1: The fate of the mentally ill
“If there is one central intellectual reality at the end of the twentieth century, it is that the biological approach to psychiatry - treating mental illness as a genetically influenced disorder of the brain chemistry - has been a smashing success.”

Shorter (1998)
The Treatment of Severe Mental Illness

Throughout much of the history of psychiatry, mentally ill patients have been ‘warehoused’ in asylums such as this one: The North Wales Hospital in Denbigh
Little evidence of improvements in outcome

Despite apparent advances in treatment, outcomes remain disappointing:

- Warner (1985) found that rates of recovery from schizophrenia have not improved since the Victorian era.

- Whitaker (2005) analysed US data on outcomes from severe mental illness 1948-2000: *greater psychiatric disability today*!

- Healy et al. (2005) examined records of service utilization in North Wales 1896-1986. *Schizophrenia patients have higher suicide rates today, and bed utilisation has not improved*!

- Data indicates that outcomes are at least as good and probably better in the developing world than in the West (WHO, 1979; Jablensky et al. 1992)

WHERE HAVE WE GONE WRONG? THERE IS A POVERTY OF IDEAS, NOT JUST RESOURCES.
2: The argument –
there is no such thing as ‘schizophrenia’

(what’s the phenotype?)
What are diagnoses for?

Psychiatry and related disciplines cannot proceed without clear ways of describing the problems encountered in the psychiatric clinic. Such descriptions should be helpful to both clinicians and patients.

They are needed to:

- Facilitate communications between clinicians and researchers
- Guide research into the causes of psychiatric distress
- Guide treatment decisions
The origins of our diagnostic concepts

Emil Kraepelin (1856-1926) created the categorical approach to psychiatric diagnosis.

Karl Jaspers argued that psychotic symptoms are meaningless.
Emil Kraepelin’s big idea

Kraepelin believed that diagnosis by symptoms would be a Rosseta stone that would lead to an understanding of aetiology:

According to this viewpoint, it should be possible to specify exactly how many psychoses there are!
Emil Kraepelin’s big idea

On the basis of symptom and outcome data, he concluded that there are three main types of psychosis:

• dementia praecox (schizophrenia)
• manic depression (including unipolar illness)
• paranoia (delusional disorder)
These assumptions have been embraced by modern psychiatrists, for example those who designed the influential third edition of the American Psychiatric Association’s Diagnostic and Statistical Manual (DSM-III), who styled themselves as ‘neoKraepelinians’…….
Klerman’s (1978) neoKraepelinian manifesto

4. There is a boundary between the normal and the sick.

5. There are discrete mental illnesses. There is not one, but many mental illnesses.

6. The focus of psychiatric physicians should be particularly on the biological aspects of mental illness.
The use of diagnoses today

Following DSM-III, neoKraepelinian diagnoses have become the dominant method of description in psychiatry. They are used in research papers, textbooks (even those written by psychologists) and clinical reports.

Emil Kraepelin (1856-1926)
The use of diagnoses today

They sometimes seem to have acquired a fetishistic quality:

Graham’, a 29 year old patient, was incensed by receiving a letter from his psychiatrist telling him that he suffered from ‘paranoid schizophrenia’. Graham believed that he had ‘PTSD’.

Graham’s difficulties could easily be understood in terms of his past experiences of a road traffic accident (after which a clinical psychologist diagnosed him as suffering from PTSD) and with the British Army in Northern Ireland. His main symptom was paranoia, and the coercive behaviour of local psychiatric services was making him feel more paranoid.
Although Kraepelin was by no means an inhumane man, the assumption that madness is a brain disease has:

- encouraged the use of drastic biomedical interventions
- discouraged attempts to address patients’ psychological needs
- denied patients a voice that might otherwise have been raised against mistreatment
The argument

NeoKraepelinian diagnoses are not fit for any of the purposes for which they have been designed.

