JOSEPH CALABRESE: So thank you, Claudia, for the invitation to come here. And thank you all for joining us today. I was thinking about, as I was walking over here from the Walker Building, how child psychiatry has grown at this institution. There was three attendings in 1989?

SPEAKER 1: Two.

JOSEPH CALABRESE: Two attendings in 1989, and now there are 13?

SPEAKER 2: Yep.

JOSEPH CALABRESE: So there's been a huge growth. I've always had an interest in studying psychiatric illness across the lifecycle. And when Finling was here, we did a lot of things together across the lifecycle. What I'll be sharing with you today has to do with an idea that came from a donor and by coincidence, the publication of the Global Burden of Disease study from 2010. And the donor gave me the idea that, why aren't we treating people younger when they have a serious mental illness?

And when I told her is that when I started here, the consensus of opinion was that very young children don't have a serious mental illness. And that was dogma. And if you asserted that that was not the case, the wrath of many people would come down upon you. When I'll be sharing with you today is new data from the GPD 2010 which shows that that was mistaken.

And so all of this came out of an interaction I had with this mother. And we talked about, how do we recognize these illnesses in children and adolescents and young adults? And I'll never forget what she said.

She said, I could have told you so from the beginning-- just like this. I knew something was wrong. I didn't know what it was. I did not know where to go. But I knew something was wrong.

And then she went on to say something along the lines that early treatment for illnesses in children really wasn't, I don't know what, acceptable or whatever? But she knew. So the problem is that when serious mental illness presents in young people, it is frequently undifferentiated and it does not conform to our diagnostic criteria until later in life.

So this is a slide that summarizes the burden of these illnesses-- mental and substance use disorders in children and adults-- by gender. So if you look at this left hand side of this slide, what you see is that age grouping. And these are males. And this is DALYs. And the WHO uses Disability-Adjusted Life Years to quantify the burden of illness.

And so boys, the burden of illness starts early, 1 through 4, and extends through 39. And the number of DALYs is 6 million. So DALY is one year of healthy life lost. So across the world, it would be accurate to say that the burden of mental and substance use disorders in boys is 6 million years of life lost.

So that's a lot. But it doesn't come that close to what it is for females. For females, whereas six million, it's eight million years of healthy life lost. So clearly, the mental and substance use disorders are disorders that originate in young people. And as you can see, later on in life, the DALYs-- the amount of impairment decreases, as does the prevalence.

So this is a slide that was in this *Lancet* publication-- a very big landmark study that summarized the findings of the WHO-sponsored Global Burden of Disease study 2010. You may recall there was one prior to this. It was 1990. And the idea is that every 20 years, WHO and others sponsor this worldwide event-- worldwide study. And they use this quite a bit.

So I'm going to orient you to the figures that they use. So on the vertical axis here, you see DALYs. Again, DALYs are the equivalent-- you could say morbidity and mortality combined.

The technical term is Disability-Adjusted Life Years. Or the definition I like is the number of years of healthy life lost. That's very descriptive.

So these are morbidity and mortality. And here is the age groups down here. So as you all know and might expect, one of the earliest disorders to afflict children and young people is pervasive developmental disorders. And you can see here the number of DALYs is about 750,000. And then above this, for childhood behavior disorders, you see morbidity and mortality associated with childhood behavior disorders is 2 million-- 2 million DALYs.

So what they did here for us is they prepared trajectories of each of all of the mental and substance use disorders across the lifecycle. And this is really going to change how we approach illness one, because age of onsets have gone down and two, because the order of these illnesses presenting has changed. So let's talk about that a little bit more.

So the biggest findings from this research and the finding that this mother I'm referring to, and most mothers really find appealing, almost a relief, is that the burden associated with these disorders, it's primarily in depression and anxiety in that these are illnesses that rise abruptly early in life, ages 1 through 10. And when you tell a mother that, they breathe a sigh of relief. They either say or they think, I could have told you so. As you can see here, these illnesses go on to peak in adolescence and young adults at the ages of 10 to 29.

Now take a look at the curve here that's blue. And you can see, just to remind you, this was pervasive developmental disorders. This was childhood behavior disorders.

And coincident almost with the onset is this skyrocketing of depression. It levels off at 7 and 1/2 million disability-adjusted life years. 7 and 1/2 million years of healthy life loss across the world.

So depression emerges first, which you guys may know this, but I didn't get that. Then it quickly worsens. I mean, it skyrockets, and then it peaks in the mid 20s. So if you see where it's peaking here, it drops down to 10, 20, 25. So I mean, that's interesting.

