence that there were structural brain abnormalities. So it was now rebranded as an organic mental disorder. But we found shortly thereafter that people with bipolar disorder also had these kind of changes in their brain, and as I'll show you, we found that these changes are even more pervasive.

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Indeed, using modern brain imaging methods, here's a paper looking across very large samples of people in 2020, and this cross-disorder analysis shows across six major psychiatric disorders that there's an enormous amount of overlap. So in major depressive disorder, bipolar disorder, schizophrenia, and obsessive-compulsive disorder, the brain abnormalities were highly correlated, and there was one shared latent underlying factor that explained more than half the variance of the brain structural variance within these disorders. So it's really quite remarkable that all of these different deficit patterns are really shared across the disorders and one thing that you'll notice in talks that touch on neuroscience is that we try to persuade you that things are true when we show you colorful pictures of the brain. And so here are some colorful pictures of the brain that show you just what I was telling you a second ago, that there's one big factor, this so-called F1, you can see on the left side of the figure, and it very highly correlates with the changes that we see in major depressive disorder, bipolar disorder, schizophrenia, and obsessive-compulsive disorder. There are some other more minor factors that can also be identified in ADHD and autism spectrum disorders, but overall, the main event is the shared neuroanatomic abnormality across these different disorders without specificity to any one of the disorders.

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Then if you may say, "Well, what about the functional patterns? That was just looking at brain structure. Maybe the functional patterns differ markedly between these different disorders." And here's another paper that came

out in 2020 where people are looking across large groups of patients and looking at the functional patterns of connectivity. What you really see is, in that study, and then in this study that looks at the genome-wide relationship across eight psychiatric disorders, they really tend to clump together. You can tease apart certain subgroups that have certain kinds of co-associations, but overall, a lot of the variance in brain structure, brain function, and the genetic relationships is all explained by common factors that occur across all the different disorders.

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Now, I think that one thing that's very interesting is we try to understand, well, what is it that's going on in the brain that could help bring all this together? And there's some brilliant investigators who have looked at the patterns of connectivity across a whole lot of different kinds of brain states and functional brains and in dysfunctional brains, and what they found is that it looks as if there is a way to look at the ways that the different parts of the brain are connected together where you can look at modular organization on the one hand and integration on the other hand. And some of the methods for integration are more efficient or less efficient, and among the modular patterns of organization, some kinds of wiring are very expensive physiologically and others are cheaper physiologically, easier to implement in a brain. But basically, there's a spectrum of connectivity landscapes that are viable and that lead to good functioning. And probably as we leave that good zone where brains function well, where there's a high level of resilience, there are a whole lot of different ways, a multitude of ways in which one could have a slightly different organization of the brain. And many of those would move in the direction of becoming less resilient in terms of one's overall connectome disorganization or organization.

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So, I think this is a model that, you know, continues to need experimental verification, but meanwhile, I think it offers a way to think about the wiring of our brains. There are many different ways to wire a brain; we are all unique, and each of us may become ill in our own ways, but we share a lot more than we are different. And just to bring this point even further, I would say going beyond brain structure and function, if we look at what codes for those brain structures and function, look at the level of genetics, what we see is that there's a very high degree of genetic overlap. You know, it was early on thought that a gene or two might explain certain disorders like schizophrenia or bipolar disorder or ADHD or major depression. Well, we now know that for any one of these complex disorders, it probably involves about a third of the entire human genome. So, there are 30,000 genes; there's probably 10,000 genes that are involved in producing the risks for disorders like schizophrenia, bipolar disorder, and major depressive disorder. So that's something that, you know, bear in mind.

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Okay, I do see some questions coming up in the chat, but if it's okay for me to wait for a while, it'll be easier for me to get through. But I hope you'll – that's it, looks like a fantastic question. Uh, so I'm eager to get to that, so I'll try to cover the rest of the slides efficiently.

