Medical Update: The Intersection between Tuberculosis and Mental Health
April 21, 2015
Archive Transcript

Slide 1 Good afternoon. Welcome to our medical update webinar series called "The Intersection between Tuberculosis and Mental Health".

Slide 2 The learning objectives for the webinar are what you see on your screen, that you'll be better able to understand the complex relationship between tuberculosis and mental health, assess the mental health status of TB patient in order to determine appropriate intervention and develop strategies to manage psychiatric complications in TB patients in order to improve overall treatment outcomes.

Slide 3 Our faculties today are Dr. Amee Patrawalla, the Medical Director of The Global Tuberculosis Institute and Assistant Professor of Medicine at Rutgers New Jersey Medical School.

Slide 4 Dr. Annika Sweetland, Global Mental Health Research Fellow under the Department of Psychiatry at Columbia University College of Physicians and Surgeons and co-founder and co-chair of the TB & Mental Health Working Group at the International Union against Tuberculosis and Lung Disease.

Slide 5 And finally, Dr. Adam Karpati, Senior Vice President of Public Health Impact at the International Union against Tuberculosis and Lung Disease.

Slide 6 Our agenda for today are to provide an overview of TB and mental health, this will be done by Dr. Karpati and Dr. Sweetland, have some case discussions which will be done by Dr. Amee Patrawalla and then finally we'll have some time for questions and discussion at the end.

Slide 7

Amee Patrawalla: Hi, this is Amee Patrawalla, welcome. So our two speakers today, I'm pleased to welcome, are Dr. Adam Karpati and Dr. Annika Sweetland. Dr.

Sweetland has a clinical background in social work and is co-founder and co-chair of the TB & Mental Health Working Group at the Union. She has previously worked with Partners in Health to facilitate psychosocial support for patients with multidrug resisted TB in Lima, Peru and are interested in international mental health including cross cultural implications and translating research into practice.

Dr. Sweetland received her Masters of Social Welfare from the University of California at Berkeley School of Social Welfare and her doctorate at Columbia University Mailman School of Public Health. She is currently a post-doctoral research fellow in Global Mental Health at the National Institute of Mental Health and at Columbia University. She has three ongoing research studies in Brazil, exploring the prevalence of depression among homeless individuals with TB, methods for integration of TB and depression treatment and primary care at a systems level and exploring inflammatory biomarkers for depression in the context of active and latent TB infection.

Dr. Karpati oversees program design to strengthen public health systems and address leading causes of morbidity and mortality in low and middle income countries. Prior to joining the Union, Dr. Karpati works for 14 years at the New York City Department of Health and Mental Hygiene. His tenure included serving as executive deputy commissioner for the division of mental hygiene, responsible for programs, policy and epidemiology around mental illness, substance abuse and developmental disabilities.

Dr. Karpati obtained his medical degree from McGill University in Montreal and completed the residency in internal medicine at New York University Medical Center. He then served in Epidemic Intelligence Service at the Centers for Disease Control in Atlanta and completed CDC's preventive medicine residency. He also has a Masters of Public Health from the Harvard School of Public Health.

And I'll turn the program over to Annika and Adam and if you need to unmute yourself, you can press pound six.

Slide 8

Annika Sweetland: So, Adam and I are going to sort of speak, our slides are intertwined, so I'm going to (lead) and then Adam is going to join in for our key points during the presentation. I'm going to begin with a brief introduction and overview of mental health issues, look at – looking at TB and mental health specifically, what's the impact on treatment outcomes, what are some other types and causes of mental health problems that emerged in the context of TB and the epidemiology and frequency of this type of problem. Then, I'm going to address some challenges and responses and finally some conclusions.

Slide 9 So to begin, why are we talking about this? People and what we know, people with mental illness and substance abuse disorders are more likely to be exposed to TB which in large part have to do with exposure in institutional settings. They're more likely to develop active TB which often has to do with inflammatory processes or health risk behaviors. The more likely to delay in seeking care, the more likely to miss doses once in treatment are more likely to default on treatment.

Slide 10 And as a consequence, they're at a greater risk for having more advance disease, the more likely to develop drug resistance due to inconsistent treatment, more likely to fail treatment and die. And infections for prolonged periods and therefore posing a risk for community transmission.

Slide 11 So, I'm going to go into each of these in a little bit more detail but that's just again an overview. We also know from other medical disorders that treating these illnesses can improve medication adherence, treatments in patient and cure rate which would have the impact in this case for TB, reducing drug resistance, reducing community transmission and reducing mortality, improving cure rates.

Slide 12 So when we talk about mental health, what are we talking about? Mental health versus mental illness. A range of emotions – there's a range of normal emotions that are normative. For example, depression and sadness, anxiety, fear, are all parts part of the normal experience. Well, what's the difference about when it becomes a disorder?

We think about as an example of an individual who's very sad, cheerful, hopeless and he finds out that the person just lost a loved one the day before, so it makes sense that the person would feel that way. The reactions are – that depresses, hopelessness and cheerfulness maybe even extreme and disabling but it's short-term and it's proportional to a very specific stressor and is in fact a normal reaction to that stressor.

If you were to find a person who presented similarly and learned that it is actually that their – their partner dies say two years ago and this is still their current state. That suggests some pathological process that is no longer tied to the specific stressor. It's significantly impairing, it may be affecting that person's ability to relate to others or to work. The duration is long beyond what it should be. And its severity, you know, it's not relenting and it's just suggestive of more clinical, unreliable disorder as opposed to a normative reaction.

Another example would be, you know, finding yourself in the middle of the woods with the wild animal feeling afraid and anxious and nervous. All these of course are normal reactions even adaptive responses that would allow you to, you know, to find your flight response. However, if you're just continuing to have that reaction, if the – if the wild animal is something like a mouse, then it's sort of changes the context in the scale of what the stressor is, what the reaction is, how disabling it is. So, that would be an example of a phobia as well as to just to give varied histories, difference between what is sort of normal, mental, emotions and behaviors to when it becomes – it comes into a different category of disorder which then requires a different type of intervention and treatment.