Now anxiety, you can see here, starts at about the same time, and it increases. And here, again, beginning in childhood, but its severity is less than half of that of depression. So that's informative. And then schizophrenia and bipolar disorder come later-- emerge during adolescence and young adulthood.

Now, I have a boatload of patients who have told me that, and frequently confirmed by their mother, that they had symptoms when they were a child. But so many people with bipolar disorder don't have the manias for years. So there's a confound here.

Some of that depression skyrocketing in the last two slides probably has to do with bipolar disorder presenting as depression, but the mania don't come around for months or years later. But you can see here, the way it's written viewed by the data is that it emerges during adolescence and adulthood and you can see it peaks later-- 10, 20 years later-- in marked contrast, to anxiety, in marked contrast to depression, which skyrocket at very, very young ages. Very intriguing.

Now, drug dependence and alcohol dependence, they looked at. They didn't look at abuse, just dependence. So you can see here-- I don't know what you guys think of this, but ages of 10 to 14, again, there's this skyrocketing up to around 4 and 1/2 million years of healthy life lost. And then alcohol comes later. It's about half the severity if you look at morbidity and mortality.

So with that in mind, let me shift gears and report something that Tom Insel, our director of the NIMH, has said now for many years, and that is that the mental and substance use disorders have been reconceptualized. And instead of calling them psychiatric illnesses or mental and substance use disorders, he feels we should be calling these illness neurodevelopmental disorders. And what he means by that is that the pathophysiology of these illnesses begin during childhood, as early as one or two or three and, as you can see in the slide, he would actually say in utero. So, I mean, this is a huge landmark change in the conceptualization of serious mental illness.

We also know that 50% of people have the onset of symptoms, across all of the mental and substance use disorders, by the age of 15, 75% by the age of 25. So that's been known for a while. And when I saw this, it was actually one of the reasons why I liked psychiatry because most of the patients we see or I've seen over the years have been young people, young adults. And it's a very pleasant, enjoyable career.

OK. Now let me shift gears and talk about this study, the GBD study of 2010-- so the follow up study to the 1999 WHO-sponsored Global Burden of Disease study. So at the top of the list, number one category of illness resulting in the highest amount of disability in the world, are mental and substance use disorders. Just a little bit about this study. So they studied 291 illnesses in 187 countries. It took place over 20 years, 1980 to 2010.

They excluded all patients who were inpatients and excluded all patients who were medicated. So I thought that was interesting, because that might have actually deflated the impairment-- symptom severity. And then they only looked at point prevalence and 12 month prevalence. Lifetime prevalence was not studied.

So years of life live disabled was number one in the world. Number five was DALYs-- was a DALY count. And a number nine was years of life lost-- premature death.

So let's explore this a little bit more. OK. So let's start off with the years of life lived disabled. Number one in the world, accounting for 23% of all worldwide disability.

That's pretty remarkable. That's a huge amount of worldwide burden. So that quantifies disability. The next category is DALYs.

And number five was the mental and substance use disorders, accounting for 7.4% in worldwide morbidity and mortality. And that went up from 1990. It was 5.4%.

So it's not surprising since DALYs are both morbidity and mortality. If years of life of disabled increase, the DALYs are going to go up, as well. Years of life lost was number nine in the world, accounting for only 0.5%. And that figure, for reasons that I'll tell you a little bit, is deflated for a variety of new research findings.

All right. So let's go into each one a little bit more. So as I mentioned, the mental and substance use disorders are number one in years of life lived disabled. It accounts for 23% of worldwide disability. And then it's followed by musculoskeletal disorders, arthritis, and diabetes and endocrine disorders, number three.

Number five, as I mentioned, was the DALY count. And that accounted for 7.4% of worldwide disability. And then that was preceded by cancer, neonatal disorders, infectious disease, and cardiovascular disease being number one. So this number five ranking would have increased to number three, which would be 8.3% of worldwide burden, were it not confounded by what has been the standard over decades-- missing comorbidity, not diagnosing and treating co-occurring illness, like the rest of medicine does, and coronary cases. And I'll go into those a little bit more.

So again, as you can see here, the morbidity and mortality is in young people, 10 to 29 years old. The top most disabling illness in the world is major depressive disorder. Number two is anxiety.

Three is drug dependence. Four is alcohol dependence. Five is schizophrenia. And six is bipolar disorder.

OK. So let's move on now and talk about years of life lost. And I think this is the category that is most suspect.

But be that as it may, it was a number nine out of these 291 illnesses. So that's pretty remarkable. And it was preceded by a number of different things-- cancer, and number one, as I mentioned before, was cardiovascular disease.

So let's just pause a second and think about this. In all of medicine, we see and treat co-occurring illness. In most emergency rooms, even hospitals, even departments of psychiatry, we don't see and treat, and if we do see, we frequently don't treat.

