

**RANZCP Auckland Training Programme**  
**Mock Objective Structured Clinical Examination**  
**Bye for Station No. 1**  
**April 2009**

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**Reading Bye for Station No. 1 - Instructions to Candidate**

**You have twenty (20) minutes to complete this station.**

You are a community mental health centre registrar and are shortly going to meet with a patient, Stuart Williams, who has a history of recurrent major depression.

You saw him once before, about 3 months ago, during this rotation. He wrote to you recently, asking for a slightly earlier appointment and enclosing several articles from the internet which he wants to discuss. These are attached.

**Your tasks are to:**

- **Refresh your memory about the details of Stuart's case from his clinical records**
- **Familiarise yourself with the material he sent you, which he wishes to discuss**

You are allowed to make marks or notes on the information provided in this Bye, and you should take your copy with you into the next Station for the appointment with Stuart.

## **Summary of history from records - Stuart Williams**

### **Demographics:**

Stuart is a 30 year old man who lives locally, in his own home. He was originally from the UK and came here as a adolescent. He is married to Liz and is the sales manager at a local Woolworths supermarket branch. He and Liz have one child, Harry, who is aged 3. Liz works part-time as a caregiver at a nearby rest home.

### **Psychiatric History:**

Stuart has had three episodes of major depression since age 20. The first episode occurred when he was at University doing his MBA, before he met his wife. At that time he was stressed by his final exams. The second episode occurred after his son's birth, three years ago, when the baby was 3 months old and Stuart was not getting much sleep, and the third episode occurred a year ago when Stuart's job was threatened due to financial problems affecting the company. Stuart did not in fact lose his job. On each occasion he was treated with antidepressants - fluoxetine 40 mgs daily during the initial two episodes, but this was ineffective a year ago, however he eventually responded to venlafaxine.

Stuart has had intermittent follow-up with the community mental health team since the episode 3 years ago. He was referred back to his GP 2 years ago, then re-referred to mental health services for follow-up a year ago when the depression recurred. Following the most recent episode he also had a course of CBT with the community team's psychologist. He had 12 sessions and apparently found this useful. When you saw him last he said that he used the techniques if he felt that he was getting stressed.

When depressed, the notes record that Stuart develops classical melancholic features with slowing, low energy, poor concentration, hopelessness, anxious and guilty thoughts, anhedonia, early waking and lack of appetite with weight loss. He has not had psychotic symptoms during his depressions. He does develop suicidal ideas when depressed but apparently only ever acted on these initially, at age 20. Stuart however told you that these thoughts worried his wife a great deal, during his last episode. At age 20 he took a moderate overdose of sleeping pills and was briefly medically admitted. His Relapse Prevention Plan notes that when he relapses he deteriorates rapidly, across 1-2 weeks. The Relapse Prevention Plan was last revised a year ago.

### **Current Medication:**

Venlafaxine 225mgs daily (75mg with breakfast and 150mg with his evening meal).

When last seen he did not complain of any side-effects on venlafaxine except for increased sweating.

### **Medical History:**

Stuart is well, with no significant medical history.

### **Alcohol and Other Drugs History:**

No history of illicit drug use. He drinks a little alcohol socially, not to excess. Is a non-smoker.

### **Brief details of Family History:**

Stuart's father also has a diagnosis of recurrent depression, which has apparently worsened since he retired at age 60. His father is treated with fluoxetine and required ECT during the two most recent episodes, so as to recover fully. No other family psychiatric history or drug/alcohol history. Stuart's mother is treated for hypertension and his father has mild COAD from smoking. Stuart is close to his parents who live locally and he has a younger sister, Julie, who lives with her husband in Nelson.

**Personal History:**

Stuart's development was normal and he described a happy childhood, although his parents were not well off so there was some financial stress. The records note that Stuart has said that this made him determined always to have a job and to provide for his family. His father worked as a taxi-driver in the UK and after emigrating. His mother worked part-time at a local supermarket, after Stuart and his sister started attending school. Stuart was an average scholar but enjoyed school, making friends well and playing sport. He met his wife Liz after leaving university and the marriage is stable and happy. Both of them are well, as is their son, Harry. Stuart keeps fit and goes jogging regularly. He is not especially religious, and his main interest outside work is sport, especially rugby and cricket, which he follows on TV or by going to matches. He has several close friends, and socialises with them and with his own and Liz's family, who also live nearby.

**Forensic History:**

Nil.

**Mental State (when last seen):**

Stuart was well and euthymic, with no residual depressive symptoms. He admitted to still being worried about the world financial climate, but felt that the company had weathered the worst of it and that his job would most likely be safe. He said that he tried not to fret about this. His sleep and eating were good, and that all was well at home with Liz and his son. He had no psychotic or anxiety symptoms, and denied ever having had manic symptoms. He had no suicidal ideas. He was alert and insightful, with intact judgement.