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Now, another thing, when we look at the patterns of inheritance of different kinds of symptoms, again, it was early on thought that there might be unique patterns of heritability that would lead to, for example, depressive disorders or generalized anxiety disorders or seasonal affective disorders or OCD. Well, modern genetic studies have actually shown just the opposite, that, in fact, there's one global psychopathology factor that probably explains most of the variants across all different kinds of psychiatric disorders. And then, if you look further, you can find additional factors that represent externalizing disorders and internalizing disorders, with the externalizing disorders being the kinds of things that present themselves to us because of acting-out kinds of behaviors. So there we have the hyperactive-impulsive subtypes of ADHD, some of the inattentive, but also oppositional defiant disorders, conduct disorders, which can include and are largely associated with substance abuse. But then, on the internalizing side, we see the affective disorders, mood disorders, obsessive-compulsive disorder. But most of the genetic liability is shared.

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That was in childhood. This slide shows exactly the same thing has been found in adults, where basically what you see are factors for internalizing and externalizing. But in this particular work, it distinguished between one set of factors that were called Axis I because they're more severe, and the other side, we see what was called Axis II, more like personality disorders. So, among the internalizing disorders, you can see we've got panic disorder, major depression, the specific phobias, etc. On the externalizing, we see anti-social drug abuse, conduct disorder, alcohol abuse, etc. And then in milder forms, again, it's just a severity axis that we're seeing here. Internalizing would include dysthymia or avoidant personality disorders, while externalizing would include histrionic, narcissistic, and borderline personality disorders. So you can see that here again, while it's analyzed slightly differently, we're talking about an overall severity axis and then probably internalizing externalizing disorders as a somewhat subsidiary set of factors. And that's the way the genetics works.

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And just to highlight that this isn't just for psychiatric disorders, this is a remarkable figure that was assembled entirely from patient medical records. We all know that we're contributing our data to electronic health records now. Well, this was an analysis across many, many, I think millions of medical records and looked at the co-associations among different kinds of disorders among people as diagnosed by their physicians. And the remarkable thing about this is not only that the mental disorders like bipolar disorder and schizophrenia that you see in the yellow circles are somewhat connected to each other, but also they're connected to a whole host of other medical illnesses, as are the medical illnesses connected to each other. So, just as I was saying in the beginning, where we can see all kinds of phenotypic expressions or behavioral expressions, other kinds of physiological manifestations of diffuse systemic illnesses, the same is true across all disorders. That we can see that physical physiological dysregulation anywhere in the body is likely to be associated with alterations in brain function and structure.

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Now you may wonder, well, what has the Diagnostic and Statistical Manual group done to address the idea that there might be dimensional aspects of these psychiatric disorders?

Because the way the DSM operates is really categorical, and there was in the lead-up to the DSM-5 something called DSM-5 Prelude, consideration of dimensional aspects across every one of the major disorder categories. So, I think for those who are academic students of these areas, it's possible now to obtain all of the rating scales that are needed to try to understand individual patient symptoms using these dimensional approaches. Yet still, when the DSM-5 was published, it continued to use the categorical model.

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I think from a patient perspective or a family member's perspective, it's important to recognize that these dimensional rating scales, which you can also freely access online, can enable you to see how severe particular problems are, what are the more severe levels of symptom expression within each of the different kinds of domains, and how many, many disorders are seen to overlap.

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Ironically, in the DSM-5, one of the key criteria in almost every disorder is the phrase "it should not be explained by another disorder." So, you may have the same exact symptoms, the same symptoms of inattention, for example, may go into the diagnosis of ADHD, may go into the diagnosis of a major depressive disorder, may go into a diagnosis of an anxiety disorder, or another cognitive disorder. Yet, you have to try to tease apart and pretend that one is not explained better by the other. So, this leads to what is called comorbidity, where we make multiple diagnoses in patients without having a category into which we can put people who have multiple kinds of symptoms.

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So, there's an implication of this kind of dimensional representation of all the different symptom dimensions, and I just want to highlight to you that with an example about depressive disorders, that we now understand that there are basically dimensions of mood that run from a lot of sadness to higher degrees of happiness, and everyone can occupy a position on this big bell-shaped curve of positive to negative mood and affective expression.

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And, when we look at this statistically or if we look at the ratings of depressive symptoms, for example, on an instrument like the Patient Health Questionnaire nine-item form, which is widely used around the world now to diagnose depression or to characterize the severity of depression, what we see is that it's really about the lowest 10%. I mean, the last number I saw was 8.4 and below; people in that range are very highly likely to be diagnosed as having a major depressive disorder. People above that are not. So, here we have a continuous dimensional measure of severity, and it's only the people in the lowest 10% who are likely to be diagnosed with depression.