They are not much better than star signs (another persistent and widely accepted diagnostic system).
3: Communication between clinicians and researchers

(reliability and related issues)
Reliability

*Reliability* refers to the consistency of diagnosis; *validity* to its usefulness (scientific value). Diagnoses can be reliable without being valid, but not valid without being reliable.

Spitzer & Fliess (1974) introduced the kappa statistic (varying between 0 and 1) to correct for the likelihood of agreement by chance:

\[ k = \frac{Po - Pc}{1 - Pc} \]

where Po is the proportion of observed agreement between clinicians and Pc is the level of agreement expected by chance.

Kappa gives a standard measure of diagnostic agreement.
Spitzer & Fliess’ (1974) review

The studies from which the data were derived were I Schmidt and Fonda (1956); II Krietman (1961); III Beck et al. (1962); IV Sandifer et al. (1964); V Cooper et al. (1972); VI Spitzer et al. (1974). The data from V (the US-UK Diagnostic Study) are analyzed separately for the New York and London samples.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>US</th>
<th>UK</th>
<th>VI</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental deficiency</td>
<td>.72</td>
<td>.72</td>
<td>.72</td>
<td>.72</td>
<td>.68</td>
<td>.71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organic brain syndrome</td>
<td>.82</td>
<td>.90</td>
<td>.44</td>
<td>.44</td>
<td>.74</td>
<td>.68</td>
<td>.59</td>
<td>.77</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute brain syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic brain syndrome</td>
<td>.64</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.64</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>.73</td>
<td>.62</td>
<td>.42</td>
<td>.43</td>
<td>.47</td>
<td></td>
<td>.44</td>
<td>.41</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>.77</td>
<td>.42</td>
<td>.32</td>
<td>.44</td>
<td>.33</td>
<td>.21</td>
<td>.26</td>
<td>.24</td>
</tr>
<tr>
<td>Mood disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurotic depression</td>
<td>.47</td>
<td>.20</td>
<td>.24</td>
<td>.30</td>
<td>.33</td>
<td>.21</td>
<td>.26</td>
<td>.24</td>
</tr>
<tr>
<td>Manic depression</td>
<td>.33</td>
<td>.24</td>
<td>.30</td>
<td>.40</td>
<td>.33</td>
<td>.21</td>
<td>.26</td>
<td>.24</td>
</tr>
<tr>
<td>Involutional depression</td>
<td>.38</td>
<td>.30</td>
<td>.32</td>
<td>.32</td>
<td>.33</td>
<td>.21</td>
<td>.26</td>
<td>.24</td>
</tr>
<tr>
<td>Personality disorder</td>
<td>.33</td>
<td>.33</td>
<td>.26</td>
<td>.32</td>
<td>.33</td>
<td>.21</td>
<td>.26</td>
<td>.24</td>
</tr>
<tr>
<td>Anxiety reaction</td>
<td>.45</td>
<td>.45</td>
<td>.45</td>
<td>.45</td>
<td>.45</td>
<td>.45</td>
<td>.45</td>
<td>.45</td>
</tr>
<tr>
<td>Psychophysiologic reaction</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
<td>.38</td>
</tr>
</tbody>
</table>
Reliability

The problem of reliability was foremost in the minds of the designers of DSM-III.

After it was published, Hyler, Williams and Spitzer (1982) argued the reliability of DSM-III diagnoses was “extremely good” and Gerald Klerman (1986) suggested that the reliability problem has, “in principle, been solved”.

Kutchins and Kirk (1997) argued that, “The DSM revolution in reliability has been a revolution in rhetoric, not in reality”.

Reviewing DSM-III field trials, in which diagnoses were made in ideal circumstances (trained raters using a standardised interview schedule, taking as long as they liked) kappa values often failed to exceed 0.70.
Comorbidity

If psychiatric diagnoses identify genuine disorders, only very unlucky patients should get more than one diagnosis.

