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Improving Long-term Outcome of Psychotic Disorders through Early Intervention

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Thank you for inviting me to share with you this afternoon some thoughts and reflections after 18 years of early intervention service development in Hong Kong. I will be going through the work here which some of you have directly contributed to in building up a system from different sectors to support improving access to mental health services to support reducing the barrier to such services.

The title of my talk is "Improving Long-term Outcome of Psychotic Disorders through Early Intervention". This is to remind us that the early intervention services are not as caring about the early outcome. In fact the ultimate goal of the early intervention has to be to improve the long term outcome for people with psychotic disorders. The rationale for early intervention is often a debated topic. Why do we concentrate resources in the early few years of the disorder?

Psychoses as a Complex Disorder

One of the reasons I will try to illustrate is that psychotic disorders are complex disorders. There are many many factors from molecular genes to molecules to physiological systems and brain network and then psychological mechanisms and symptom networks. There are many factors that are interacting in ways that can form loops in ways that they can be self-reinforcing once these loops are formed. And clinical psychologists will know very well how at the psychology cognitive level these loops can lead to the reinforcement of certain symptoms and behaviour. It is not just at the psychological level as the symptom phenomenon level at the physiological level as well as the molecular level. Increasing knowledge suggests to us that many hundreds of genes are likely to be involved and are responsible for a disorder like schizophrenia. From the genes you have downstream mechanisms, many of which are still unknown but are increasingly being worked out. These systems do not work in isolation. There are interactions between these systems with the possibility of forming loops and cascades so that things become self-perpetuating later on, just very much like a psychological mechanism. The rationale for early intervention is to try to reduce this process. The accumulation of self-made processes we don't even know about the exact nature, but we know they must be there, affecting the brain, affecting the expression of the disorder. There is evidence that the final expression of a psychotic episode may be related to dopamine. We know this from dopamine synthesis study but as has been emphasised by researchers in this area. It is very complex, including early and late factors, psycho-social, biological factors. Psychosis is actually the final expression of complex processes so the factors interact. The question we ask is, "What can we

Transcript of Dr. Gerald Choa Memorial Lecture of 65th Anniversary Symposium on Mental Health on 10th December 2019.

do once the network has been disrupted to the extent that psychotic symptoms appear?"

Another biological fact about the brain that has become increasingly known is the phenomena of the critical periods in the brain. What this refers to is that there are specific periods during development that the brain is open to particular influence from the environment. Here, for example, Konrad Lorenz was doing an imprinting experiment. When he exposed himself to ducklings that at a certain stage after the hatching, the brains of the ducklings adapted to him as an attachment figure and thereafter they would follow him as if he were their mother.

So there are time windows in which the brain is open to particular influences and interact and develop the necessary schema to then cope with life adaptively (Figure 1). What is becoming increasingly known is that these different periods of openness to influence from the environment actually extend into adolescence and youth periods. So we have early development of sensations of the language and early years, the things we learn within the first 18 months. But there are some higher functions. The part of the brain that is responsible for social functions and decision making actually has this period of openness, in the youth period. So that is a suggestion of why many of the mental disorders actually have an onset time around the youth period from 15 to 25. We are all beginning to know about the mechanisms which control the opening and closing of these brain systems. What it suggests is that there are tiny windows in the brain and once the window is closed, things become fixed and less easily changed. So that is another reason why intervention in the youth period can be very decisive over the long term outcome.

When we talk about the outcome of psychotic disorders, something as complex as schizophrenia, it is important to notice that there are different dimensions of outcomes, so functioning is a very important outcome. The presence or absence of psychotic symptoms, as