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However, if we plot that a slightly different way, here's just a cumulative way to plot the normal distribution where we look at the percent of the population that's involved. So here, this depicts that bright blue line is the line that separates, in the current condition, what the bottom 10% looks like on this curve. Those are the folks anybody below that line is likely to get the diagnosis of depression based on having low stress resilience, as what I've called it on this x-axis.

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However, let's just imagine for the moment, and then we'll talk about how that could happen, but let's just imagine for a moment that we could help everyone to be a little bit more stress resilient, that we could help everyone to be a little bit healthier. And here, I'm talking about a little bit healthier, is the amount that's just above the threshold that we could notice. That we could notice ourselves, and maybe one of our family members, or maybe a doctor could notice that we're actually feeling a little bit better. If we could move that much, and in this graph, and for you statistical gurus out there, what I'm talking about is a move of about a half a standard deviation, which is widely considered to be a difference that is noticeable clinically. That movement of the curve by one half of a standard deviation would change the overall number of people below the bright line from 10% down to 3.5%. So effectively, just by making everyone a little bit healthier, we would have cured, so to speak, or prevented, that's another way to say it, almost two-thirds of the people who have depressive disorders. And I think that's pretty remarkable and highlights the virtues of having universal interventions that may enhance well-being.

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So let's talk a little bit about well-being. Among the different well-being indicators, there are lots of measures that have been developed, and I think it's worthwhile thinking a little bit about them, to think about how they work, and that gives us clues as to the kinds of things that we can do, to understand our own well-being and to enhance that of us as individuals. This well-being in the nation network is really interesting because it identifies indicators of well-being that work across entire countries and continent, so I think that's fascinating in terms of global approaches to understanding well-being. But when we drill down to the individual level, there are a number of ways to do that, and the simplest way to do it is with something called Cantril's ladder. This basically lets you rate yourself on a 0 to 10 scale from the worst possible life to the best possible life. So you could imagine a ladder, and I say, "What's the best possible life for you? Where are you at today?" And you can make a mark there on the grid and say, "Oh, for example, I feel like I'm six today." And then there's a second question that's often asked, "On which step do you think you'll stand about five years from now?" So let's say I respond, "Well, I think in five years, I'll be at eight on Cantrill's ladder." Well, what that shows is a degree of optimism that is also highly correlated with a number of well-being outcomes. And you can do the same thing with financial out-

comes, but interestingly enough, this extremely simple measure, it doesn't get much simpler than this, is able to predict the number of people thriving, the number of people suffering, the number of people who have hope for the future, just with these two simple questions and has been administered millions of times, well validated, and the scores on this measure are related to all kinds of illness morbidity, also to mortality, death, and to the costs that are associated with illness. So, this is a global measure that's useful for stratifying risks, and it works well across sectors and has worked well internationally as well.

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But when we dig into the literature on well-being, we find that the well-being researchers have identified a number of different areas of well-being that are a little bit more refined and get into certain kinds of specific practices that we might consider if we're interested in enhancing well-being. And so, this is from a well-known well-being researcher Carol Ryff and her colleague Burton Singer, and they identified six key factors and also the historical antecedents in the world literature where these ideas really came from. The components include self-acceptance, purpose and meaning in life, a sense of autonomy, environmental mastery, personal growth, and positive relationships. And these, depending on how you go up measuring them, these can be identified as independent dimensions, each one of which can be supported independently, even though they often work together and are highly correlated within individuals.

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One other point I'd like to make about these ideas that highlights the virtue of focusing on dimensional approaches, and that is that if we think about where attention has been focused globally, most of the attention and effort has been focused on eliminating and targeting the eradication of disease rather than on well-being. So basically, the bottom of this figure is focused on trauma, exclusion, adversity. These are the kinds of things where efforts are largely directed, and I think that there's an increasing recognition that by focusing on the top of this diagram, by focusing on the positive aspects rather than the illness aspects, focusing on dignity and inclusion, on well-being, that these are the kinds of interventions that may have equal or even greater effect than focusing just on the impairments and dysfunctions that we see.

