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The ‘better prognosis hypothesis’ for schizophrenia in poor countries. Is it the medication?

Glenn Brady The Schizophrenic, the bipolar and the manic-depressive

Since decades the ‘better prognosis hypothesis’ keeps looming in international research and debates. It’s the assumption, or conclusion, from international research, that outcomes for schizophrenia are better in developing countries compared with developed countries..

This complex matter continued to intrigue me. Suppose there is a difference in the course of schizophrenia between rich and poor countries (and sometimes it seems there is), what could we learn from this? Could this give us answers on how to treat people with (and after) a psychosis? Could it give us clues for more effective models of care, new protocols, new ideas and inspiration for the difficult roads to recovery? And what is the role of medication? Must we stick to the current biomedical model of treatment?

Still, in all the efforts to get a definitive and clear confirmation or rejection of this best prognosis hypothesis, more and more new questions seem to arise. Controversies about the research quality and validity, as well as the conclusions drawn from the data, are not solved yet.

Let’s start at the beginning…

In the late 1960s the World Health Organization (WHO) started a series of cross-national research on the outcome of severe mental disorders like schizophrenia. The first was the International Pilot Study of Schizophrenia (IPSS), the second the Determinants of Outcomes of Severe Mental Disorders (DOSMeD), and the third the International Study of Schizophrenia (ISoS).

In the IPSS study (Schizophrenia: An International Follow-Up Study, 1979) for example, researchers find that after a five-year follow-up, India had the most success, with 42% of schizophrenia cases reporting ‘best’ outcomes, followed by Nigeria with 33% of cases. By contrast, the rich countries performed poor: ‘best’ outcomes were seen in only 17% of cases in the USA, and in fewer than 10% in the other developed nations.

The DOSMeD figures (article in Psychological Medicine, 1992) supported these findings with rates of complete clinical remission of 37% in low income countries and 15,5% in high income countries.

In the ISoS study (article in the British Journal of Psychiatry, 2001) more than 1,000 people with schizophrenia from 16 centers around the world were followed up after the passage of 12 to 26 years. Most of them had participated in the IPSS and DOSMeD as well. The researchers concluded that the findings of this study confirmed the ‘better prognosis hypothesis’ of the 2 earlier studies.

There have been lots of discussions and doubts about the research models used in these WHO studies, which could make the results unreliable, but I will not probe too much into that here.

I want to look at the conclusions drawn from these early results about the cause of

the 'better prognosis'.

What happened after the so called WHO studies?

Is it all 'culture'?…
For instance the conclusion in the ISoS study was as follows: "A significant proportion of treated incident cases of schizophrenia achieve favourable long-term outcome. Sociocultural conditions appear to modify long-term course. Early intervention programmes focused on social as well as pharmacological treatments may realise longer-term gains." There were no hypotheses about other possible reasons for the differences find, and without any further examination one concluded that 'culture' was the main parameter.
But what's culture in this context? It could be the ongoing support and tolerance of the families in developing countries (but is this true? is there not a lot of stigma and exclusion as well?), or 'the disorganized rural labour markets', which offer more opportunities, such as field work, for people with mental illnesses and contribute to there recovery? Or is it yoga and meditation that make people in certain countries recover better?
The WHO studies did not give any answers on these questions. Or as Kulhara wrote in 2009: "We suggest that in course and outcome studies, culture should not be used as a synonym for unexplained variance and research designs focusing at other potential factors impacting course and outcome of schizophrenia are much needed." Culture is even called a Black Box (by Naren Rao cited in an article by T.Padma, Nature, 2014).
In an attempt to refine the assumptions in the WHO studies, Cohen et al (2007) reviewed 23 longitudinal studies of schizophrenia in 11 low and middle income countries. They examined clinical outcomes and patterns of course, disability and social outcomes, and mortality and suicide in people with schizophrenia. They also considered evidence about the role of families, gender effects, and the implications of evidence concerning persons with schizophrenia who have not received biomedical treatment. In their conclusions they urged for more clinical, epidemiological, and ethnographic research and: "Although a host of sociocultural factors have been cited as contributing to variation in the course and outcome of schizophrenia, e.g. family support and styles of interaction, industrialization, and urbanization, there is little direct evidence, and what exists provides little help in unpacking the "black box" of culture."
Building further on the earlier research the INTREPID 3-year pilot study by Morgan et all is now running. Morgan et all seek to understand 'the determinants of cross-cultural variations in the incidence and outcome of schizophrenia' with research in three settings in Nigeria, India and Trinidad and Tobago. They want "to identify and recruit incident cases of psychosis and representative controls, follow individuals over time while minimising attrition, and establish a core set of cross-culturally valid instruments and procedures to collate data on psychopathology, social and biological exposures, and outcome".