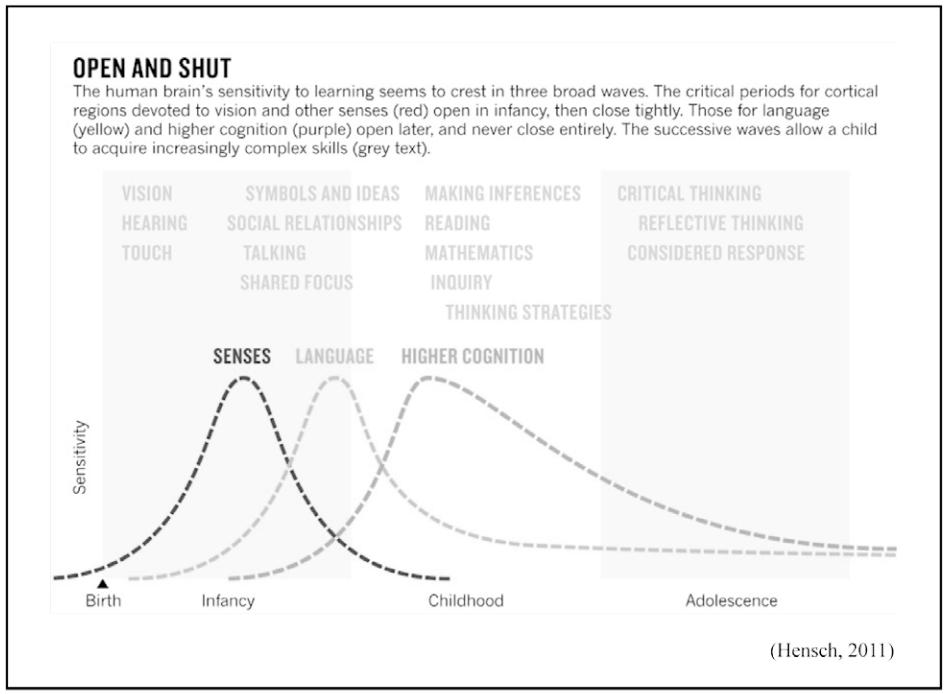


Figure 1: Critical Periods in the Brain

well as things like suicide. There have been a number of longitudinal studies that look into the long term outcome of schizophrenia. This is one from Chennai, India, basically showing more or less a similar picture with variation. There are people who have one episode and then it is in remission, with hereafter, a small percentage. There are many people who have episodic disorders, recurrent disorders, with good remission intervals in between. There are people who had episodic disorders without a good recovery. There are some residual problems in between. And some unlucky people who don't really recover from even the first episode. And there are those who actually end their life in the course of the disorder.

Early Intervention of Psychoses

What we are talking about with early intervention is asking ourselves, "Is there something we can do in the first few years of a patient's illness that could have an effect on the long term cause of the illness?". There have been several studies that followed patients for ten or even 20 years. Data from these studies suggests that the outcome in the first few years, the first three or four years, and the outcome ten or twenty years later actually contributed to the majority of the variance of the outcome ten or twenty years later, suggesting that whatever happened in the first few years are the predominant, decisive factors in deciding the long term outcome. That is the sort of data that have driven the early intervention approaches.

When we talk about early intervention, it is a very popular term. It sounds good. But we have to be a bit more specific about exactly when we mean by early intervention. In fact there are some different components to early intervention work (Figure 2). The first is detecting the illness earlier so to reduce the period of untreated psychotic illness reducing the DUP (Duration of Untreated Psychosis). The second approach is once you have detected the patient, to focus the resources to try to achieve as good an outcome as you can in the first few years of the illness, and that is phase specific intervention. Phase specific intervention means that we want to focus our expertise and knowledge about the early stage of the illness, because the early stage is actually quite different from the stage where the patient has been ill for many, many years due to the accumulation of factors that we talked about earlier. To have that expertise and ability to shift the cause of the illness in the early few years, and then combining the early detection and the phase specific intervention, we hope to get a better outcome in the first few years, what is called the critical period in the field now, the first turbulent years. After, the cause of the illness tends to settle, whether it is good or bad, it tends to become stabilized. Hopefully if you get a good outcome after the first few years, you can maintain that for the longer outcome.