So this has become a huge problem. And a post-hoc analysis was done to see how much more morbidity and mortality that generated and the impact. And this is what was done.

So axis one comorbidity, increased the lifetime risk of suicide. The addition of one illness to a prior illness increased the risk of death due to suicide from 0.5% percent to 1.8% years of life lost. And when it came to DALYs, as I mentioned before, it increased from 7.4% to 8.3%.

So the stuff that's in red is burden that resulted in suicide. And the stuff that's in blue is disability not resulting in suicide. So this is fairly robust increases.

So the take-home message here is that single diagnosis patients should be rare events in psychiatry. And it's quite uncommon to see a psychiatric patient come and be diagnosed with one illness. It's a huge problem.

Comorbidity increases morbidity and mortality. And each and every illness that a patient has requires individualized treatment. The treatments are different.

So if you had heart disease and somebody had three or four coronary arteries occluded, well, you wouldn't just go to surgery. I mean, you might think about it, but you'd want to find out if they're diabetic, if they got high blood pressure. And you'd be treating all three differently.

That hasn't happened a lot in psychiatry. The same thing is relevant to psychiatry. Each additional illness not only increases morbidity, but shortens life span due to premature onset of suicide.

And now, we know there's actually more death due to the premature onset of chronic medical illness than there is suicide. So the primary cause of premature death in patients with mental substance use disorders is not suicide. And I'll show you the data in a minute.

This is a slide I put together about 15 years ago. And what it does is it details the amount of comorbidity each and every illness has. So having a special interest in bipolar disorder, I found this interesting 10 years ago.

So the rate of co-occurring illness in bipolar disorder is 99% percent. This is NIMH data. But look at the second line. The rate of co-occurring illness and antisocial behavior-- the rate of co-occurring mental and substance use disorders is 96%. Now, you never hear about that.

So Claudia and I are going to be meeting in a couple of weeks with a group of people down at the mental health board. John's going to be there, as well, and we're going to be talking about just this. How do we get people in the community to first be diagnosed, and then to treat co-occurring illness, including people in jails and prisons? So you can see at the top, it was 99%. But even with alcohol abuse, the illness that has the least amount of comorbidity, 62% of people have another co-occurring mental or substance use disorder and the most benign of these illnesses, alcohol abuse or misuse.

So this is why this is important. This is a really important slide. This slide focuses on the impact of co-occurring illness and the probability of a first suicide attempt. So if you see over here, if somebody has one mental disorder on top of another, the risk of the first suicide attempt goes up 3.7; two, 6.8, three, 12.1, four, 16.4 and six, which you actually get not infrequently with bipolar disorder, 29-fold. So I mean, you can see there's a huge amount of morbidity and mortality associated with these co-occurring illnesses.

Another way of looking at this is to look at the relationship between mental and substance use disorders and stages of suicide behavior. So in the natural history of a suicide, there are four stages-- people who think about suicide, ideators, people who plan, people who attempt, and people who complete an attempt. So 65% of ideators have a mental and substance use disorder. 75% of planners have a mental or substance use disorder, 80% percent of attempters, and 90% of completers. So that's important for a whole host of different reasons.

Nearly 1 million people suicide per year, and 84.5% is attributable to mental and substance use disorders-- 1 million. And let's go through this a little more. So 5% are children and adolescents.

I'll never forget the first time I treated a young-- it was an adolescent. I was at the clinic, so it was in the 80s. And she went into her closet and she stood on a chair and she put her neck inside of a big wood hanger and jumped off of the chair. So these children, adolescents, young people, regardless of age, suicide-- 33% suicide during the ages of 20 to 39, 42% 40 to 59, and 20% late in life.

So let's pause a second and focus on not just suicide, but the other things that are co-occurring. So this is really groundbreaking data published recently in *JAMA Psychiatry* that looks at how non-psychiatric medical burden shortens lifespan and how it does so more than suicide. So first of all, right now in the United States, the general population gains four additional months of life every year. Well, that's pleasant hearing that. I thought that was, hmm, not bad.

However, the mental and substance use disorders have a lifespan that's decreased by 10 years despite-- not only is lifespan not increasing, it's decreased. Now, the biggest new finding here, and actually, the biggest finding I'll be sharing with you today, is actually of that mortality, only 18% was suicide. Now that mortality, around 70% had to do with the premature onset of other illnesses-- chronic medical illnesses. At the top of the list, cardiovascular disease.

There are 10 pathways in bipolar disorder that overlap with cardiovascular disease, if you look at OMICS profiling. So these illnesses, they don't share phenotypes, but they share a pathophysiology. And then there are 15% of non-suicide deaths that remain unknown.

