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Schizophrenia: The Past, Future, and Options for Recovery

"Ask A Researcher" with Dr. Fidel Vila-Rodriguez
From the 2020 BC Schizophrenia Society Donor Appreciation Event

Dr. Fidel Vila-Rodriguez is Director of the Schizophrenia Program and Non-Invasive Neurostimulation Therapies Lab at University of British Columbia's Department of Psychiatry. He also serves as a Volunteer Board Member on BCSS' Board of Directors.

Q: What do we know about schizophrenia today?

We all know that schizophrenia is a prevalent condition around the world that affects 20 million people - that's around 1% of the population.

We know that schizophrenia is an illness of the brain. The most characteristic symptoms of this brain illness include (but aren't limited to):

- cognitive impairment
- negative (the person loses drive, motivation, and will not do the things they like)
- hallucinations (hearing voices or seeing things that are not there)
- delusions (fixed, false beliefs)

Schizophrenia is a devastating illness associated with considerable disability and can affect educational and occupational performance and achievement. People with schizophrenia are two to three times more likely to die earlier than the general population. This is not only a result of treatments, but also the result of the toll the illness takes on physical health - i.e., the ability of people to take care of themselves and embrace healthy habits around diet and physical activity.

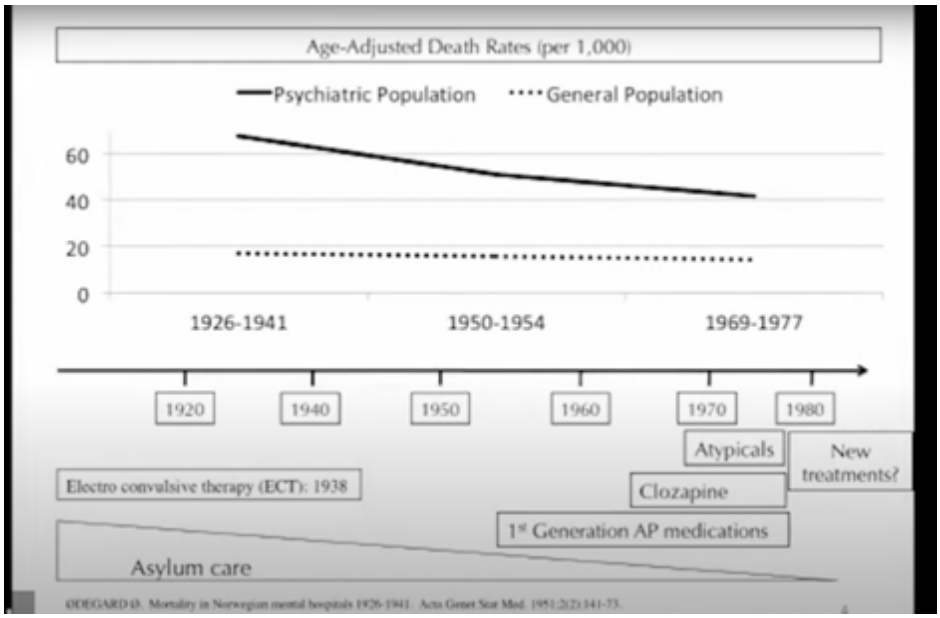
But it's important to note schizophrenia is treatable. Treatment with medicine and psychosocial support is effective, and people do get better. There are strategies that can help people who suffer from schizophrenia perform at their potential. Strategies like supportive housing and supportive employment are effective management strategies for people with schizophrenia.

Q: How does today's picture compare to the long term outcome for schizophrenia in the past?

When you compare the mortality rates in the psychiatric population to the general population, in the early 1900s, before we had any treatments like medications, the mortality rates were significantly higher in the psychiatric population - many of these people had severe schizophrenia and psychotic disorders.

Over time, you can see that things have improved based on the ecological data that exists. We cannot definitely establish that it's a causal relationship, but we can see that the life expectancy gap has narrowed with time. This coincides with the availability of more treatments.

So I think the key message here is that like any severe illness, mental health illnesses left untreated are lethal. But treatments do work, and make a huge difference to the outcome.



IMAGE

This screen shot is of a slide referenced by Dr. Vila-Rodriguez when speaking to the mortality rates in the psychiatric population compared to the general population.

Q: What are the most used medications to treat schizophrenia?