Slide 13

The most common types of mental disorder include mood disorder which are depression, the bipolar disorder and previously known as manic depression, anxiety disorders and phobias, nonaffective or psychotic disorders which is schizophrenia, PTSD or other trauma-related disorders and substance abuse disorders. I know that these psychoses, some symptoms can be present in any one of those disorders.

Slide 14 And Adam wanted to say a few words about terminology and about the U.S. Health System.

Adam Karpati: There's some or lot of confusion when speaking about mental health and mental illness as Annika just described. We have some ways of distinguishing clinical syndromes from less significant experiences. I just wanted to say that we often used some of these terms interchangeably, mental health, mental illness and I think, you know, mental illness is the much more descriptive term.

There's a lot of different words that were used to describe substance abuse disorders or substance abuse. I listed some of them here and I think there's – there's – also it's important to think about severity and think about impact. So, substance abuse can refer to a behavior or practice, substance dependence for example is a much more clinical syndrome and substance use disorder is probably the most specific of all.

I'm worried about about serious mental illness and what people may refer to severe and persistent mental illness. These are meant to be situations where your clinical mental illness is more serious and more impairing and more disabling between severe and persistent mental illnesses us typically use to describe individuals who may have had experiences and the long-term institutional care or have clinical syndromes consistent with having that experience.

Different terminologies for people suffering from mental disorders and let's get some of them here. We're talking in this presentation mostly about mental illnesses such as depression and anxiety. We're also speaking to some degree about substance disorders and often referred to me under the term behavioral health. Mental hygiene is another term which often used. So, I'm not saying let's do – to point out what – what should be normative or what the right terminology is but really just to highlight some of the words we talked about (this) and I think it's important for us to be as specific as possible when discussing these issues.

Slide 15

Annika Sweetland: Sorry, I thought that's the other slide. So, what are some of the (kinds) of mental health disorders, what is the genetic predisposition, in particular with relation to say depression, schizophrenia, there's a large hereditary element. What that means is not that just because someone's parent has schizophrenia that they're – that they're going to definitely get it.

What it means is that there some amplified risk for that person and if they – during the course of their life had some triggering event which tend to be sort of trauma experiences, they will have more than likely than the average person to develop schizophrenia or depression in that context. So, it's a – it's a hereditary risk and it's not prescriptive.

Other causes of mental illness, exposure to trauma, violence, abuse, family disruption, psychosocial stressor such as incursion status, job loss and medical comorbidity which gets into more what we're going to talk about today.

Slide 16 Many mental – many – depression in particular has comorbid with a lot of the medical illnesses. And I just pulled up four systematic review or meta-analyses that found the prevalence of depression. I know people with HIV, cancer, chronic obstructive, pulmonary disease and diabetes to be very high, ranging from zero to 49 percent in some use cases. And this is important because it's – depression is associated or other medical illnesses are associated with poor medical outcomes as discussed before.

Slide 17 So in this case for example, depression and anxiety are associated with three times greater risk of not adherence to medical treatment, and just for a range of medical conditions. It is associated with lower quality medical care and premature deaths across the board and such estimated by the WHO that people with serious mental disorder die an average of 10 to 15 years earlier than healthy – healthy individuals.

And they don't die from schizophrenia or depression, they die from sort of – they die not taking their treatment or not going for care, for other physical conditions, infectious disease, suicidal behavior and all of the secondary health risk behaviors, etc.

Slide 18
And so now Adam is going to talk about the U.S. Health System.

Adam Karpati: So, I think part of the theme here today is to try to talk about bridging what are – what are often very separate systems for medical and the mental health system. In the United States, mental health is often typically regulated and reimbursed separately from the medical – the medical system. In many state agencies for example, physical health and behavioral health are units with a separate – separate agencies and reimbursed separate ways.

Managed care models often – are often distinct as well, where there may be a different insurance system, different payment model for behavioral health and for physical health at the federal level is all replicated. Behavioral health patients have one federal agency dedicated just – just for that. Increasingly in the United States, the Medicaid System is particularly influential in driving the system of care for mental illnesses and substance abuse disorders. And this is interesting because the – typically the state agencies that we're seeing regulate the systems are distinct as I said from the Medicaid System which is often in – associated with health departments, with a health department.

Another good feature of the mental health system in the United States is that it is – it's characterized for a wide variety of clinical practitioners from psychiatrist, physicians, to psychologist, social workers, nurse practitioners, etc. So there is a wider variety of practitioners than typically seen in the medical system.

And the last thing I want to say about the system in the United States is that the mental health system in some ways is – has a long history of acknowledging and building in attention to social factors for integrating community-based rehabilitation, social services for people with serious mental illnesses and really practicing in sort of holistic so called recovery approach to mental health and I think that there are areas in the medical side, on the physical side that do this as well and within TB, TB care is one of them. I think that these are principles that are needed to really combine and to bridge these, the two symptoms that we're talking about today.

Slide 19 This is just the slide to indicate – to show some information about the treatment gap for mental disorders in the United States. This is the – this is the national representative survey called the National Comorbidity Survey from early 2000. This was an interview-based survey, national representative and these are the proportions of people who had a diagnosable mental disorder at least according to the – these are the pretty rigorous surveys according to the very rigorous techniques that were employed in the survey to make a diagnoses and the percent of the respondents receiving care for their – for their physician.

And you see that – if you go to the right of the slide, any sector that reported only 4 out of 10 people suffering from a mental disorder were receiving care. The most common setting was general medical provider, only about 12 percent for a psychiatrist, 16 percent are other mental health specialist. This is the data that's often used to talk about how most mental health care is actually provided in general medical setting and also to make it a point that most people with known mental disorders are not in fact being treated for their conditions.