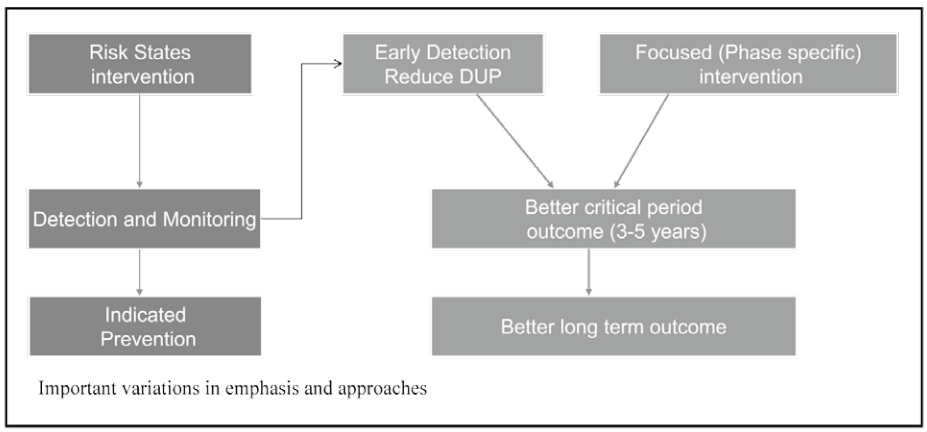


Figure 2: Early Intervention Aspirations

There is another different component which is about identifying people at risk but who have not yet developed a full-blown psychotic disorder. If we can identify them, we can actually either monitor them or provide some preventative intervention. It is usually not medication but usually some sort of psychological intervention or neuro-protective agents, in the hope that preventative action will reduce full-blown psychosis.

This guy here is not Patrick McGorry. This is actually a 19th Century psychiatrist from Glasgow, and I will tell you a bit more about him. He was one of the early people who actually proposed the idea of early intervention. I won't go through the detail of this but it shows the pathway of what patients may go through in the first few years, two or three years, in the course of the first episode of psychotic illness. What it tries to highlight is in each of these stages – the first episode, the first remission, recovery stage and then relapse and some people get into the refactory stage and then co-morbid stage. In each of these the very specific early intervention idea would be to develop a targetive mode of intervention, to specifically tackle, for example, the first relapse, which is different from the second relapse, different from the first episode. To have this refined, tailor-made intervention that actuates that particular event in the hope that we can focus and then we can deliver a bigger impact. So this is the whole idea behind early intervention work.

Now, David Yellowlees is this guy long ago. He used the term insipient insanity, and he discussed it in 1903 in the British Medical Journal in very much the same way we would talk about early intervention nowadays. I will return to him a little bit later.

So the idea of early intervention is not new. Since 1903 it has been around, since about the time the concept of schizophrenia was formed and consolidated, even a little bit before that time. Right from the very early days his idea of early intervention was there. Is it surprising? Not surprising. We had early intervention in all fields of medicine, in cancer, in all the diseases. What is surprising is how we actually lost the idea later on. Early intervention had to be re-proposed as if it were something new. I think this is something we should reflect on as well.

Early Intervention Services in Hong Kong

Now I want to share with you some of the data we have in Hong Kong about what we have been doing and what sorts of results we can get in Hong Kong. As I said, many of you here participated in this as well. The first is, "Can we actually delay the treatment for psychosis?" The program in Hong Kong started in 2001, and we have some data to show how the DUP has changed since 2001 and in the early 2010s. We don't have more recent data but you can see some of the patterns. First of all, the DUP of the period from clear onset of psychotic symptoms to effective treatment. You notice here, from 2001, this is the data we have, showing that the distribution is not a normal distribution (Figure 3). A lot of people did not have much delay. This is 30 base, the number of people, about over 100 people from Hong Kong Island. About one-third, 30%, present within 30 days. Too late. Then if you go to ask how many people would have presented within half a year, 180 days, you look up this curve, about 50%. So about half of my first episode patients present within half a year. The other side of the coin is that the other half present a little bit longer than half a year. It is actually very easy to remember. What about one year? One year two thirds of the patients have presented, about one third have a DUP longer than one year. This is the basic situation we have for early intervention.

The question is whether we can shift this curve upward so that more proportion of patients will have presented by a particular date. This is a challenging task and what it means is that the medium DUP is about half the patients. We need some calculations. We estimate every day in Hong Kong something like eight to ten people would have developed psychosis for the