Most of the medications that have been and continue to be used to treat schizophrenia are variations that target one chemical in the brain- dopamine. They antagonize, or bind, to the dopamine receptors which decreases symptoms, particularly hallucinations and delusions.

Clozapine is a very different treatment because it does not act fundamentally on these dopamine receptor mechanisms. It affects other chemicals in the brain, and probably has other effects like regulating the immune system and levels of inflammation. It's a very different type of medication in that way.

BCSS MEDICATION UPDATE

BC Schizophrenia Society regularly updates a fact sheet that provides some brief information on some of the more common medications used to manage symptoms of schizophrenia. This information is available on the BCSS website at: https://www.bcss.org/wp-content/uploads/resources/Medication-Update-2018.pdf

Q: What are some significant recent developments in medication to treat schizophrenia?

Historically, medications have focused on targeting the neurotransmitter dopamine. Some of the most recent advances and research in medication target other neurotransmitters, other chemicals in the brain.

As an example, there's a lot of interest to regulate the level of glutamate in the brain to treat schizophrenia. Glutamate is the main excitatory neurotransmitter. There's a lot of new research and emerging medications aimed at regulating the levels of glutamate. In the same vein, I think we'll see more medications that target the inhibitory neurotransmitter GABA. Another approach is medications that target the acetylcholine receptor. So the key message here is that new medications are coming out for the pharmacological treatment of schizophrenia that are targeting chemicals other than dopamine.

Another aspect of a new pharmacological approach is medications that already exist dispensed in a different form. For example, some of the new medications

coming out allow for a person with schizophrenia to have an injection once every three months, where they used to have to take the exact same medication by mouth every single day. It's the same medication, but now we've made it much more convenient, and probably you increase the chances that people will take the medication.

Q: What are some new approaches to treatment beyond medications?

There are a new array of treatments that are non-pharmacological. There's a series of treatments that address one very important aspect of schizophrenia- the cognitive difficulties that people with schizophrenia have.

Cognitive remediation is one of these treatments. Cognitive remediation is a cognitive rehabilitation treatment that consists of helping people with schizophrenia train thinking skills in order to improve everyday life functioning. Metacognitive training is another cognitive treatment which targets the tendency that happens in people with schizophrenia, where they jump to conclusions without all the information causing delusions and false beliefs. There's a lot of evidence building up in clinical trials in favor of these two interventions.

There are also non-invasive neurostimulation treatments. These are treatments that leverage the capacity to stimulate the brain by eliciting electric currents. And some of those include transcranial magnetic stimulation. Also, electroconvulsive therapy is returning as a very effective treatment to treat delusions and hallucinations.

Q: What are the long term effects of Clozapine and other medications?

Let's start with side effects, because that's definitely a question that comes up a lot. First of all, side effects are one side of the coin of any intervention. If you have any intervention that can help to treat an illness, it will have the potential of having some side effects. That applies to pharmacological interventions, arthritis treatment, antibiotics- to any treatment.

It's important to understand side effects, and what we can do to mitigate them. Some of the long term side effects associated with medications for schizophrenia and psychosis have to do with the risk of developing abnormal movements. These are in the form of something called dyskinesia. Dyskinesia are abnormal movements that consist of involuntary movements that are repeated. Other abnormal movements are called dystonias, which is the contraction of a muscle group.

Other side effects have to do with the levels of a hormone called prolactin. Many medications increase prolactin levels and that can have an impact on the reproductive system and sexual function.

The risk of side effects accrue over time, so the longer someone has been on these medications, the more risk of a side effect there is. One way to mitigate side effects is to always follow your healthcare provider's direction and to work with them. Perhaps it's possible to take another medication that can help mitigate any side effects, or maybe the dose can be adjusted. There are options but always check with your health care provider before making any medication changes.

Q: What should a person with schizophrenia do if they want to change their medications?

Again, it's very important to check-in and to engage your healthcare provider before making any changes to any medications. If a person feels strongly about making changes to his or her medication, it's critical to engage in discussion first, to talk with the patient, their family, and the medical team.

Q: What is the role of family members in a patient's treatment?

When it comes to treatment, I think it's always important whenever there are family members who want to be engaged, that they join in the discussion, but only to the extent that the patient allows. It's just as important to consider a patient's preference, as it's a complex and dynamic part of treatment. As a professional, I do see the perspective of how important it is to have the family engaged in an individual's treatment.