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So how does this work out in individuals, though? There's a really nice summary of how these kinds of measures, you know, relate to what's called emotional intelligence or the so-called EQ. But again, the dimensions may begin to sound very familiar because on the well-being dimensions, we have areas like trait optimism, happiness, and self-esteem. Sociability is involved in that, emotionality as well, which includes empathy and emotion perception. But again, a focus on relationships, other aspects of self-control that enable one to have emotion regulation and to control one's impulses and to manage one's stresses, along with other facets of motivation and adaptability that help to promote well-being.

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Interestingly enough, a review that looked across a whole lot, almost 100 self-report measures for looking at well-being in adults, found dimensions that again, are going to start to sound very familiar: mental well-being, social well-being, physical well-being, spiritual well-being, activities and functioning, and personal circumstances. This is a slightly different way to slice the pie, but I think you're getting a sense of the kinds of aspects that we can identify that go into psychological well-being.

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Similarly, if we look to see what's been identified so far by our big health agencies as aspects of well-being, the NIH has identified both mental, physical, and social health outcome measures separately, and the CDC has actually gone a little bit further in trying to identify aspects of emotional well-being and psychological well-being and satisfaction with life, along with domain-specific satisfaction and the values of engaging activities and work that may be critically important. In fact, it brings to mind what Sigmund Freud once said, "What are the keys to men-

tal health?" He said, "To love and to work." So, I think that if we consider the elements of loving relationships and productive engagement in work life and to have a work and life balance, these are probably cornerstones of successful well-being.

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Now there's another sort of astonishing thing that I want to bring up that has to do with the value of a focus on psychological well-being. You may say, "Well, why do we care so much about behavior, particularly if our interest is on medical illnesses?" And this chart I think highlights that when we look at the burden of disease and try to explain biomedical illness and try to figure out what are the key factors that are associated with physical illnesses of all kinds, what's found is that physical environment accounts for about 7% of the variance in medical outcomes. Medical care, that's where we spend most of our health care dollars, accounts for only about 11% of medical outcomes. About 22%, this is reassuring I guess to all of us biomedical scientists, genetics and biology, which we've been studying for years and investing a huge amount of research effort into understanding, accounts for about 22% of the outcomes. But more than half of the outcomes are due to social circumstances and individual behavior.

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So, you can see the social circumstances that we live in, the so-called social determinants of health, account for about a quarter of all the outcomes, more than genetics and biology alone, and double that of medical care in accounting for health outcomes. Individual behavior accounts for more than a third of health care outcomes, 36%. So, that's really, I think, remarkable. That's a very clear justification for why individual behavior is important, and if you think about it, there are a number of psychological assets that go into enhancing physical and physiological functioning—conscientiousness, self-efficacy, optimism, etc. Negative moods and affects that if they're lower, lower stress, lower hopelessness, lower anxiety, lower depression, and there's a whole bunch of other risk-related behaviors including gun violence, irresponsible sexual activity, bad driving, other physical activity, sleep patterns, and diet, account for a huge amount of our health care outcomes. So, yeah, if we think about smoking habits, sleep and exercise patterns, sexual activity, and mood, these are all examples of where individual behavior is a critical determinant of health and a good rationale for why we should really be thinking about it.

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So, let's focus now for a moment on what about being satisfied with one's own life? This is, you know, you may think one of the goals of life is to be satisfied with life. And students of this area have identified that social relationships, work, school, and personal relationships, and health all go into satisfaction with life, and there are five questions there on the right. If you could answer those questions, yes, then you know you're gonna probably be pretty satisfied with life, and if not, then there's work to do.

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Now, let me talk about one other dimension of well-being, and that is something that was discovered back in ancient Greece when they were discussing the kinds of happiness that exist. On the left side of this diagram, you see the older Plato; he's identifying, signifying by holding up his finger, there's only one kind of happiness. On the right is the younger student, Aristotle. You can say, "Hey, he's saying, 'Hold on, dude, it's not...don't go so fast. I think there's more than one kind of happiness." And it was Aristotle who brought to us the idea that there are really two kinds of happiness: one of which is hedonia, the immediate gratification of needs, in contrast to that, the sustained happiness that comes from living a life filled with meaning and purpose, and you refer to that as eudaimonia or the true spirit. And that's the highest recognition of oneself, and this has been developed further by a number of scientists; Deci and Ryan have a well widely read paper that focuses on the hedonistic tradition where there's a focus on happiness, typically that's defined as high amounts of positive affect and low negative affect. But in this eudaimonic tradition, the focus is really on living a life that's in a full and deeply satisfying way and that provides more sustained happiness. And again, in psychology, we don't believe something exists if we can't measure it, so there are some nice scales. Alan Waterman has a lovely scale that focuses on