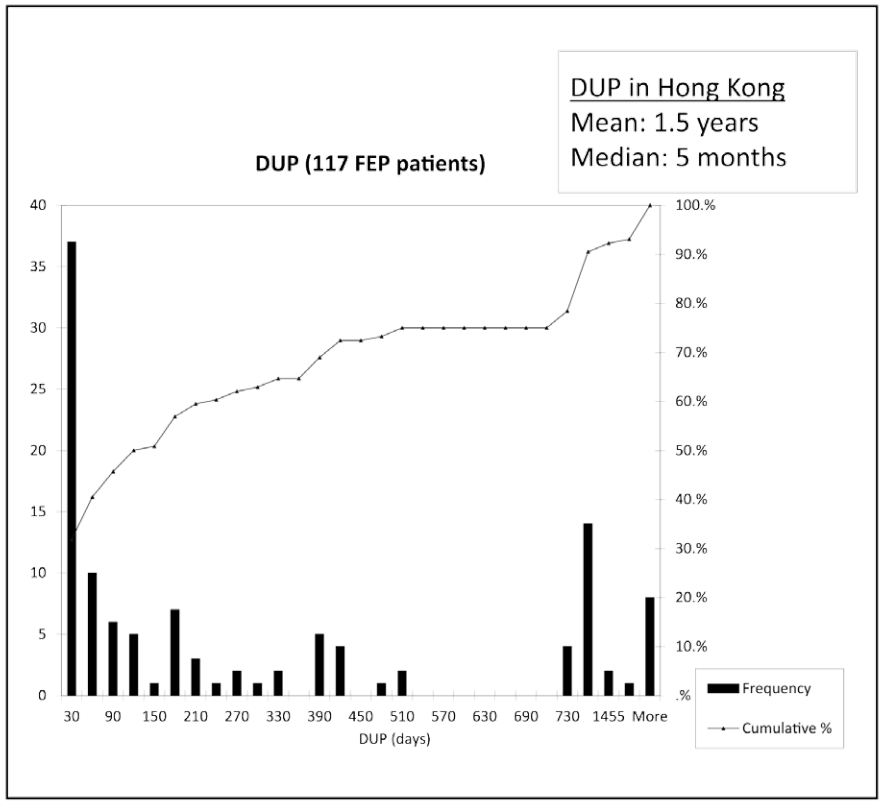


Figure 3: Duration of Untreated Psychosis in Hong Kong Since 2001

first time in different districts, different areas of Hong Kong. We don't know about them. There is nothing we can do to screen them. We cannot image the brain. There is no appearance that would tell them apart. These people who develop clear-cut psychotic symptoms today, it would take them five months before they receive effective treatment. That was back in 2001. We have improved a little bit since then. That is the sort of challenge. As you can see, this would immediately bring us out of the clinic and out of our centres and hospitals. In order to reduce this DUP we have to do something that allows people to come earlier. They cannot just sit there and wait.

What are some of the factors which affect the DUP even within Hong Kong? This is important. I think it may be population-specific. In Hong Kong we found that actually having a family member who already had a psychotic illness helped. If the family had an experience with a psychotic illness, the DUP is shorter. This suggests that even something as basic as knowing what to do, recognizing the symptoms, is important. Then it is not surprising that the mode of onset of the illness, how sudden the illness present, is an important factor. But that we cannot control. What we can control is the family information about mental illness. The two factors interact so you have the worse situation, the slow onset situation in a family with no experience of psychosis. In order for families to have the information to act and the challenge that we cannot predict in which family a psychotic illness is going to strike, we have to have some strategy to educate the public, and that is what we have followed a little bit. So there has to be some public education, some mass media work. Then we can focus on some specific groups.

These are some of the groups we have worked on, the so-called gate-keepers, the

people who are more likely by their jobs to encounter people who become ill – the social workers, teachers, police, estate managers. In Hong Kong we live in large public housing estates and each block of flats will have a manager. They are often the people the residents will come to if they want to complain about a neighbour, noises and voices and so on. So a very important profession in Hong Kong to educate. As we embarked on this work in a project - the Mental Health Association of Hong Kong was a partner - we then discovered the size of the estate manager population. Any idea how many people? Ten years ago there was something like 200,000 estate managers in Hong Kong, probably one of the most numerous professions. Educating them becomes a severe challenge.

Youth at School is a priority because they are just moving into the age of onset psychotic disorders and because they are still in the school system, which makes it relatively manageable to have a more in-depth sort of access. Regarding the social work we have been doing in Hong Kong, we found first of all that the original Chinese name for psychosis (嚴重精神病) didn't work. It is not informative, but is highly stigmatising and negative. We want to communicate that psychosis has different degrees of severity. We came up with this term (思覺失調) which has been in use for 18 years. Actually it surprised me the resilience of the term with negative connotations. I would have thought that it would have walked off in years, and then when people use this term, it would be the same as the term for schizophrenia, the usual term for madness. Somehow the negative connotation didn't catch up as fast as we expected. I suspect that one of the reasons is that it has four syllables, making it more difficult to swear and scold people with this term. That was unintentional in the design.