Slide 20

Annika Sweetland: OK, so now (we'll) start to talk more specifically about TB and mental health. What we know so far that there are three review studies in the last two years, one that looked at TB and depression exclusively, one looked at TB and depression anxiety and one looked at any mental disorder associated with TB.

And they all sound very high prevalence from 11 to 80 percent, looking at all the three studies and I can speak to the first study which I was involved in. And the top one that – it is likely to be as a caveat going to be an overestimate for a number of reasons, mostly the scales for most of the countries. It was 12 countries, 33 studies and most of the studies used screenings scales that tend to overestimate and the quality of studies are variable but this is definitely suggestive of a very high rate and the fact that the other two studies are also very extremely high rates.

So, this is something that we need to pay attention to, particularly as it relates to the negative outcomes which I'm going to discuss in the next slide but also as a final note, TB and HIV coinfection amplifies risk for depression by 1.7 percent, 1.7 times high risk of depression.

Slide 21 And so from the TB literature, we find that alcoholism is associated with treatment delays, that mental disorders are risk factors for higher drug resistance, the substance abuse, indications with MDR TB are the associated treatment default.

But alcoholism is (associated), has 1.6 times greater risks of death and mental disorders, have 1.8 times higher risk of death with general TB and this was from a large, over 300,000 population study in Brazil. For MDR TB having any psychiatric conditions are associated with higher risk of death as well.

Slide 22 We're talking about this TB in the U.S. It's a little bit different than in other countries. We know that it's about 65 percent foreign-born, although that rate can vary across the country.

For example in, New York City it's probably closer to 80 percent foreign-born and there's some research that suggest that foreign-born individuals have lower rates of substance abuse but there's no way of knowing if that went to those particular populations. About 6 percent are homeless, 4 percent incarcerated, 7 percent HIV positive. And although we don't have specific statistics about what proportion of people with TB in the U.S. have serious mental illness, we can presume that it's relatively high – a little bit higher than the general population given these other shared risk factors.

Slide 23 So, there's five basic types of mental health problems that can come up in the context for TB. First is the psychological reaction to diagnosis and treatment. Second, psychiatric side effects associated with TB medications. Third, physiological consequence of the disease itself. Four, exacerbation or emergence of mental health issues, so either re-triggering or relapse or new onset with mental health issues based on the stressors. And finally comorbidity as a result of shared risk factors.

Slide 24

So in terms of the psychological reaction to the diagnosis, one of the mechanisms which just happens particularly in lot of other countries is I think there's less social stigma in the U.S than in other countries but the social stigma are manifests in two ways, externally and internally. Externally, people with TB can be rejected or how degrading, discriminated against because of – because of the social stigma.

The flip side is that if they have internalized these stigma beliefs, they may direct those stories inwards in terms of feelings of shame and guilt and they withdraw socially or isolate themselves and they have feelings of depression. Social impairment related to either to the disease or the treatment itself can be psychological stressor.

And the risk of infectiousness or exposure to households can be a stressor and as I was just discussing this, TB tends to impact very vulnerable populations in a general sense, so people living in poverty. In which case, this can be exacerbating of poverty, people with severe mental illness, homelessness, incarceration and coming from low-income countries. All those stressors which can be exacerbated by this – the illness and treatment. And finally infection with HIV can be a significant risk factor for greater depression.

Slide 25

For psychiatric side effects from anti-TB meds, most of what we know that psychiatric side effects is based on case reports. So, there is very little if any studies that have looked to the prevalence of side effects exposure to these medications that were case reports, meaning you know of a case in hospital at this time. And these case reports brings back to the 50s and all the way through – and the majority of the cases that are part of the literature has to do with isoniazids.

And so in this case, I looked at a review by (Hachi), and all and then we did sort of a manual search just last week trying to sort of identify a range of TB medications that had been associated with psychiatric effects. But again, this is just, you know, one case here, one case there. This is not – this does not speak to the frequency but isoniazid and cycloserine are most commonly associated medications link to TB (put) to psychiatric reactions.

Slide 26

So isoniazid, it is mostly case studies and that overall observation is that the reaction tends to be more psychotic in nature, tends to be severe, so it's rare but severe. So, it's unusual to find this – the side effects of isoniazid but when you find that it tends to be specific and it finds itself, you know, in the literature as the case studies. The other thing to note in terms of isoniazid in the context of mental health system is the liver toxicity which is a significant factor to consider with patients with alcoholism.

With cycloserine, there's fewer studies available and mostly because the medication hasn't been used this frequent. It is used in MDR TB and but when it is used the prevalence of psychiatric side effects tends to be very much more common so a recent systematic review and med analysis found that 5.7 percent of individuals receiving cycloserine has some sort of psychiatric side effects.

Other studies, for example one that I was involved in Peru found that new onset of depression anxiety psychosis to be 13, 12 and 12 percent respectively, other reviews of the literature of case studies found frequencies between 10 and 50 percent. So it is less common in terms of its use of the medication but the frequency of side effects is more common and more varied in presentation.

Slide 27

Finally, you know the physiological reaction to the disease, there is some suspicion that inflammatory processes involved with TB maybe related to mental health reactions or vice versa that inflammation related to say depression for example maybe a risk factor for activating TB. TB and its treatment may lead to exacerbation and it may exacerbate your line of health issues and comorbidity maybe as a result of shared risk factors such as substance use and socioeconomic status which are also have higher risk for psychiatric conditions.

Slide 28

So some of the main challenges in addressing TB and mental health currently are that the problems tend to be under and misdiagnosed and this is for a number of reasons. One, some of the symptoms are overlapping pursuing with depression for example, anhedonia or lack of pleasure, lower appetite or fatigue. A lot of the symptoms mimics depression and therefore can be confused with depression.