**Diagnosis:**

- I Major Depressive Disorder - recurrent, severe.
- II nil
- III nil
- IV Financial climate affecting job security
- V Currently 70-80 (functioning well)

## Breaking News February 2008:

### New Study: SSRI Antidepressants 'Clinically Insignificant'

#### For Most People

A new study recently published is sure to set off another storm in the ongoing debate about the widespread prescription of antidepressants. Professor Irving Kirsch at the University of Hull and colleagues in the US and Canada report that new generation 'SSRI' antidepressants like Prozac or Seroxat mostly fall, "below the recommended criteria for clinical significance" (Kirsch et al. 2008). In other words, the most modern drugs prescribed for depression generally don't work.

*These are the articles I want to discuss with you.*

*I'm wondering what this means in terms of my treatment - maybe the venlafaxine isn't doing much?*

*Anyway, I'll see you at the clinic.*

*- thanks, Stuart*

The study was particularly interested in whether the drugs had different effects on people with different levels of depression. Here is what they found:

1. Mild depression: not tested as mild depression is usually treated with a 'talking therapy' rather than antidepressants.
2. Moderate depression: antidepressants made "virtually no difference".
3. Severe depression: antidepressants had a "small and clinically **insignificant**" effect.
4. Most severe depression: antidepressants had a significant clinical benefit - but see below...

#### Effectiveness limited even for severe depression

When Professor Kirsch and colleagues looked more closely at the data for those who were most severely depressed they uncovered more bad news for drug manufacturers. The antidepressant effect the drugs appeared to have, though small, was largely due to differences in the effects that the placebo had on the control group rather than better response to the drug.

Let's unpack this a little. The placebo effect means that even when you give someone a 'fake' antidepressant they still improve a little, simply because they expect to. This effect is so powerful and reliable that to be taken seriously drug studies have to compare depressed people taking an antidepressant to a control group taking a placebo.

What Professor Kirsch and colleagues found was that while the placebo effect was present for moderately depressed people, it disappeared for those who were the most severely depressed. This meant that antidepressants weren't having any more effect on those who were more depressed, it's just that *in comparison to the control group* that's how it appeared. In reality what was happening was that the control group weren't responding to the placebo.

The authors, therefore, conclude that there's no point prescribing SSRI antidepressants to anyone but the most severely depressed people, unless other treatments have been tried and have failed.

### **Can we believe this study?**

So the question is: can we believe the results? Well, the study used data from 47 clinical trials that had been submitted to the US Food and Drugs Administration (FDA). The FDA already has a rigorous set of criteria for including studies, so this suggests only quality studies were included.

The data from all these studies were then combined using a statistical technique called 'meta-analysis'. This means all the studies were collected together and analysed as though they were all one huge study. By doing this you can increase the power of the study significantly.

Like many statistical techniques, though, there is some debate about the use of meta-analyses. For example it is often argued that they lump together studies with different protocols so that effectively you end up comparing apples with oranges. Whether this sort of criticism is valid depends on the study's nitty-gritty details.

### **High stakes**

More broadly, we have to be careful about drawing conclusions from a single piece of work. There's no doubt how high the stakes are for everyone: Professor Irving Kirsch has built a career on showing the power of the placebo effect, pharmaceutical companies have built their fortunes on studies proclaiming the benefits of SSRI antidepressants, while patients are stuck in the middle.

Despite this, the evidence does seem to be mounting up against SSRI antidepressants. Although previous studies seemed to show SSRIs were effective, recent work has suggested this might be due to a bias in the way research is reported (Turner et al., 2008). Studies which show no effect have a tendency to be 'filed' rather than being submitted for publication. This can result in a much more rosy picture being painted of a drug's effectiveness than is really the case.

Either way, considering the number of people worldwide currently taking SSRI antidepressants, we can be sure this isn't the end of the story.

### **References**

- Kirsch, I., Deacon, B. J., Huedo-Medina, T. B., Scoboria, A., Moore, T. J., & Johnson, B. T. (2008). [Initial severity and antidepressant benefits: a meta-analysis of data submitted to the food and drug administration](#), PLoS Medicine, 5(2), e45 EP
- Turner, E. H., Matthews, A. M., Linardatos, E., Tell, R. A., & Rosenthal, R. (2008). [Selective publication of antidepressant trials and its influence on apparent efficacy](#), New England Journal of Medicine, 358(3), 252-260.

## **Human Givens Institute welcomes Irving Kirsch's meta analysis of antidepressant drug trials**

**This week, Professor Irving Kirsch and his colleagues at the University of Hull released the long-awaited results of an extensive meta-analysis of clinical trial data for new generation antidepressants. Their findings were splashed (in simplified terms) over the front pages of most of the major newspapers: "Antidepressants do not work".**

The Royal Society of Chemistry's website

**<http://www.rsc.org/chemistryworld/News/2008/February/26020802.asp#>**

summarises the research and its results eloquently:

"Kirsch and colleagues found that there was a statistically significant benefit in the use of SSRIs over placebo - but that the difference was smaller than the standard of 'clinical significance' set down by the UK's National Institute for Clinical Excellence (NICE) for all but the most depressed patients. ... Interestingly, the team also found that patients' response to placebo across all the trials was 'exceptionally large' - an indication of the complexity of the disorder. It was only the fact that the most severely depressed patients showed a much lower response to placebo that made the drug response clinically significant in this group of patients."