these different aspects of eudaimonic well-being, including self-discovery, perceived development of one's best potential, sense of purpose and meaning in life, being intensely involved in activities, and that leads to investing a lot of effort in those activities, and enjoyment of activities that are personally expressive. So, I think that's the path to eudaimonic well-being, and I picked my three favorite questions from this, and if you can answer these positively, then I think you're well on your way to a life filled with eudaimonic well-being. If you have core beliefs that give meaning to your life, that you feel best when doing something worth investing a great deal of effort in, and when you can say that you found your purpose in life, then you're there.

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Now, I wanted to touch briefly on some of the challenges we've had to our psychological well-being, and the last couple of years have been something that I think none of us expected, and I hope that we are beginning to emerge into a new life that's somewhat better. But to try to shed a little bit of light on what I think people have experienced, it brings to mind, again, an old finding from 1956. Hans Selye identified what he referred to as the general adaptation syndrome about how we respond to stress. The bottom line is that we can actually do pretty well for a period of time in the early stages of alarm. Of course, we have a little reduced ability to cope, but we can pretty rapidly pull things together. And then for a month or two or maybe three, we can continue to maintain resistance, but after that, we get into a phase of exhaustion: fatigue, burnout, depression, anxiety, decreased stress tolerance. And Selye identified some of the key physiological changes that take place when this happens. And I think that's something we've been seeing a lot in the pandemic.

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Another thing that's happened, I think during the pandemic, is that we've all been forced into a world where we are narrowly focused, like you are right now, on a little screen, perhaps, and a lot of our meetings are held with zoom screens where we have our little squares where we're looking at people with miniature, and it's a fascinating thing from the study of psychology and anxiety states is that if you experimentally ask people to narrow their attention like you see in the right side of this figure, it increases anxiety. In contrast, if you have an experiment where you induce anxiety, for example, by giving people an incredibly hard math test and telling them it's easy, well, that leads them to narrow their focus of attention. And so, what I think we've seen is that in the context of an anxiety-producing pandemic, we have simultaneously been asking people to narrow the focus of their attention, thus accelerating further the development of anxiety. And so, I think this is something that leads to the suggestion that we really need to get our heads out of the zoom sphere and get out into the world, expose ourselves to nature, preferably to seeing the horizon, and to the extent that it's safe and possible, to interacting with other humans in real three-dimensional space.

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This fascinating thing occurred to me as I was talking to some students at UCLA, as the pandemic started, is that they started telling me that their time was all messed up. They couldn't keep their schedule straight anymore. I couldn't understand at first, how could that happen, when the pandemic has not messed up their schedule; it's just kept their locations in a more narrow frame than they were used to. And then I remembered this old literature on what are called zeitgeist or time cues for our biological clocks. And it turns out that what comes in through our visual and other senses are clues that help to regulate our daily rhythms.

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Yeah, so the exposure to light, the alterations in feeding schedules, alterations in sleep, exercise schedules, and changes in temperature, to the extent that those are messed with, it changes our central genetic clocks, it changes all of our cellular clocks, and that, in turn, changes all of our metabolic functions, which affect our brains and other organs, so I think it's no surprise that people were getting their sense of time messed up by some of the changes in their spatial activity levels. And this contributes also to problems during the pandemic that I think can be helped by insisting on a regular schedule, getting out in the light, in the middle of the day, not looking at bright lights later in the day, keeping the feeding regular, focusing on sleep, getting exercise, regulat-

ing temperature—all these things. So yeah, bedtime is a good thing, low temperatures at night help sleep, waking up at a fixed time—alarms, you may hate them, but they're worth it—eating regularly, exercising regularly, and then yeah, focusing on exposure to sunlight at midday and limiting blue-green exposure at night. These are some keys to helping to regulate that.