There is also a lot of misconception which is what I was touching on before and we'll talk about more, misconceptions about situational distress before – versus critical illness and the tendency to conflate poverty and illness with depression. So there is often a misconception that you know you have a person with TB who is depressed. A lot of clinicians will say you know "of course they're depressed, they're poor, they're sick" and there is a lot of recognition of the distinction between depression and sort of sadness as a normative reactive response versus when it becomes more clinically entrenched issue that requires a different type of intervention.

Screening and identification is not integrated as a standard protocol which is another challenge and there's often a low priority for mental health services and limited services available so this can lead to reluctance to identify them as a health problem, and that's there's nothing you can do about it then there's no service available, its hard to rationalize the identification and finally there's a limited evidence based for best practices which is one thing that is definitely needed in the fields. The TB mental health working group that Adam and I co-founded with the International Union against TB and Lung Disease as one of our main objectives is to find ways to build an evidence base to identify practices that work and to disseminate those practices to different settings.

Slide 29

So in terms of how to respond to mental health issues and the conflicts of TB, there's sort of three general areas. First is interception and screening, so the identification of whether or not there is a clinical disorder present, what is it and once you know that then we need to think about what types of intervention would be appropriate.

So for more of a situational distress, normative reactions with TB being a very difficult life event and the fact that it tends to happen with people who have lots and lots of other psychosocial stressors and difficulties is the treatment to help them complete therapy, should it be more supportive, problem solving, harm reduction, or do they require more clinical intervention such as individual group therapy or psychopharmacology, and how can we help with health and mental health systems integration to those – when you go to reach those three?

Slide 30

So screening for mental disorders, I think mental disorder is different than other medical conditions as it is not observable. There is no blood test that can tell you that the person has depression or schizophrenia. You have to rely on clinical assessments that are often generally done by mental health specialist and that's often not possible at primary care settings or at low resource settings and so what we've come to use often times is what are called screening instruments.

And these screening instruments are brief questionnaires, they're often health assessments and they're not diagnostic. They're not intended to find cases of clinical disorder but they're designed to flag potential cases. So they're often – so a lot of these scales are you know maybe 2 to 20 questions, its not too long. They're often – their either yes or no or more frequently likely scaling you know how many times in the past two weeks have you felt this, like none of the time, some of the time, most of the time, all of the time.

Then usually the responses are scored, you may get a total score and then they use validation studies to determine what the cut off point should be to determine case versus noncase. And I'm going to explain that a little bit more. These are meant to be tools – they're not diagnostic. They're intended to be triage tool so that you can identify and flag cases that should – that requires further assistance.

Slide 31

When I go through two very common tools used in the US, one is for depression and the other one is about substance abuse. For depression, there is a questionnaire called the PH2Q and PHQ9. The Patient's Health Questionnaire 2 and 9; two is the first two items that are highlighted in that and those are intended to be just very, very short screener and what's often found in primary care settings for example in the hospital where every single primary care patient who comes in has to respond to these two questions, as part of their general check in and if they respond positively to either one of those questions then they're asked to answer all nine questions and then their score on those 9 could determine whether or not the primary care doctor is alerted and they need to ask more questions to this indvidual.

So if you look at the bottom in terms of sensitivity, the PHQ sensitivity and specificity, sensitivity is the ability of the screen to identify true cases, and specificity is the ability to rule out noncases. So in terms of the PHQ2 it has a fairly effective rate of identification with a cut off of 2 or more, it can identify probable cases at 86 percent and rule out most noncases.

When you go through PHQ 9 there's more questions and you have a need to hire with a sensitivity of 74 percent but he is in higher specificity at ruling out noncases and importantly the PHQ9 also included the last question which is about suicidality which is as a screening question would always trigger a referral.

Slide 32 A common example of an instrument for substance use is the audit fee, which involves three questions, how often do you have drink containing alcohol, how many drinks do you have on a typical day, how often do you have six or more and based on these three questions, the slight difference between man and women in terms of – in terms of reporting that affects the way in which he interprets the scores but for men, a cut off of 4 has a sensitivity of 86 percent and a specificity of 78 percent for women and there's a higher sensitivity but a very low specificity which has to do with under reporting by women but this is another example of the three item scale that can be used to do as a screening instrument, as a flag potential – to identify cases in which further questions should be asked so sort of whether or not this is a clinical disorder.

Slide 33 And in terms of treatment, there are various types of treatment, there's pharmacological, psychotherapeutic and supportive as I mentioned before.

Slide 34 Adam is going to talk a little bit about this intervention with regard to substance abuse.

Adam Karpati: So the reason for bringing this up in this conversation is the applicability of some of these brief intervention models to primary care settings or other nonspecialty settings and this is part of the theme of suggesting that more attention to mental disorders can have positive benefits on individuals with tuberculosis but that integrating this attention in to practice is doable and can be effective – can be effective.

So the expert at screening intervention referral to treatment is an evidence based model that – that's a united services – a United States preventive services task force B recommendation so it's a – its recommended, its part of a primary care preventive service package. It involves, it involves screening with the audit C – three question tool that Anika just mentioned and then followed up with – with high scores with a 10 questions. It's much like the PHQ 2 followed up by the PHQ 9 and then involves engagement by the primary care provider with the individual in a brief way, supportive way.

And using principles of motivational interviewing and with relatively low intensity, a few sessions perhaps has actually been show to decrease binge drinking frequency, decrease average consumption and reduce hospital admissions.

So again the principle here is this model of screening for referral and treatment can be incorporated into basic clinical practice and primary care settings, it does not involve overly intensive – overly intensive amount of time, can be relatively easily integrated into a standard protocols and gets good results.

Slide 35

Annika Sweetland: OK, so other interventions include psychopharmacological treatment, there's several types of psychiatric medications, antipsychotics, antidepressants, mood stabilizers, stimulants, anxiolytics or antianxiety medications. Of note, these using pharmacological treatment has best impact when used in combination with other types of nonpharmacological therapies.