Is it all culture? No clear answers yet. Work in progress.

Is it the medication?…
For example Cohen et all (2007) find 4 studies of schizophrenia (China, Ethiopia, two in India) where the influence of 'the lack of biomedical treatment' was measured. Overall, people who did not receive antipsychotic medication seem to have a worse clinical outcome after follow ups between 1-4 years. Cohen et all concluded that "In sum, these findings suggest that good outcomes cannot be assumed for untreated schizophrenia in low- and middle-income countries and that (biomedical) treatment does make a significant difference." But in these 4 studies the follow-up period was


Glenn Brady Medication time at Rosemount

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quite short and not representing patients who may have been recovered after say 10-20 years. And the main focus was 'clinical state' or the improvement in positive symptoms (hallucinations, delusions, thought disorders) and not the general level of functioning or wellbeing.
And Kulhara (2011) stated that "Patients seem to be doing better in poorer countries, despite limited resources such as health facilities and health infrastructure, and treatment facilities".

But what happens if you turn this around and say: 'Patients seem to be doing better in poorer countries, because the limited resources such as health facilities and health infrastructure, and treatment facilities'?

This is what Robert Whitaker seems to be doing in his article A Schizophrenia Mystery Solved? (2010). Whitaker writes about the WHO research series: "Any thought that a variance in medical treatment might be the cause of the disparity in outcomes was mostly forgotten. But, if we return to their initial hypothesis today, it seems fair to raise this long-neglected question: Is it possible that a paradigm of care that involves selected, limited use of antipsychotics would produce better long-term outcomes?"
Whitaker sees extra support for his hypothesis in the W-SOHO report by Karagianis et al, 2009. In this, also called Eli Lilly study, with data from more then 17,000 patients with schizophrenia in 37 countries, almost all patients studied used antipsychotic drugs at a regular base. The Eli Lilly investigators concluded that patients in 'developing' and 'developed' countries showed a 'substantial similarity' in their outcomes, which could be described as fairly poor. Which led Withaker to conclude that: "In this Eli Lilly study, the disparity in outcomes between patients in developing and developed countries had disappeared. The patients in the developing countries were no longer enjoying the 'exceptionally good social outcome' they had in the earlier WHO studies". So, it seems that when one leaves patients out who are not on antipsychotics, the best prognoses hypothesis vanished.

Is 'no-medication' the main factor in the best prognosis hypothesis?
Recent research from the USA and the Netherlands seems to give his hypothesis some extra fuel:

What happens if people living with schizophrenia are followed for longer periods?
In the Chicago Follow-Up studies Martin Harrow, followed 145 people diagnosed either with schizophrenia or a milder psychotic disorder for 15 years (published in 2007) and 139 patients for 20 years (published in 2012). These were prospective, naturalistic studies, which means that all the patients were initially treated with antipsychotics and then Harrow followed up at regular intervals to assess how they were doing, and whether they were using antipsychotics.
His results: At each follow-up 30–40% of all patients with schizophrenia were no longer on antipsychotics. Starting at the 4.5-year follow-ups and continuing thereafter, patients with schizophrenia not on antipsychotics for prolonged periods were significantly less likely to be psychotic and experienced more periods of recovery; they also had more favorable risk and protective factors. Patients with schizophrenia off antipsychotics for prolonged periods did not relapse more frequently.

But Harrow's study was a naturalistic one and not randomized. This means that the group of patients on medication and the group of patients off medication, could have had different characteristics beforehand (selection bias). Maybe they were already better off or had more protective factors like support and work.

This weak point in the Harrow results was overthrown in the randomized study of long-term outcomes by Wunderink, 2013. In this Dutch study of adults with a first episode of psychosis, all 128 patients were stabilized on antipsychotics for six months, and then they were randomized either to a 'drug discontinuation/drug reduction' group (the DR group), or to standard drug maintenance (the MT group). In other words, this was a randomized study designed to see which treatment protocol produced better outcomes: tapering first-episode patients from their