Different NGOs – I couldn't list all of them – but there is one NGO, Episo, which focused on psychotic disorders to engage celebrities and others to sort of make the image of mental illness more positive. One thing I must mention here is that over the years we see a transformation in the posters about mental illness workshops and the quality of the posters. That is led by New Life, actually very high quality posters, well-designed posters. Even those posters are a signal of stigmatisation. Somehow, for mental health topics you don't need well-designed posters as well as in other illnesses. This is the JCEP (Jockey Club Project). Do you recognize the young people there? We have many dedicated colleagues from the Mental Health Association of Hong Kong participating in this project. This is our logo for the JCEP project, about ten years ago.

These are the things that we have been doing – giving public talks, workshops, exhibitions – and it is still on-going, in various platforms. Now we have women's mental health and youth mental health. The question is, "What effect does it produce?" We'll take a snapshot into the potential effect. Around 2010, ten years after the initial project, it is time to take another snapshot. What happened here is we look at how much this DUP curve shifts upwards (Figure 4 & 5). If it shifts upwards, it means a higher percentage of people would have presented by a particular time. The situation is that we managed to shift the DUP for people in the adult population, but we didn't manage to change the DUP for young people. That is something we need to think a little bit more about. Knowing already that the baseline in the young people is not as bad as that of the adults, so maybe there is more room to improve. Then there is a ceiling in which the sort of work we are doing would be hitting the ceiling, the limit of its usefulness, so that is something we have to consider. There are several studies around the world to look at whether the sort of promotion program can actually change the DUP, and the results are mixed. In fact not many places report a clear-cut change in the DUP. One of them was actually Singapore, which was able to change the DUP very substantially. But their original DUP was very long, like two and a half years.