So the public health message here is that there exists a need to reduce mortality, but not by treating the mental illness alone, but by recognizing and treating co-occurring chronic medical disorders at the same time. So part of this is shared pathophysiology and part of it is the consequences of having a mental and substance use disorder. There's lifestyle changes-- smoking and activity, no exercise, poor diet-- that go along, especially with the psychotic illness. So it's pretty clear that it's not just psychiatric burned that shortens a lifespan, but [INAUDIBLE] psychiatric burden.

So I guess the issues that we want to talk about next is, how do we identify this burden, where and when do we treat it, and what's the role of the family? OK. So let's talk about emergency rooms. So our patients frequently go to emergency rooms.

And suicides are frequently missed in coroner cases-- a patient who has died, they present to the emergency room. Even if the mental or substance use disorder is diagnosed, frequently, coroners just report the cause of death-- the proximal cause of death. So you'll see gunshot or asphyxiation if it was a suicide.

So the reason I'm bringing that up is that the years of life lost, that's deflated by what happens in emergency rooms. So the burden associated with undiagnosed patients is something else. It's just entirely missed. It's like 30%, 40% of people who have mental and substance use disorder are just not diagnosed. So all the statistics I shared with you before are probably deflated, just simply because the proportion of people who had these illnesses and are not diagnosed and treated is so high.

Now let me share with you an example of probably the most egregious or worrisome development in all of medicine, when it comes to psychiatry. So it's when a young adult, usually young adult male-- not always. But the young adult male comes to the emergency room.

They're loaded. They're intoxicated. What happens? You can't do anything with them, because they're out of it. They frequently don't come with a family member.

So you give them a bed to dry out and you come back in 12, 24 hours. So nothing happens there. And I'm not faulting anyone. I mean, it's not like you can talk and get a sophisticated history done.

But it's a huge problem. And it's a huge problem because mental health assessments are not done. Again, good reasons. They're sedation or agitated and usually, frequently, no family member.

But once the patient's mental status clears, they're usually diagnosed. So if they've been there for 24 hours and they're in the ER, the last thing ER infrastructure is going to want to do is take another two hours to find out what's going on, especially if it's 3:00 in the morning. Because they're not going to find have family and they're not going to be able to schedule an appointment.

So the take-home message here is that a [INAUDIBLE] co-occurring mental and substance use disorders, predictors of suicide, frequently go away, are frequently unrecognized completely, just by virtue of how these illnesses present. They don't present and talk about depression. They're intoxicated and you can't get anything out of them.

So why is that a huge problem? It's a huge problem because these comorbidities increase the risk of suicide. So what is the risk?

So just to refresh your memory, 62% of those with alcohol abuse have a co-occurring mental disorder, usually depression, 81% if its alcohol dependence, 89% if it's abuse, and as I mentioned before, 96% for drug dependence. So it's not a small subgroup that have mild to moderate cult illness. It's the vast majority who never get diagnosed and treated.

So at this meeting that we're going to be attending on May 11-- this is something that cops don't know. All cops know is that somebody is intoxicated. They're loaded. They're annoyed by them. And they never think about this being driven by an unrecognized serious mental disorder.

So let's get back to these slides here and talk a little bit more about alcohol and drugs. So as I mentioned before, anxiety and depression precede everything, with the exception of pervasive developmental disorders, basically. So here you see that the drug dependence is out about 10 years later. Alcohol dependence, not quite as bad, but still, about 10 years later.

So this is why this data's so remarkable. It shows, for the first time, hard, reliable data that what I was just talking about is in fact the case. This is worldwide data-- 291 countries. Alcohol and drug abuse follows the onset of depression and anxiety.

So what happens typically in chemical dependency treatment infrastructures is that people get dried out and then they see what's left. They go home. They're dry. The depression comes back and they relapse. This is a huge issue.

And this is a very, very common. I would say 90% of the CD treatment centers in the country do not get a history of mental disorders prior to the onset of alcohol or drug abuse because they don't meet with family. You got to meet with family.

You can't ask somebody who's dependent. You got to go back and ask family, what were they like when they were 9, 10, 15 years old, before they started using? And then when you do that, you find that they had just what this slide shows-- mood and anxiety.

So we have to identify these things, I guess, is the most important, probably, take-home message here, and particularly in emergency rooms, but really, everywhere. Lots of psychiatrists don't do this because in order to do this, you have to meet with family. And you can't do this with family in 20 minutes or 30 minutes, or really even 45 minutes, because it's just too labor intensive.