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So again, bringing back this sort of six-factor model of well-being, we can see how the COVID pandemic has challenged some of the cornerstones and foundations of well-being. So, in the COVID era, our challenges to our autonomy and environmental mastery have been markedly impacted where we have mandates to restrict our activities to certain locations, to adopt certain behaviors like wearing masks and not interacting socially that are really against the development of positive relationships, and they can undermine our self-acceptance. But if we double down on trying, however we can, to enhance our relationships, increase our self-acceptance, and the challenges, focus on our purpose in life, and focus on personal growth, then I think that leads us to a brighter future filled with well-being despite the impacts of the pandemic.

[00:43:22]

Yeah, the social influence is one that's hard to overemphasize. Here on the right, you see a picture of really cute little prairie voles. They're well known for showing side-by-side behavior. In fact, studying these animals has led to the oxytocin hypothesis about social relationships. And indeed, getting support as a stress buffer is critically important, and getting emotional sustenance and coping assistance from others is a key to psychological well-being.

[00:44:02]

I've gotten this kind of support from my support animal. You can see that over the course of the pandemic, we've started to look more alike. But interestingly, I shared this photo with some of my colleagues and friends, and look what I got back. And I didn't even know German Shepherds were experts at billiards or how cute and handsome they could be in other settings as well. So just by sharing my own experience, I also developed other relationships with my friends that opened up new avenues of exploration.

[00:44:34]

And then finally, I think that David Brooks, many of you may know, has developed a project called the Social Fabric Project. And I think that's something that we all should be thinking about is, as social distancing ends, we have an opportunity to rethink the world that we want. What do we want to do as the pandemic ends, given that we've broken pretty powerfully with the past? How do we want to live from here on in? Do we want to continue to be isolated, or do we want to double down on our social interactions, engagements, and relationships? Do we want to focus on those things that are really important to us, now that we know that there are many things that we can live without? These are the kind of questions that I hope we'll continue to ask and come up with great answers for in the future.

[00:45:20]

And so, with that, let me thank you and see if we have time for some questions.

[00:45:26]

CHIH-CHING HU: All right, thank you so much, Dr. Bilder, for the wonderful presentation. So we are open up for the Q&A. Our panelists are reading questions as they're coming and summarizing them and sending them to me, so I will read it to you.

[00:45:41]

DR. BILDER: All right. And I don't have to look at the Q&A, huh?

[00:45:46]

CHIH-CHING HU: And we also have some pre-submitted questions. So, the first question: "Can you recommend 10 to 15 minutes of mental health hygiene that people can practice daily? For example, what can we do every day that is equivalent to brushing teeth daily for oral health in order to maintaining good mental health?"

[00:46:12]

DR. BILDER: Yeah, I think that there are a number of things one can do. One of the things that I think, in terms of having a daily practice, is meditation. You know that here we are in the modern world talking about the brain and neuroscience, but it turns out that there are four or five thousand years of tradition of trial-and-error experimentation in perfecting techniques for meditation and mindfulness that are very valuable and known to have positive effects on all kinds of mental, you know, psychological well-being outcomes. So, I think that also, you don't need to travel to the Himalayan mountaintops to find experts in contemplative practices anymore. And I think that there are a lot of apps available online, and one thing I would recommend is a colleague of ours, Dr. Schueller, at the University of California, Irvine, has a guide which he calls the "PsyberGuide," but instead of being C-Y-B-E-R, it's "P-S-Y-B-E-R Guide." But what he's done is a careful review scientifically and then in terms of the user interface, so that it's evaluated also with how people who are not scientists evaluate the apps. And so you can see for every app a combination of what's the scientific validity of the thing and then how friendly is it going to be to use. And there, there's an evaluated a bunch of different mindfulness apps; I don't, you know, have any stock in nor do I have any strong recommendation among those—Headspace is very widely used, I know, and then also I know UCLA, the Mindful Awareness Research Center, or MARC, M-A-R-C, has some other free apps that were designed by Norman Belzer and Diana Winston, who are big leaders in international training in mindfulness meditation, and it's a completely secular practice. There's not any specific spiritual overtone to that meditation practice. I think those are very accessible.