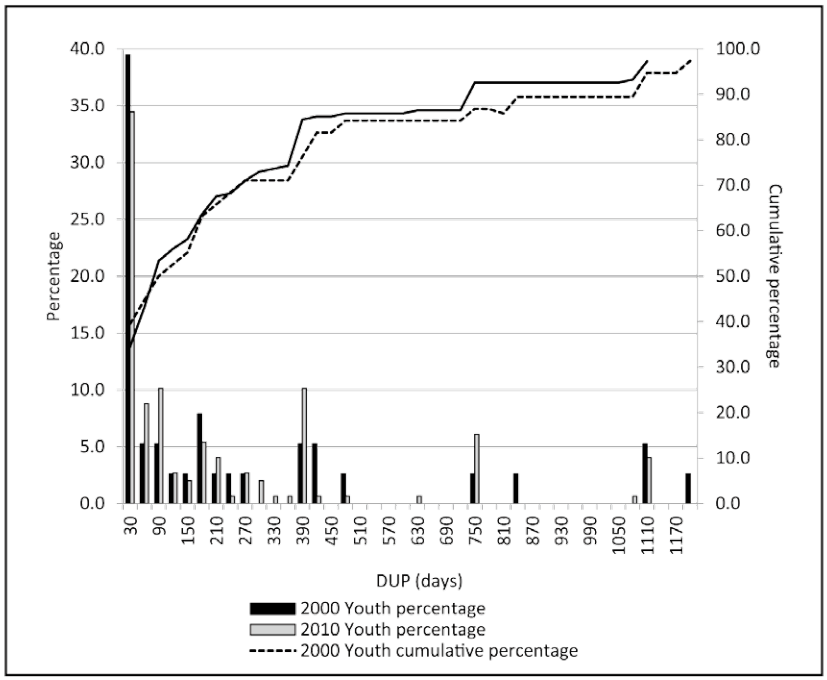


Figure 4: Comparison of DUP of Youth Patients in 2000 and 2010

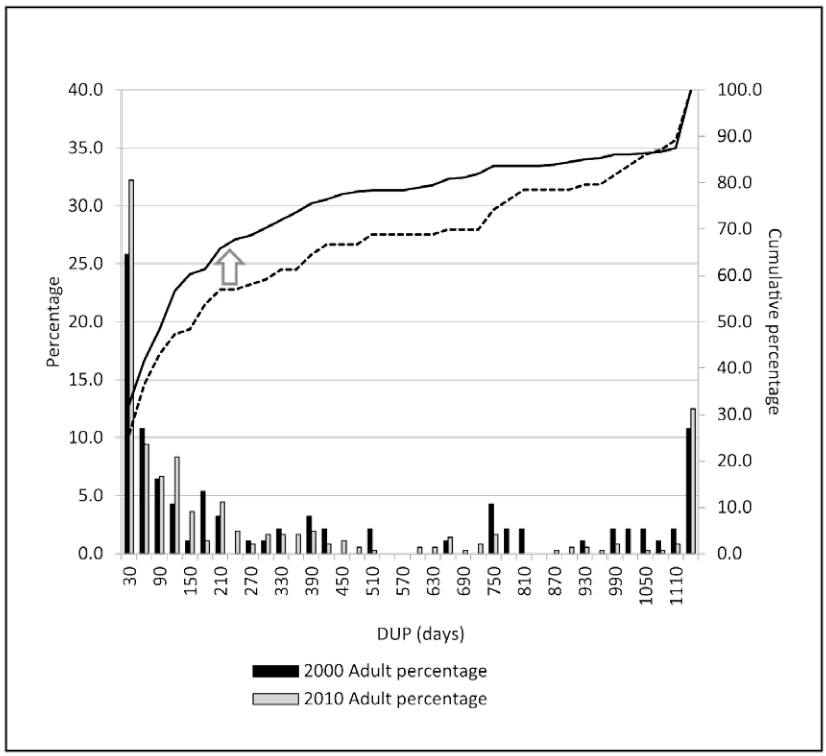


Figure 5: Comparison of DUP of Adult Patients in 2000 and 2010

Once the patient has been identified, can we do something useful for the patient? Can we make an impact on the outcome? We did some evaluation. This is to point out that there are many different programs, each one has a name and they are very proud of their own identity. In Hong Kong our program is called Early Assessment Service for Youth with Psychosis (EASY). In Singapore the EPIC program. Later on we have a JCEP program. In Asia there are many people working on early psychosis, and we actually meet regularly to discuss the issues and challenges specific to the Asian culture. This is one book Early Intervention in Psychiatry we published several years ago as a result of those discussions. We are talking about 40 minutes of work which spanned 20 years, two decades, and how the people actually grew and aged along with the work.

Back to this very specific intervention, we tried to be as specific and focused as possible, using multi-disciplinary teams in which there were case managers, who were mostly from the nursing profession. We have tried social workers and OTs in some other hospital units. This shows one of the teams, all very happy, energetic and enthusiastic. This picture was perhaps 10 or 12 years ago. Nowadays if you take another picture, I think you would be reminded of the talk about stress, inadequate resources. I am talking about the reality.

One of the things is very heavy caseloads. In the other program which I mentioned, the caseload is about 20 to 30. In Singapore it is about 35. It may have been better but now it is about 35. In Hong Kong it is about 60. The aim is 50 and the reality is 60 and 80 actually because often you just cannot get the people on the team. We have these teams of nurses, social workers, occupational therapists, clinical psychologists. Our poor clinical psychologist – she is the only one and has to cover the whole of Hong Kong from Queen Mary to Castle Peak, so travelling each day to a different hospital. This has changed a little bit now. That shows you the very skeletal resource that we have been working with since the beginning of the program and why we are now sort of trying to consolidate, to get just adequate resources to do the job properly. We have a system there but you need adequate manpower to do it properly.

This is Professor Byron Good, a medical anthropologist from Harvard. He actually helped to interview a number of patients and workers in the early intervention program to try to find out the experience of working in this setting and the culture. He identified several factors which distinguish the early intervention service from a more generic service. First is the longitudinal contact. You are with the patient for two years and now three years. This once only opportunity is very strong, so the first few years in the illness are a unique time for the patient. Once it is passed, it is past. The good feeling is past and it will never be there again. So the sense of responsibility for the worker to have to try to do their best during that once only opportunity of the early years of the illness is very strong in the patients.