We're not going to get into specifics around these treatments but rather go in a little bit and talk about what we know in the literature about potential drug to drug interactions and how that might play into treatment.

Slide 36 So in terms of isoniazid to start, isoniazid was actually interestingly developed initially as an antidepressant and has antidepressant properties and it has been recognized as a weak MAO inhibitor. Its effects against tuberculosis were recognized and so it has been used mostly in the case of – is now primary TB

drug and medication. It is also theoretically contraindicated for use with SSRIs and tricyclic antidepressants – because of the interaction.

As I've said it is theoretical because there is no cases reported of this. This was just based on – our understanding of underlying mechanisms, this could be a risk. So certain antidepressants maybe contraindicated in conjunction with isoniazid and further examination of this should be pursued before combining treatment. There are also some antianxiety medications doses that interact with isoniazid and antipsychotic medications isoniazid may inhibit metabolism therefore they inhibit the metabolism of certain antipsychotic medications, such as haloperidol therefore it might be necessary to lower doses of haloperidol during isoniazid treatment.

Again, these are very broad observations. There have been very few if any clinical trials so this is all – little we know based on the literature to suggest these potential interaction in all areas for future research.

Slide 37 With rifampin, although it hasn't been associated with necessarily psychiatric side effect, it has – it does interact with a number of psychotropic medications and in an important way and it is believed to actually lower the effects of these medications including antidepressants, antianxiety medications, antipsychotics, mood stabilizers, sleep disorder, substance abuse, all of these medications which means that when people are taking these medications and they take rifampin, the enhanced metabolism means that they may need – they may require higher doses of these psychotropic drugs to reach the same effects.

So it has led to symptoms of withdrawal in that case and so it might be necessary to higher the doses of these medication so if the patient is already on them prior to treatment is treating with rifampin.

Slide 38 Other drug and drug interactions newly used for TB its more in the experimental phase for use within XPR cases but it also has weak MAOI properties and therefore maybe contraindicated with SSRI due to risk of serotonin syndrome.

A very interesting line of research which is sort of emerging recently is that there is some antipsychotic medications that may increase the bacterial activity of some anti-TB drugs or strengthen the effects of certain antiTB drugs meaning it might be possible if combining some antipsychotics with the anti-TB drug may strengthen their effects, there's mixed evidence.

Evidence in both directions from animal models and there's also some related evidence that they may independently have their own anti-TB properties. So this is very interesting the study sort of happened just in the last two years shows a lot of promise that explored in the context mostly of MDR TB and it certainly just earmarked for future studies.

Slide 39 Now, Adam's going to talk a little bit about more – more talking about health and mental health systems integration as an approach to address TB and mental health problems.

Adam Karpati: OK, so I spoke earlier about clinical strategy, screening free for prevention that is applicable in primary care settings to addressing in that case substance use disorders and this –what I'm going to speak about now is a model that was really developed around managing depression but has also held evidence for managing other mental illnesses and again, the theme here is pragmatic and expected methods of integrating behavioral, attention to behavioral health into primary care.

And so the so called collaborative care model is one that provides a level of assistance and a consultation to primary care providers to allow them to successfully diagnose and manage you know mental illness and just to make a point, I made earlier that to the degree that mental illnesses are identified and treated in the medical system, most of them will not be treated on the specialty side.

Most of them will but be treated by psychiatrist, social workers and psychologist, most in fact would be managed by primary care, need to be managed with primary care practitioners, this is not only a matter of resource limitation but also a matter of patient preference and frankly, for most mild to moderate conditions they should be managed in primary care.

And yet, there are big challenges to doing that and the collaborative care model acknowledges that primary care physicians and other practitioners need support, need an opportunity to refer when cases are very complicated or severe but that – with the level of support many of these cases can be managed in primary care.

And so the key to the collaborative care model is that it is a team based approached with primary care, specialty care and of course the patient working together, the use of registries which is the systematic and regular followup with individuals to assess progress, the need for adjustment of treatment and the use of quantitative monitoring of the treatment progress for example using the PHQ9, to quantitative score of the PHQ9 to monitor treatment progress,

But the core of the model is that it's a team of – it involves the primary care provider, a care manager that is and listed here are some of the functions of that care manager. The care manager could be a social worker, doesn't necessarily have to be a social worker and you see here that many of the tasks and functions of the care manager are things that could also be applicable to other, other conditions as well not just in health conditions.

And then the psychiatric consultant, the specialty consultant available not only for referral but for short term consultancies and also in the use of the registry for its systematic review of all patients under treatment on a regular basis. So the principle is that the care manager and the psychiatric consultant provide to the primary care provider the support, the technical expertise and when necessary referral destinations to allow comprehensive approach in managing – managing these conditions in the primary care setting and just to say that this has been evaluated in a variety of setting and is bound to have impressive benefits for variety of disorders.

So again, the challenge of implementing the models like these are often in that issues of billing and fiscal considerations and of course building those relationships to the primary care provider and the specialty sector but these are I believe issues that can be managed. It can be overcome increasingly safe health departments and local health departments and behavioral health

departments are providing a level of technical support and expertise and technical assistance to help practices develop these sorts of models and implement them properly.

Slide 40

Annika Sweetland: OK, so finally to wrap up, were talking about there's a number of research gaps. First of all is gaps and research gaps so operational and research. The first is this awareness – raising awareness about the difference between situational and reactive mental distress and particularly the way it may require a different type of intervention which we have been talking about today. For examples with a more psychosocial situation with lots of stressors and TB is just one of them, they might require extra support to be able to complete treatment.

Whereas if someone has natural clinical disorder in addition to their TB, it might require an additional clinical intervention in order to really improve the effect of TB treatment and so understanding the difference between those and how it affects treatment is very important and that is something that we'll discuss a little bit when we go into the case studies in the next.