Q: What is the value of involuntary treatment for a family member? How can families work to protect the BC Mental Health Act for the benefit of those suffering from mental illness?

This touches on a very sensitive topic, where different stakeholders at a societal level have different and sometimes strong opinions. To protect the very important and helpful resource that is involuntary admission, we need to bring some perspective to stakeholders who do not know the reality of what can happen at home when someone is experiencing severe mental illness but cannot understand they need to seek help.

I think that professionals and people who have strong opinions against involuntary treatment have never experienced firsthand a situation where someone close to them stops eating and sleeping, is harming themselves, and doesn't realize that they are suffering an illness of the brain that prevents them from having the insight that they do need treatment. If they had that experience firsthand, they would understand immediately that sometimes in very concrete situations, as families, professionals, and a society, we have a duty to take care of people. I think that's very important to convey to those who don't understand the necessity of involuntary admission.

Q: What is being done currently to test relatives of people with schizophrenia for pre-existing tendencies for the illness? Is anything being done to alleviate those tendencies?

We know that part of the etiology of what causes schizophrenia is likely driven by many different genes. So there's a genetic component. Studies have shown that there might be more subtle cognitive difficulties in relatives of people who suffer from schizophrenia. So, that's the background- we know that this link exists.

In people who don't have the diagnosis of schizophrenia, don't have those set of symptoms, but may have some of what we call liability, researchers are finding ways to look for biomarkers linked to schizophrenia and similar disorders.

Right now there are a lot of different biomarkers that researchers are investigating. They're using imaging tools like electroencephalograms. They're also looking for biomarkers in the bloodstream. These tests are designed to detect people who may be at risk of developing schizophrenia or at a transition. Not a lot of this has been applied to studies of relatives.

I would say that if someone is concerned about that potential liability, it's then extremely important to really stick to some of the fundamentals of looking after oneself (and these should not be treated as medicines). But it's a good idea to be very respectful with your own rhythms, prioritize good sleep hygiene, and be as physically active as possible- things like that. Avoid substances like cannabis, excessive alcohol, and other drugs. These things are going to be protective factors.

Q: Is an MRI at birth to determine ventricular size a reliable predictor of the development of schizophrenia?

No, it is not. I think this idea comes from a paper that was published 2 months ago showing that we're able to harness machine learning to see certain patterns in an MRI scan that would distinguish two different groups of people with schizophrenia. But we need to pay attention to the fact that this research was done on thousands of people who suffered from schizophrenia, once they had developed their condition, not before.

The most reliable marker of future instances of schizophrenia and related disorder in children and young people is cognitive impairment. Cognitive impairment is typically present years before delusions and hallucinations emerge. This takes the form of strong difficulties with learning and adjusting to the school environment. These are the markers that are the most promising in my opinion, and there's some research to back that up.

Q: Will COVID–19 vaccines be safe for people taking medications for schizophrenia?

I have to admit that I've not looked at the data just yet to make a 100% firm claim and statement. From what I've read so far, like many other vaccines, there's no risk reported of having an interaction with pharmacological medications. So I think the key message here is from what I know about vaccines is that they are safe for people with schizophrenia, and any medications they might be taking.

That's not to say that we shouldn't be mindful and monitor what happens as we progress in vaccinating the entire population. In large studies for these COVID–19 vaccines, they've treated more than 30,000 people. In the UK, they found two people who had very severe allergies to the vaccine. So it means we need to take care with vaccinating and monitor for these rare side effects, and then learn from it. But the general statement is that vaccines are safe and people should be vaccinated.

Q: How far away are we from a cure for schizophrenia?

That's an excellent question. On one hand, it's uncertain. On the other hand, as you can see from the graph above charting the lifespan of people living with schizophrenia and related illnesses, we've made a lot of progress in decreasing mortality rates. Investing in clinical research is a way to achieve not only excellence in current clinical treatments, but to develop treatments that push forward and advance better outcomes in schizophrenia. It's extremely important to continue that research.

I don't know when we'll have a cure for schizophrenia, but I know we're definitely closer now than we ever have been before.

A full recording of this event is available at https://youtu.be/Fd55tIbA0Tc

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