[00:48:31]

There's a bunch of other things that one can do. There are a number of websites; we have at UCLA our Healthy Campus Initiative, we have the MindWell pods, so there are a number of recommendations there as well for psychological well-being. I would also recommend the Greater Good Science Center, has a website with lots of great tips. And then one of the founders of positive psychology, Martin Seligman, at the University of Pennsylvania, also has a website that has many recommendations for the kinds of practices one can get involved with. When I leave this talk, I'm going to go downstairs to the sneak preview of a movie, "Gratitude Revealed," from our alumnus Louie Schwartzberg. He's the guy who brought us "Fantastic Fungi," the movie, but he has a new movie called "Gratitude Revealed," which is a full-length feature film on gratitude practices and of gratitude writing, gratitude letters. These are also known to be associated with psychological well-being, so there's lots of practices that you can build into a daily routine.

[00:49:39]

CHIH-CHING HU: Yeah, okay, great, thanks for those information. We will check out those information and also those apps. Okay, so the following question is, for the F1 difference in brain anatomy, were the subjects having active symptoms or in remission?

[00:49:59]

DR. BILDER: Oh yeah, so in that particular study, the diagnoses were based on lifetime diagnosis, and then the brain structure was identified inter-episode, so it was not just a byproduct of people being in active phases of illness that those observations were made. With the functional imaging study, I'd have to look back at the details of that study to see exactly what controls they had over clinical state, whether people were in remission or not.

[00:50:40]

CHIH-CHING HU: Okay.

[00:50:42]

DR. BILDER: It does. It makes clearly a huge difference in terms of the functional connectivity effects if someone is acutely in illness. Also, probably makes a big difference what medications they're on. We see very stark differences in functional brain activity as a result of either an acute state or medication state. Interestingly, though, there are effects as the questioner might well know, that even in brain structure, you can see these differences. There is a shift as you go from symptomatic to non-symptomatic states that you can see in the brain structure itself. I was fortunate enough to be one of the groups that first showed a medication effect on basal ganglia volume, leading us to believe that there may be effects of certain antipsychotic drugs that actually led the basal ganglia to expand. And then that was subsequently validated in studies of other species. So, it's interesting... you know, how much plasticity there is in the structure of the brain, not just the function of the brain.

[00:51:42]

CHIH-CHING HU: Yeah. Okay, next question: "Why are so many genes involved in brain disorders instead of just a few the way some diseases are?"

[00:51:53]

DR. BILDER: Yeah, yeah. So, I think that's a fantastic question. And, you know, of course, there are some diseases like Huntington's disease that we think is due to a mutation essentially in a single gene. Now, with complex syndromes, though, I think that we find that typically, for any complex trait, there is this kind of incredible heterogeneity and multiple paths. What it may be is that we just haven't identified what are the discrete syndromes, you could make that hypothesis at least. So, let's say among all of the people who experience and get or get the diagnosis of schizophrenia, which itself is heterogeneous, you know, we know that it's very heterogeneous. And when we know that the genetic risk for people who have that diagnosis is, you know, is like 80%, that's the heritability of it. So, you know, it's exceptionally high heritability, but that probably is due to about eight to ten thousand different genes that are working together on some pathways that regulate the connectivity of the brain, the regulation of a whole bunch of different neurotransmitters. So, in the same way that I talked about the systemic illnesses leading to the same symptoms of all the major psychiatric disorders, I think that there's a mass action of these genes that are involved in brain development, brain structure, brain function. And again, those circuits are so complicated in terms of their regulation that you need to have probably multiple different hits on different genes, different combinations, that end up converging on anomalies in the development of certain neural pathways. So, I think that's the best explanation for why these very complex traits have very complex genetics.

[00:53:59]

And so, I think that's the best we know so far. Now, it doesn't mean that we can't, you know, at one point find what is the function of a particular gene. But I think that more and more, we're understanding that, you know, if you really think about it, these genes never work in isolation. You may have a gene that expresses a particular protein, but what that protein does changes completely as it goes from one organ to another. I think about, you know, some of the same proteins. Or, well, think about it even this way. You have the same DNA in every cell, yet some of those cells are producing fingernails, and some of them are producing noses, and some of them are producing brains and neurons. So, you know, the environment where those cells live and the unique expression, the silencing and expression of different genes changes depending on a whole bunch of other genes. And then I'm not even getting into the parts of this control system that are not genetic, that are other that are in the so-called silent areas of the genome.