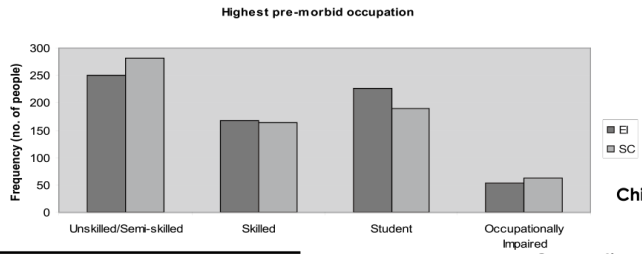
In the early days of the program there were some feelings between the early intervention services and the generic and rehabilitation services. People were saying, "Why do you have these fresh patients you can do a lot of things with? We have (a very bad term but it was a term actually used by the workers) the 'bad fish' and we can't move anything. Things are fakes, not movable". I think first of all it sort of emphasised the responsibility of the early intervention service, the people who have the chance to work with people in the early phase. But I think things also have changed a lot with our recognition of the plasticity of the brain, of how the brain is modifiable even after long years of illness with age and so on. I think that sort of view is now untenable, so the responsibility is now more equally shared between the early years and the later years.

The other thing about the unfolding journey is that while at the beginning of the illness, it is an unknown that both the worker and the patient are going to embark on this journey. Nobody knows whether the patient will be able to get back to the previous functioning or will have a relapse or will have some residual symptoms. So there is a lot of unknown that the worker has to take the patient through.

Improving Long-term Outcomes

Let's look at the result. We do have some sort of quantitative evaluation. We were not able to do an randomised control trial. We did the next best thing which is to have a cohort of patients just before the early intervention started. They matched with a cohort of patients who received the early intervention, with a separation of about one and a half years between them. The unlucky patients became ill just before the early intervention service. Those lucky patients were the first batch who received the early intervention. They were well-matched in terms of diagnosis and pre-morbid functioning. That is the outcome (Figure 6).

We only did very simple occupational function (Figure 7). If you had a full-time job, you scored one mark. Part-time 0.5, and no job, 0. This basically showed that there was an advantage for early intervention patients that more of them had jobs, actually right from the beginning. So the effect, I suspect, may have something to do with avoiding hospitalisation during the first episode.



Chi-square test - n.s.

***Occupational impairment* includes unemployment and prolonged educational stagnation**

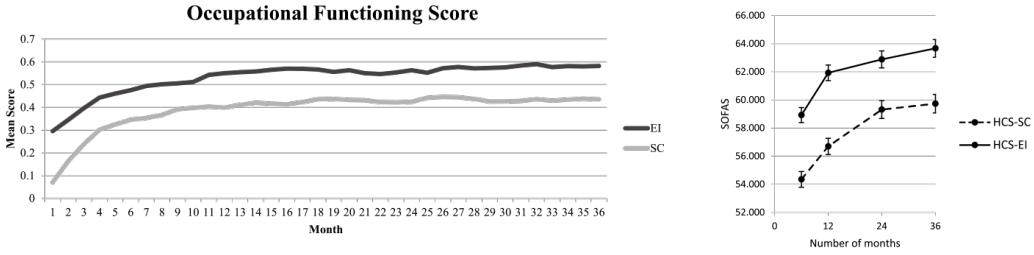
Diagnostic category	EI	SC
Schizophrenia and schizoaffective disorder	484	486
Acute and transient psychotic disorder	87	87
Psychosis NOS	46	44
Bipolar disorder with psychotic symptoms	54	54
Severe depression with psychotic symptoms	29	29

		EI	SC
Gender	Male	359 (51.3%)	359 (51.3%)
	Female	341 (48.7%)	341 (48.7%)
Mean age		21.12 (±3.41)	21.27 (±3.44)

Figure 6: Well-matched Cohorts of Patients Before and After EI

	EI	SC	F/OR (95% CI)	P
Occupational functioning score, mean (S.D.)	0.53 (0.34)	0.39 (0.35)	13.54	<0.001
SOFAS, mean (S.D.)	61.5 (10.4)	55.3 (10.9)	27.09	<0.001

a. Quantification of occupational functioning: patients obtained 1 mark for each month of full-time employment and 0.5 mark for part-time employment. An average score over 36 months was generated for group comparison.