Other research steps involve understanding the prevalence of psychiatric issues. Like I said there's evidence to suggest that depression for example is very high. There is evidence that substance abuse is very high particularly in some populations although that tends to be regionally specific, you know for example in Russia, it's extremely high alcoholism rate amongst TB patients so it's somewhat more regionally specific but we need to have a better sense of numbers but really we need to more than that understand and identify best practices that can be disseminated through vehicles like these types of webinars for supportive interventions, psychosocial in terms of psychotherapeutic and pharmacological interventions, better understanding of drug interactions and we need to find ways to use existing data not just necessarily the data like we did all the time but we have lots of data already that could be analyzed to help begin to respond to some of these question.

There's also lots of clinical trials in TB that makes it possible to integrate mental health question into which would help increase the evidence based and

finally we have the need for prospective studies to address some needs of these challenges.

Slide 41 So the International Union against Tuberculosis and Lung Disease that we mentioned earlier, Adam and I are leading a TB mental health working group our primary objective are at a global level although there's – there's also interest at a domestic level.

Linking researchers in the field including you know participants perhaps listening to this webinar, people who have a lot of experience working with mental health issues who can share their experiences. We want to link clinicians, frontline workers that are having – that are encountering these issues and navigating positively and negatively these types of cases we want to learn from.

We want to link researchers with these types of clinicians, we want to build an evidence based for best practices and develop guidelines that can be disseminated nationally and internationally. So anyone listening who has interest in joining the working group or learning more about it or participating you can let either of us know. So that's the end of our full presentation for now. If anyone has any questions.

Slide 42

Amee Patrawalla: So that was great. Thank you both to Anika and Adam for that. we'll open it up to a few questions right now and then we have a couple of short cases to discuss, so if anybody on the phone has a question or a comment. # six to unmute yourself and go ahead.

If there are no questions on the phone, we did have one that was sent in. Maybe Annika, you could comment. It was a general question about what serotonin syndrome is.

Annika Sweetland: I'm not a psychiatrist so I'm not actually the best person to respond specifically to that question personally.

So I guess I can add I mean I have seen it once or twice in my experience. It can be either a mild or a severe reaction usually to a combination of medications that are acting on the same pathway and patients will present with tremor, agitation, maybe some neuromuscular rigidity, although that may not be the predominant feature and again in some patients at least when you read the textbook, you know, it said that can be very mild so they – it's not like they may not present to the emergency room necessarily, they may present, you know, to their outpatient physician or it can be very severe, they can have a lot of autonomic dysfunction and have high fever or some things like that so it can be very severe, it can be life-threatening, but it could also be something quite mild and it can be seen really with a variety of these medications acting together.

Amee Patrawalla: OK. So another question, would you recommend screening all TB clients with mental health screening or substance abuse screening tool? I think that's probably a question that a lot of the TB Control Programs have at this point. Should we be screening everybody since, you know, our patients in general probably are at risk?

Annika Sweetland: I mean my inclination is to say yes, given that it's – even these brief screens can be, you know, two or – two questions for depression or three for substance abuse, it's so simple when, you know, the basic standardized intake for TB patient has all sorts of, you know, I mean nationally protocolized, you know, these protocols for, you know, for inpatient at a national level in U.S. and other countries that it seems like it would be relatively simple to integrate, you know, a few of these screening questions in that for a page just to – just to flag something at the beginning rather than wait until, you know, months into treatment, you know, if someone is not taking their medications and they have all these problems one could really potentially sort of identify that upfront and be able to incorporate that into the clinical plan for each patient so in my opinion I think it would be very wise to incorporate that as a routine measure and I think Adam has speak to it a little bit in terms of the Collaborative Care Model. It uses basically that strategy and uses sort of mandatory screening of for example depression of any medical client when they come in and that's how an integrated model of care can emerge or Adam if you have any …

Adam Karpati: You know – You know I would – I would just echo that and say that, you know – you know, the recommendations are these – that this sort of screening does occur in primary care setting. The evidence for – The evidence for the ability to screen and detect these disorders and then affect outcomes is there and that's the basis for the recommendation.

In the case of depression screening in particular, if you read the (U.S. Preventive Services) Task Force recommendation, it talks about recommending depression screening as long as there is consistence for follow-up. I think that that's when considering implementing these types of as Annika was saying simple approaches. It is important to build in that protocol and the procedures for follow-up, but again those types whether it's, you know, brief intervention in that in the primary care setting or in the TB setting or it's referral or it's, you know, some form of collaborative care, the point that we're making is that these are – that you require work that you require thoughtful implementation that they are doable and they will improve outcomes both to the mental disorders as well as to the outcome so I think it's very compelling to consider doing this routinely in TB setting.

Amee Patrawalla: Yes, I think – I agree. I think that's right. I think that, you know, the screening tool certainly found like something we can implement. The bigger question obviously is what do we do with that afterwards.

There's a related question and I love to hear from anybody on the phone as well who may have done this, if anybody has an example of how some of these tools have been incorporated into their – into their TB assessments, is there any programs that are actively doing this or Annika or Adam if you know of any specific programs either here in the U.S. or outside that are – that are implementing something like this.

Annika Sweetland: Well the key elements of Adam and my sort of core strategy is to try to get programs to do this, but I think that there probably are some that do it, but it's definitely not systematic and just the fact that TB treatment is so – because it's an infectious disease, because there's such – there's just so much potential for integrating and to standardize protocols that this would be having a few

questions here and there I think will be very simple and that's sort of what we're – we're advocating to do at the government level.

Amee Patrawalla: Great. So I think if there are no more questions on the phone. We'll have some time for questions later on as well. We'll move on and talk about a couple of clinical cases.

Slide 43 So I'll just present the cases. These are very abbreviated cases and I can certainly add more detail, but Annika and Adam please feel free to jump in at any point.

Slide 44 So the first one is a young patient – young man, 28 years old who is a migrant worker from Mexico. He immigrated to the U.S. about four years prior. His family has all remained in Mexico and he speaks minimal English.