So there are three strategies I'd like to share with you to consider. One is history taking from an informed adult family member or significant other while they're in the ER. So it's feasible. It's time consuming. But it requires that they come in with somebody, and many times, they don't.

Another option is to delay the assessment until they're sober, and usually, that's 12 to 24 hours, and then do the assessment with them on the spot. That's kind of hard to do because they're still not ideally suited to go through a lengthy assessment. The other thing is to create follow-up teams.

So there's a colleague in the mood disorders program, Dave Kemp, who left recently. And he's doing just this. So what he does is he assembles a team of people in a capitated environment. And anybody who's got alcohol/drug abuse problems, they're followed up by this team to uncover this axis one comorbidity.

That would be great if our ER was capitated. But we get everybody, so it's hard to afford doing that. But these are three options that people have tossed around in the literature.

OK. Let me I'll close up by talking a little bit about substance use disorder and dependence, in particular, worldwide. So as you can see here, we have the distinction of being the worst in the world when it comes to substance dependence. The US is number one; UK, number two; Russia, number three; Australia, number four. And substance dependence accounts for 0.8% of all global DALYs.

And as most people now know, opiate dependence is number one worldwide, and nothing comes close-- the DALY count of 2.25 million. Now that's, to me, somewhat perplexing, because we don't see that much opiate dependence. I mean, I think people who are dependent on opiates are going elsewhere. And I'm not quite sure why it happened that way. We see people with alcohol dependence, cocaine or crack, and cannabis, but not opiates so much.

And as you can see from this slide, there's a huge increase in opiate dependence compared. So again, this is 2,250,000 DALYs for opiates, and nothing comes close to it. Again, opiate dependence peaks during the mid 20s, and more than doubling any other drug dependence.

I thought I would just assemble for you the top seven associated morbidity and mortalities associated with drug dependence. So these are things that I don't think we normally think about. But number one is injecting drug use is a risk factor for AIDS-- 2.1 million DALYs, right at the top of the list.

Number two is amphetamine dependence as a predictor of suicide-- 854,000 DALYs. Opiate dependence, 671,000 DALYs, as a predictor of suicide, specifically. Injecting drug use as a predictor of hep C, 500,000. Cocaine dependence as a predictor of suicide, 324,000. And somewhat in a different category, but still showing a significant increase, is injecting drug use as a risk factor for hepatitis B and cannabis for schizophrenia.

You always hear about cannabis being a predictor for schizophrenia. It's real. But as you can see here, the morbidity and mortality associated with it is very low-- nothing compared to injecting drug use as a risk factor for HIV.

So I think the reason why I'm here today-- we were talking about this public health initiative and how do we get people, not just the general population, but providers, to recognize and treat mental disorders that preceded the onset of alcohol and drug abuse, and in what setting? These findings, I think, do have public health policy implications for not just adolescents and adults, but also young children. It's, I think, at the top of the list, the most robust, worrisome finding, as most premature deaths as a result of mental and substance use disorders is not due to suicide. Somehow, these illnesses share pathophysiology.

So on average, if somebody says, what's the impact of having bipolar disorder on lifespan-- never say this, but you will die 10 years earlier. That's the mean. In some subgroups, the range is actually from 2 years earlier to 20 years earlier.

So I mean, how do you tell somebody who's 15 or 20 or 25 that your lifespan is going to be shortened by 10 years if you don't get treated? I mean, nobody thought about that. It's a very difficult sell. It's very difficult to articulate.

The prevalence of alcohol, opiates, and cocaine abuse has increased substantially. So in the last 20 years, from GBD 1990, it increased, but the mental disorders did not increase. Mental disorders stayed the same prevalence. The substance use disorders, dependence in particular, increased.

And I guess probably the biggest take-home message from a clinical perspective is if somebody has a mental disorder and a substance use disorder, they both need to be treated. And you can't get that history unless you assess the period of time that preceded the onset of alcohol and drug abuse. And you usually can't get that if you meet with the patient alone because they don't have that much illness related insight to recollect these things for you.

So I wanted to leave lots of time for discussion because we'd be interested in what you have to suggest about how to go about doing this. But it seems to us that there's a need for a community-based intervention that involves the prevention of these things and an intervention that's appealing. So how do you talk to people about these illnesses? How do you get them engaged? How do you get them to come to an auditorium-- all of these sorts of things.

Now, morbidity and mortality induced suicide among young people, again aged 15 to 19, has also changed. So it used to be quite a bit lower, but now it's starting to approach the morbidity and mortality in adults. So it's almost as if the illnesses are of earlier onset and more severe. And males, in particular, continue to have the highest rates of suicide in all age groups, but females, 10 through 19.