By carrying out a meta-analysis (a statistical review of many trials which combines all the results into one overall conclusion), Kirsch and his colleagues were attempting to discover any trends that have not previously shown up in individual studies.

One of the reasons this latest research is so significant is that it also included a number of previously unpublished studies which Kirsch obtained from pharmaceutical companies

under the Freedom of Information Act. By so doing, Kirsch says that his meta-analysis avoids the data bias caused by pharmaceutical companies selectively reporting only positive results. Although these additional studies had been submitted to the Food and Drug Administration (FDA), not all of them were made available to NICE when it was drawing up its guidelines.

An interesting, related article ('It doesn't work, but do it anyway') in the forthcoming issue of the 'Human Givens' journal ([LINK](#)) discusses the limitations of the current 'Gold Standard' of evidence-based healthcare – the randomised controlled trial (RCT) – and how easily the results from such trials can be distorted to mean almost whatever the agency funding the trial wants it to mean (whether they choose to publish trials or not).

The Human Givens Institute welcomes Kirsch's research as it throws more light on whether SSRIs are as helpful as is often maintained and supports the position we have maintained on antidepressants for many years. However a caution is needed as antidepressants have been shown to be demonstrably beneficial for certain patient groups, particularly those with severe cases of depression, and until we have enough people trained to treat depression effectively by other methods, such as psychotherapy, they still have a helpful role to play in relieving distress.

# Depression drugs don't work, finds data review

David Rose

Millions of people taking commonly prescribed antidepressants such as Prozac and Seroxat might as well be taking a placebo, according to the first study to include unpublished evidence.

The new generation of antidepressant drugs work no better than a placebo for the majority of patients with mild or even severe depression, comprehensive research of clinical trials has found.

The researchers said that the drug was more effective than a placebo in severely depressed patients but that this was because of a decreased placebo effect.

The study, described as "fantastically important" by British experts, comes as the Government publishes plans to help people to manage depression without popping pills.

More than £291 million was spent on antidepressants in 2006, including nearly £120 million on SSRIs. As many as one in five people suffers depression at some point. With that in mind, ministers will today publish plans to train 3,600 therapists to treat depression. Spending on counselling and other psychological therapies will rise to at least £30 million a year.

The study, by Irving Kirsch, from the Department of Psychology at the University of Hull, is the first to examine both published and unpublished evidence of the effectiveness of selective serotonin reuptake inhibitors (SSRIs), which account for 16 million NHS prescriptions a year. It suggests that the effectiveness of the drugs may have been exaggerated in the past by drugs companies cherry-picking the best results for publication.

The National Institute for Health and Clinical Excellence (NICE), which is due to review its guidance on treating depression, said that it would consider the study.

Mental health charities say that most GPs admit that they are still overprescribing SSRIs, which are considered as effective as older drugs but with fewer side-effects. SSRIs account for more than half of all antidepressant prescriptions, despite guidelines from NICE in 2004 that they should not be used as a first-stop remedy.

American and British experts led by Professor Kirsch examined the clinical trials



submitted to gain licences for four commonly used SSRIs, including fluoxetine (better known as Prozac), venlafaxine (Efexor) and paroxetine (Seroxat).

The study is published today in the journal *PLoS (Public Library of Science) Medicine*. Analysing both the unpublished and published data from the trials, the team found little evidence that the drugs were much better than a placebo.

“Given these results there seems little reason to prescribe antidepressant medication to any but the most severely depressed patients, unless alternative treatments have failed,” Professor Kirsch said. “The difference in improvement between patients taking placebos and patients taking antidepressants is not very great. This means that depressed people can improve without chemical treatments.” He added that the study “raises serious issues that need to be addressed surrounding drug licensing and how drug trial data is reported”.

The data for all 47 clinical trials for the drugs were released by the US Food and Drug Administration under freedom of information rules. They included unpublished trials that were not made available to NICE when it recommended the drugs for use on the NHS. “Had NICE seen all the relevant unpublished studies, it might have come to a different conclusion,” Professor Kirsch said.

Tim Kendall, a deputy director of the Royal College of Psychiatrists Research Unit, who helped to formulate the NICE guidance, said that the findings were “fantastically important” and that it was “dangerous” for drug companies not to have to publish their full data. He added: “Three of these drugs are some of the most commonly used antidepressants in this country. It’s not mandatory for drug companies to publish all this research. I think it should be.”

SSRIs are not prescribed to patients under 18 because of the risk of suicide. Drugs watchdogs in Europe are considering tighter controls on the development of new medicines, *The Times* reported this month, and may soon require regulators to monitor psychiatric effects and the risk of suicide more closely during clinical trials.

A spokesman for GlaxoSmithKline, which makes Seroxat, said: “The authors have failed to acknowledge the very positive benefits these treatments have provided to patients and their families dealing with depression and their conclusions are at odds with what has been seen in actual clinical practice. This one study should not be used to cause unnecessary alarm and concern for patients.”

A spokesman for Eli Lilly, which makes Prozac, said: “Extensive scientific and medical experience has demonstrated that fluoxetine is an effective antidepressant.”