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We now know that there are all kinds of controls over whether a gene gets expressed or not that isn't in the non-coding regions of a gene. The term "gene" is used to identify the part of the DNA sequence that actually codes for protein, but that's not the majority of the genome. The majority of the entire three billion base pairs that make up the human chromosomes are other stuff that isn't coding for proteins, but it is probably critically

involved in whether those genes get read or aren't read, and it has to do with the molecular expression patterns and how genes get turned on or off. So, I guess the best answer is, it's complicated.

[00:55:53]

CHIH-CHING HU: It's very complicated. Okay, so I guess that's the lead to the next question: "Are we able to identify the underlying mechanism of mental illness yet, or how close are we?"

[00:56:09]

DR. BILDER: Yeah, I think we're still a long way from understanding the real causes, but I think we're gaining a greater humility and perspective on how complicated these problems are. They're not like simple diseases, and I guess students of other diseases may say, "Oh, those diseases aren't that simple either." But when you get the flu and you have some viruses replicating and wreaking havoc and causing an inflammatory response, that's a little bit easier to wrap your head around as opposed to problems that occur with the brain and behavior that impact our social functioning in a complex social environment. You know, we know that the impact of certain brain differences varies markedly depending on things that have nothing to do with the individual but have to do with other people's reactions to that individual, how tolerant we are of the quirks of a person who has those kinds of difficulties. And having an appreciation of all the social and contextual factors that lead to what we call mental illness, and how we can help people who have difficulties adjusting in our social world. I think this is our responsibility as psychologists, psychiatrists, scientists of the brain, to try to think about how we can address these uniquely human problems in a uniquely human way that serves the greater good and the benefit of global society.

[00:57:56]

CHIH-CHING HU: All right, we have a question about COVID-19: "Have we seen COVID-19 caused the same pattern of a mental disorder that the 1918's influenza caused?"

[00:58:09]

DR. BILDER: You know, it's interesting. There have been some people looking at it, and I would say, yes and no. I don't think there's been enough detailed collection of data about the psychiatric consequences to have seen a number of the manic and other psychotic states emerging, but I think part of that has to do with the way we classify things now. There's been lots of evidence that people become more neurotic and depressed when they're impacted by COVID and they have, you know, in addition to the fatigue, there's been less documentation about the emergence of other kinds of manic or agitated and psychotic states. But there has been a lot of information about increases in irritability. And then when people get bad enough to be what's called psychotic, then we have a new word for it: it's called delirium. So, I think it's actually a great point. Whoever the question is, thank you because now I'm going to go back and look at the symptoms with that lens and see, "Oh, maybe Llopis and Menninger have now already been replicated in the world literature, so we can have a little revival in 2022."

[00:59:23]

CHIH-CHING HU: Yeah, okay. So probably one, one more question: "Are any aspects of well-being associated with particular disorders either as a cause or therapy?"

[00:59:40]

DR. BILDER: Oh yeah, so if I understood the question right, you know, are any of these factors of psychological well-being associated with particular mental disorders or to help particular mental disorders? And, you know, it actually turns out that the answer to that is probably probabilistic in terms of the prevalence of the different disorders. We have a ton of information that positive psychology practices help people with mood disorders, depression, and anxiety, because these are the most common symptoms, but we have also seen benefits of positive psychology practices in people with psychotic disorders. But I think that's been less frequently shown

than the almost ubiquitous impact on depression and anxiety. I think one of the key benefits following this dimensional model is that if we could widely adopt positive psychology practices, I think there's a good chance that a lot of people who end up developing anxiety disorders and depressive disorders would never develop them, because they would have the tools to keep themselves above that 10% bottom, 10% threshold and never have the sort of snowballing of problems that lead to a diagnosable mental disorder. So, I think that's the hope that it's good to follow these practices good for everyone, because even if you're in the top part of the curve, you could be functioning even at higher levels of satisfaction with life and well-being, but if you're closer to the threshold for having a disorder, it's more likely that that will bring you up away from that threshold. So I think it's good for everyone.

[01:01:21]

CHIH-CHING HU: All right. Thank you, Dr. Bilder. It's after 7:30 now. Okay, so thank you so much for the wonderful presentation and the Q&A.

[01:01:33]

DR. BILDER: Thank you, kindly. Thank you so much for having me.

[01:01:35]

CHIH-CHING HU: Thank you. And we are going to close the event.