Chen et al. (2011) Early Intervention in Psychiatry

Figure 7: Occupational Functioning 3 Years

Because of time I may have to cut short some of my presentation. But I want to go through this next part because this is important. The critical question is whether you do something, focus your resources in the first few years and you work on the group outcome in the first few years. According to our rationale, some of those effects should be able to be maintained in the longer term. That actually is on our data. In other words, whether the critical period hypothesis can be demonstrated. In order to answer this question, my colleague Shirley did this 10-year outcome study. One group of patients was well-matched, but one group of patients received early intervention for the first two years of the illness. The other group had received standard generic service. After the first two years, everybody received generic general adult psychiatry service.

The question is whether after ten years there is still a difference between those groups or whether the better result is only bare and it becomes sort of faded in ten years. This is occupational functioning data. What it shows, to cut a long story short, is that it works not only for the first three years but some of the effect is still detectable in the subsequent years. Basically what it shows is if you look at the patients, there are two patterns of occupational functioning. One is a relatively good functioning, both in the early intervention and the standard care group. Then there is functioning that is not so good. In the early intervention you can increase the functioning of that group, but it subsequently dropped. What difference the early intervention made is that it actually shifted some of these patients into the higher functioning plane, so that more proportion of the early intervention patients ended up in this sustainable, higher functioning group. This is what the analysis showed (Figure 8).

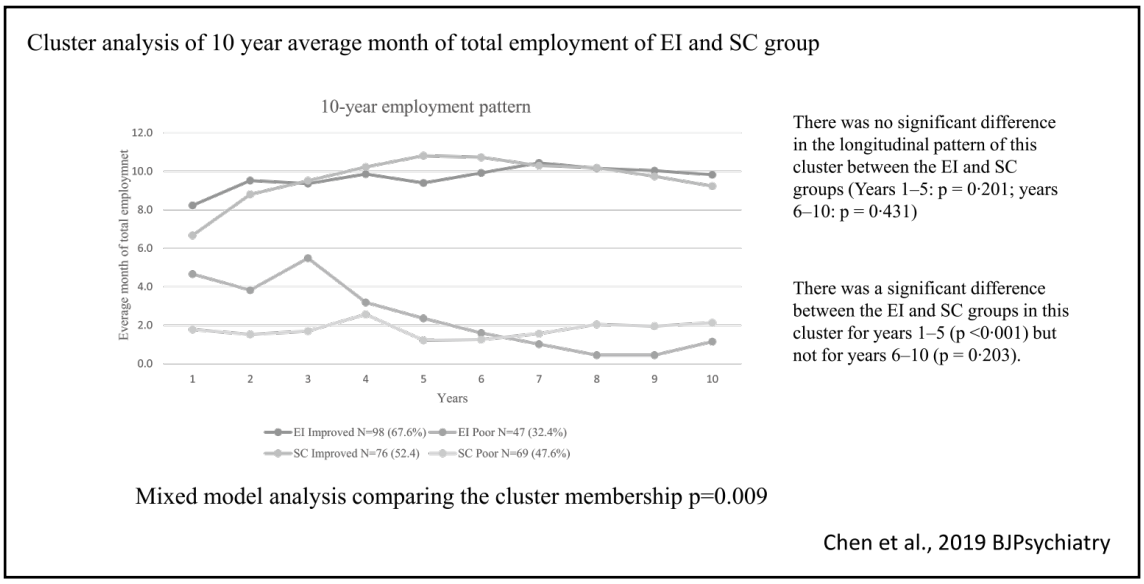


Figure 8: Longitudinal Occupational Functioning

We didn't manage to change relapse. The proportion of relapse is the same for both groups. The other thing we managed to change was suicide. We managed to reduce the number of suicides in the early days of disorder. There were some late suicides that we were not able to prevent. We actually cut down suicide by nearly half in the first three years, so again this is an important outcome for early intervention. The other important thing is hospitalisation. This was drastically reduced by something like 50% with the early intervention service. If we put all this together in a healthy economic model and calculation, the situation is that the cost of the early intervention team is about the same as the hospitalisation cost. And you are getting a better outcome. You have a situation where the improvement outcome would have justified the model.

I should end here. I do have more slides to share, but maybe another time. Thank you.