antipsychotics (or down to a low dose), or standard drug maintenance, at usual doses.
After 7 years, 103 patients (80.5%) of 128 patients who were included in the original trial were located and consented to follow-up assessment.
Results: At the end of seven years, those in the DR group had a much higher recovery rate (40.4% versus 17.6%.). The difference in recovery rate was due to the fact that those in the DR group had much better functional outcomes. At the end of 18 months, there was little difference in functional outcomes. The divergence in functional outcomes began to appear after that point.
In terms of risk of relapse (control of clinical symptoms), the relapse rate at 18 months was in fact higher for the DR group (43% vs 21% for the MT group). But from that point on, relapses occurred at a greater rate in the MT group, such that by the end of three years, the relapse rate was roughly the same for the two groups. At the end of seven years, the relapse rate was slightly lower for the DR group (61.5% versus 68.6% for the MT group).
This led to the following conclusions:
-Schizophrenia treatment strategy research should include recovery or functional remission rates as their primary outcome (like daily living and self-care, working and studying, and relationships with others);
-Schizophrenia outcome research should also include long-term follow-up for more than 2 years, even up to 7 years or longer;
-Antipsychotics could hamper long-term functioning and recovery.

The long-term benefits of antipsychotic maintenance treatment following a first-episode psychosis is doubted and there is a strong need for studying alternative treatment strategies and protocols for prescribing antipsychotics.

A new era in psychiatry?


Schizophrenia by Craig Finn

After decades of a psychiatry with the optimistic belief that one could cure or control severe mental disorders with psychotropic medication, an new era in psychiatry seems to emerge.
There have always been people and organization pleading for alternative treatments for people with psychosis like e.g. (for further reading) Mad in America, the Icarus Project, the Open Dialogue Approach in Finland, Paris Williams in Rethinking Madness and the Soteria network. But recently even Thomas Insel (director of the National Institute of Mental Health USA) writes in his blog in 2013: “It appears that what we currently call ‘schizophrenia’ may comprise disorders with quite different trajectories. For some people, remaining on medication long-term might impede a full return to wellness. For others, discontinuing medication can be disastrous. For all, we need to realize that reducing the so-called positive symptoms (hallucinations and delusions) may be necessary, but is rarely sufficient for a return to normal functioning. Neither first nor second generation antipsychotic medications do much to help with the so-called negative symptoms (lack of feeling, lack of motivation) or the problems with attention and judgment that may be major barriers to leading a productive, healthy life. Family education, supported employment, and cognitive behavioral therapy have all demonstrated efficacy in reducing the likelihood of relapse events, increasing the ability to function in daily life, and improving problem-solving and interpersonal skills. NIMH is supporting research on interventions that focus on a combination of approaches—symptom remission, family engagement, and functional recovery.”

In a recent editorial in the British Journal of Psychiatry (‘Towards a more nuanced Global Mental Health’) White and Sashidharan warn against an over-reliance on the Western biomedical model as well. They argue that in the efforts to scale up of mental health services in low and middle income countries (like the WHO mh-GAP initiative) “we must critically reflect on the merits of biomedical conceptualizations of mental health and weigh these with local perspectives and local resources (including indigenous healing, social support networks, rights-based organizations and family support)” and “Unlike physical health problems (such as polio, influenza, and HIV), the evidence for biomedical causes of mental illnesses (such as depression and schizophrenia) remains fairly weak. There is also growing evidence that aligning the treatment of mental health difficulties too closely to a biomedical model may have potentially detrimental effects. For example, a reliance on biomedical causal explanations of mental health difficulties has been associated with increased prejudice, fear, and desire for distance from individuals diagnosed with psychiatric disorders. Although, psychotropic medication can be helpful in managing distress, there are also limitations to this approach. For example, long-term use of antipsychotic medications can contribute to increased morbidity (including metabolic disorders and cardiovascular conditions), and risk of premature mortality linked to sudden cardiac death. Important questions have also been raised about the methodologies employed by pharmaceutical companies to evidence the effectiveness of psychotropic medication. There is a danger that biomedical explanations of mental health difficulties and an over-reliance on psychotropic medication may serve to inhibit the utilization of alternative forms of support.”

Conclusions:
The ‘better prognosis hypothesis’ for schizophrenia in poor countries. Is it true? Is it the medication? And what does this mean for future research, and treatment protocols?

1. It seems plausible that generally people living with schizophrenia in poor countries are better off regarding there overall functioning and recovery. But, due to limitations and inaccuracies in the studies so far, this is still more an interesting hypothesis then a strong fact.
2. Although limited in scale and generalizability the Harrow and Wunderink studies give some evidence in the direction of negative long term effects of anti-psychotic drugs.
3. So, whether it is true or not that people with schizophrenia in poor countries have a better prognosis, it seems obvious that the possible (long term) negative effects of anti-psychotic medication is bigger then assumed in the last decades.
4. It’s possible that not/never receiving or discontinuation of anti-psychotic medication, is one of the main determinants in the ‘better prognosis hypothesis’, and underestimated thus far.
5. In order to get a full picture of the onset, nature and long term outcome of schizophrenia in individuals, or in countries, or even between countries, one must take medication as one of the possible variables in the study.
6. There is a strong urge to develop and study alternatives in the treatment of psychosis and schizophrenia. Maybe, in this regard, we can learn a lot from poor countries!
7. The call for new standards of care for people living with schizophrenia is heard here and there, but, given the hypotheses and evidences mentioned above, I think not hard enough yet.