He was hospitalized for typical symptoms of pulmonary TB, cough and shortness of breath. He was noted to have some liver test abnormalities at admission and he was subsequently diagnosed with pulmonary TB and he was then initiated on standard treatment and discharged after that. The sort of bulk of the case really occurred as an – when he was an outpatient and so there were multiple visits to his home by TB Program staff. Both the patient and his roommates were often found intoxicated and again the patient appeared to clinic intoxicated.

The patient denied having an alcohol problem. He reported that he was consuming just two beers a day, but he did have difficulty remaining employed. He had unstable housing and he was intermittently adherent to his treatments.

So I guess, you know, I think we've talked about this a little bit, but one question I would have again is, you know, this is sort of a – it doesn't even need screening, it seems fairly obvious what the problem is, but sort of how do we intervene and how does the TB Control Program intervene in order to sort of get the best outcome that we possibly can. Is this somebody who should definitely be referred to, you know, specific substance abuse counseling services and really sort of what can we expect, you know, from that approach.

Adam Karpati: I can speak to sort of the system level of issues here and perhaps Annika you could – you could talk to some of the more individual level of clinical strategies. From a system approach, I think that this case illustrates the need for a very close collaboration and connection between tuberculosis clinical providers and other systems operating in communities and this is – this is standard practice for TB Programs. I'm not seeing anything new here, but in the case of for example substance use disorder treatment, there will be a network of providers available in communities for treating substance use disorders. I would say that the screening is unlikely – I mean screening in the very simple sense may not, you know, the issue may be already well known, but there certainly would be a need for more – for more in-depth characterization of the substance use problem.

There may be some possibility of managing it in the primary care setting, but perhaps (come to) low severity requires referral, but that needs to be intentional, it needs to be thoughtful and those relationships need to be established ahead of time and then an idea that's being just to say is again nothing new to folks in the control world, but there needs to be a very close relationship not only with substance use treatment providers, but with social service providers that would be able to address things like stable housing and in some cases and in many cases there's a strong interaction between the social factors and the clinical providers.

Amee Patrawalla: Annika, do you want to say anything about sort of what sort of, you know, with these sorts of interventions, what the TB Program can sort of expect as a best case scenario?

Annika Sweetland: Well what I will say is that so what like Adam was saying with substance use disorders the identification isn't always the hardest part – the hardest part of figuring out (what is used) so substance use disorders tend to be – it becomes very obvious in the case with this patient who is intoxicated at each of the different contacts and is truly interfering with treatment. I guess the piece that is different between substance use disorders versus like depression for example as we're talking about earlier is readiness for change and, you know, in a six months – six months' treatment by referring that to a substance

use treatment program assumes that the person actually is ready to enter treatment, which may or may not be the case.

It would be helpful I think if people within the TB Clinic have some skills and training related to motivational interviewing, which is a strategy intended to assess readiness for change so if a person, you know, is really in complete denial of having any sort of drug use problem, referring them to a treatment is, you know, may or may not be effective, but if the person has some insight and recognition that there is a problem and they want treatment that would be a very useful course.

If they have no interest in treatment then it may be necessary for the patient to be managed at the clinic level – at the TB Clinic level, which would mean having skills around harm reduction and sort of working with the patients to be able to find ways to not necessarily stop their drinking, but find ways that they can continue to prioritize taking the medications in a way, you know, that – if not so the outcome is not stopping drinking and the outcome is taking the medications at all so (that they get advanced) treatment and so the management is slightly different.

I think the combination of (making) the referral systems when there is readiness for actual treatments and there isn't readiness for treatment is having (done the skill base) at the – at the clinic level for harm reduction strategies to be able to improve adherence, treatment outcomes (to work along) with those substance abuse outcome.

Amee Patrawalla: Go ahead. There's a question here in the room.

(Alfred Lardizabal): Thanks Annika and Adam. This is (Alfred Lardizabal) here in Newark. I think it's great that we're talking about mental issues and behavioral disorders as they relate to tuberculosis and really bringing to front recognizing that this is fairly prevalent in many of our patients.

Going back to this case, I think fear is a very good motivator and why not just use that. Many jurisdictions have and I mean this is just trying to be a devil's advocate here, a lot of jurisdictions have legal interventions and why not just

go that way, it's a lot readier rather than picking out mental health clinics. They seem to respond to fear. Is that the wrong way?

Annika Sweetland: Are you suggesting like incarceration or that was a …

(Alfred Lardizabal): Yes maybe your opinion with regards to, you know, there are other options that are available to use out there, which have to do with sort of being forced to go through (such change) treatments a judge will have to order a certain things and in situations such as this where adherence becomes a problem that may be the first step that a program might approach or might use so I guess there's no head-to-head comparison, which would have a better outcome, but would you – how do you – what would be your opinion on something that is again a collaborative multidisciplinary approach or - I think most of the problems that we confront is that we don't have people to approach in terms of for health support.

Adam Karpati: Yes, I mean, you know, it would just be because you know tuberculosis control and behavioral health actually share some – the system share some like characteristics, one of them is the (legal) basis for mandatory treatment, but in the behavioral health world first of all those are very rare cases and what I would say is that there is, you know, there is a – there is a, you know, there's a temptation, there's a potential for resorting to (holistic) methods of obtaining, you know, of treatment when, you know, and attributing issues of compliance or adherence on individual patient, (therapies and location) to decision making when in fact in many cases they represent the (age of assistant) to successfully engage and to make treatment acceptable to individuals so you know, not necessarily talking about force treatment for tuberculosis, but for behavioral – for mental health disorders, the real issue and the real strategy is about creating (NDS) methods for engaging patients and for making the treatment system welcoming.