Roos Korste, psychologist, international trainer and blogger

By in2mentalhealth, on October 5, 2014 at 4:28 pm, under in2mentalhealth Blog Posts. Tags: antipsychotics, developing countries, LMIC, mental illness, psychosis, recovery, schizophrenia.
8 Comments

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Comments

Dr Sam Obasi On October 6, 2014 at 10:34 pm Permalink | Reply

It might not be advisable to completely disregard the role of the sociocultural environment on the noted disparity in treatment outcome of schizophrenia between the developed and developing nations. Other interesting studies may also indicate a huge disparity in prevalence in the two socio-cultural -cum-economic environments.

in2mentalhealth On October 8, 2014 at 4:08 pm Permalink | Reply

Yes, indeed. Thanks for the reply!

Ron Unger On October 13, 2014 at 6:23 am Permalink | Reply

Thanks for writing about the disturbing yet important possibility that antipsychotic drugs are worsening mental health outcomes – on top of all the ways they impair physical health and often subjective sense of wellbeing!

in2mentalhealth On October 15, 2014 at 9:39 am Permalink | Reply

Hi Ron. Thanks for your comment. I like your work and website (http://recoveryfromschizophrenia.org).
Hope this blog post helps to improve the understanding of the positive and negative effects of anti-psychotics. Much more research and writing about this must be done.

Desmond Raymond On April 20, 2016 at 2:27 pm Permalink | Reply

My son has schizophrenia when He was 17 years of age as a result of a car crash, for 6 years i was really fed up with taking care of him as there was no improvement on his condition. Just taking the government money and Not looking at the progress part, I really needed some help to get him back to the way he used to be as a normal son. Because he doesn't go anywhere apart doing screaming at the voices he hears and saying abusive words to me. A member of my church gave me Dr Joseph's email address, i contacted him and i narrated all to him and he told me to wipe my tears. He sent me this very powerful medication which i gave my son and to my amazement within the space of days he was back to normal self and nothing has changed since. Contact the doctor on this email josephakormah@gmail.com

wesley blake On August 24, 2016 at 1:44 am Permalink | Reply

This was how i got a cure for my son who was diagnosed with schizophrenia 9 years ago when he was 19. He told us that he got messages and he heard people telling him that he should hurt himself. He had a terrible temper with cursing and violence towards me and his dad. The doctor gave him different anti-psychotic drugs like Zyprexa, prolixin, risperidone but all this even elevated the condition because he became worse over the years not until last two years that

help came our way. I got Dr Joseph’s contact from an old colleague of mine who relocated to Kansas city and he told me about this herbal medicine that can put an end to my son’s condition. I contacted the doctor and i explained it all to him and he told me all will be well. I got the medicine and gave him as instructed and before i knew it he was normal again, no side effects at all. I am writing this today because i needed to be sure the cure was a permanent one which it is. I know what schizo is and how heart aching it can be but i tell you today that there is a cure for it. Contact the doctor on josephakormah@gmail.com for psychosis, schizophrenia, bipolar disorder, he can help you too

Robert Drake On January 25, 2017 at 11:07 pm Permalink | Reply 

Well written, though the conclusions and perspective are actually not challenging or very brave. There is more research supporting the conclusion that the treatments are deleterious and suppressive of health and longevity than there is justification to pacify societal elements that do not conform. Not to mention the intellectual costs of the narrowing of “permissible” knowledge and experience. Though the advocates of keeping it in place are biasing your account of this. Thanks for referencing Whitaker, he can debunk the results on the basis of the treatments alone, not withstanding the location.

Trackbacks

By „Wir benötigen mehr psychiatrische und psychotherapeutische Hilfsangebote.“ – psychoriginal on October 16, 2016 at 8:49 pm

[…] Die Rückfallraten bei Psychiatriepatienten sind generell sehr hoch. Ergebnisse einer Vielzahl an Studien, unter anderem der WHO deuten darauf hin, dass die Verläufe für „Schizophrenie“ in […]

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