For example substance use disorder treatment, the majority of – many individuals in those systems are actually mandated to be in those systems, you know, by court. It's not the – It's not the ideal profile of the Patient-Centered System to have such a high proportion mandated into care so I think it's dependent upon us who are involved in this – in the care to think about ways

to make – ways of engaging and ways of making sure it's appealing rather than (having them taking some of these course of attention).

Slide 45

Amee Patrawalla: So just to give a little follow-up on this case and then we'll move on to the next one.

This patient was as you can expect lost to followup after about two months of treatment. Four months later, he presented to a different clinic due to continued symptoms. He was found to be AFB smear positive at that time.

He was then admitted to the hospital for one month both for medical reasons as well as for public health reasons and then upon discharge unfortunately the case management team had similar difficulties as before due to his unstable employment.

Slide 46 They did ultimately – They were ultimately able to find housing for more stable housing for the patient, which was provided by the American Lung Association and the Department of Health and the patient did ultimately complete treatment, although 18 months after initiation due to these multiple interruptions as well as his underlying presumably alcoholic liver disease and so while the outcome was positive in the sense that he was completely treated, it certainly took about a year longer than you would normally expect it to and so I think that the housing was certainly one of the main issues in terms of getting him to complete his treatment in addition to really sort of dedicated case management services and some other incentives as well and I think Annika mentioned, you know, throughout this process, the field staff didn't notice that he was never completely sort of abstinent from alcohol, but he did cut down significantly once he have the housing so sort of unsimilar lines of what we've been discussing.

So if there are no – if you have any comments on that last case Annika or Adam, otherwise, I'll move to the next one.

Annika Sweetland: There are none.

Slide 47

Amee Patrawalla: OK. So our next case so this is a 50-year-old African American woman who was diagnosed with HIV in 1998 during her last pregnancy. She has four male children, two of which are currently incarcerated.

She has a remote history of cocaine and alcohol abuse. She has a history of depression, although never treated and a suicide attempt in 2007 and she has had some interaction with the mental health – with mental health services, although never continuous.

She was diagnosed with extrapulmonary TB, lymph node TB in 2013. This was complicated by drug-induced liver injury as well as other side effects and other medication intolerances and so she is currently on a TB regimen that will likely take about 18 months of treatment as well as her antiretrovirals.

She has missed along the course of saying appointments both with the TB Program as well as her infectious disease physician. She has been referred in the past to mental health services, but she never went, at least not in the last couple of years and currently she is employed and her social situation is a bit better than it was before and she seems to make most of her appointments with the TB practice and so she is doing well.

At the same time, she has missed about four or five months' worth of appointments at the infectious disease practice and so, you know, one of the issues here is clearly this is a very complicated patient. She has a lot on her plate to deal with. You know to how and she has both sort of short-term and long-term goals and objectives and short-term and long-term, you know, mental health issues as well.

So what should be our best approach with her and what's our, you know, best chances of sort of preventing future decline of her – of her mental health?

Adam Karpati: Well maybe I could just again take it from one of those system perspective and I think that this is a – this case illustrates many of the challenges (facing) the medical system in the United States where many, you know, especially for individuals with multiple comorbidities and a variety of social challenge, social stressors and psychosocial challenges and in this case it's hard to know

exactly what the clinical status is and obviously that would be an important sure step to better characterize the clinical need around mental health services, but in the totality there should be other points we need for a lot – for team-based care, for collaborative models, for a – and for care coordination across multiple disciplines and I think that increasingly there are – there are models for this – for this kind of work and in the case of mental health and HIV in particular such care coordination (model) is good, although not necessarily at the level that's really needed, that with the Affordable Care Act and new models especially in Medicaid for care coordination for complex cases isn't exactly becoming the kind of things needed and I think the message ultimately here is that Tuberculosis Programs and (with those with) permissions should be finding ways to participate and to be actively engage in these care coordination case (conferencing), you know, multidisciplinary models of patient care and it's no one practitioner that will have the answer, but it's really that coordinated approach that's necessary and that includes both the specialty behavioral health providers, specialty infectious disease providers, primary care and of course the case manager or care coordinator of the hospital.

Annika Sweetland: Yes just to add on to that, this seems like Adam said and I feel for those case requiring case management because when I see, you know, for example patients missed multiple appointments, there is a history of this and then that and there's not reporting on, they are referred for care and so all of this suggest that there is a need for some person either a social worker or a case manager, someone who is there to say OK first of all what is going on, is this – is there active depression, suicidality, is there current, you know, abuse issues going on, what is the active substance use, what are the diagnostic concerns first of all, why is she missing appointments, you know, this involved conversation engagement with the patient finding out what is it that's interfering, what are the issues (actually), you know, more, someone should be asking more questions and if she was referred to mental health services and didn't go why not, did she not want to or did she not have transportation, did she not have a baby-sitter, I mean there's – there's clearly in a case that's so complicated there's clearly a need for some person to play the role of asking these questions and trying to figure out how to address the very complex needs to support such a patient to complete treatment.

Amee Patrawalla: Yes, I think that would certainly be useful at least in this patient's case and I think, you know, part of the issue is that if things are going OK from the TB Program's point of view, you know, it doesn't necessarily spark a whole lot of sort of proactive questioning of the patient about their mental health and things like that so hopefully from some of, you know, as this Collaborative Care Model or Patient-Centered Home Model comes closer and closer and closer to the ground to us, to the providers and to the patients, some of that will be, you know, implemented in a more standard format that it would be beneficial for many of our – many of our patients.

So, you know, I want to take a moment Adam and Annika to thank both of you for an excellent presentation and for really developing this topic so nicely. If there are no other questions on the phone, I'm going to turn it back over to Anita and I also just want to thank our audience as well.

Slide 48

Anita Khilall: Thanks Amee, Annika and Adam. There were several questions that we didn't get to, but those were typed in and we can try to get answers for you and respond by e-mail.

Slide 49 And finally just again to want to thank everybody for their participation and to thank all of our faculty. Thank you and this concludes the conference.

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