Soon after DSM-III was published, it was noticed that the exclusion criteria in the definitions led to underestimation of the ‘comorbidity’ between symptoms. Robbins et al. (1981) suspended these rules on data from the Epidemiological Catchment Area Study:

- Given schizophrenia, the odds ratio for mania was 46
- Given schizophrenia, the odds ratio for depression was 14.

Amazingly, they concluded: “The most likely explanation for co-occurrence is that having one disorder puts the affected person at risk of developing other disorders”
### The vanishing consensus effect

Different diagnostic systems diagnose different patients as schizophrenic (Brockington, 1990). Data from van Os et al. (1999):

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>RDC</th>
<th>DSM-III-R</th>
<th>ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Schizophreniform disorder</td>
<td>20</td>
<td>2.8</td>
<td>-</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>268</td>
<td>38.0</td>
<td>371</td>
</tr>
<tr>
<td>Schizoaffective manic</td>
<td>98</td>
<td>13.9</td>
<td>13</td>
</tr>
<tr>
<td>Schizoaffective bipolar</td>
<td>129</td>
<td>18.3</td>
<td>-</td>
</tr>
<tr>
<td>Schizoaffective depressed</td>
<td>118</td>
<td>16.7</td>
<td>-</td>
</tr>
<tr>
<td>Major depression</td>
<td>16</td>
<td>2.3</td>
<td>71</td>
</tr>
<tr>
<td>Mania</td>
<td>18</td>
<td>2.6</td>
<td>87</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>16</td>
<td>2.3</td>
<td>66</td>
</tr>
<tr>
<td>Unspecified functional psychosis</td>
<td>43</td>
<td>6.1</td>
<td>68</td>
</tr>
<tr>
<td>Delusional disorder</td>
<td>7</td>
<td>1.0</td>
<td>10</td>
</tr>
<tr>
<td>Not classified</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
**Construct validity**

Do the symptoms of schizophrenia correlate with each other? The evidence is that they do not:

Studies have shown that there are at least three clusters of schizophrenic symptoms (first demonstrated by Liddle, 1987, much replicated):

- **Positive:** hallucinations and delusions
- **Cognitive disorganisation**
- **Negative**

More recent studies (Blanchard & Cohen, 2006; Braga et al., 2005; Cuesta et al., 2003; Demjaha et al., 2009; Emsley et al., 2003; Grube et al., 1998; Klimidis et al., 1993; Peralta et al., 1992, 1994; Smith et al., 1998; Toomey et al. 1998) have pointed to more dimensions which encompass both schizophrenia and bipolar disorder.
New diagnostic proposals

van Os and Kapur (2009) have argued that bipolar disorder, schizophrenia and schizoaffective disorder can be explained by five dimensions.

But other researchers have argued for a meta-structure of psychosis, with one all-encompassing psychosis syndrome (First, 2009; Carpenter et al. 2009).
4: Is ‘schizophrenia’ genetic?
What’s the phenotype?

Lichtenstein, Yip. Bijork, Pawitan, Cannon, Sullivan & Hultman (2009) - linked multigeneration registers containing information on all children and parents in Sweden with hospital discharge registers - 2 million families with 9 million participants!

- 36,000 schizophrenia and 40,000 bipolar patients

<table>
<thead>
<tr>
<th>Relation to proband</th>
<th>Risk for schizophrenia when proband has schizophrenia</th>
<th>Risk for bipolar disorder when proband has bipolar disorder</th>
<th>Risk for schizophrenia when proband has bipolar disorder</th>
<th>Risk for bipolar disorder when proband has schizophrenia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Biological relationships</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent</td>
<td>9.9</td>
<td>8.5-11.6</td>
<td>6.4</td>
<td>5.9-7.1</td>
</tr>
<tr>
<td>Sibling</td>
<td>9.0</td>
<td>8.1-9.9</td>
<td>7.9</td>
<td>7.1-8.8</td>
</tr>
<tr>
<td>Sibling</td>
<td>3.6</td>
<td>2.3-5.5</td>
<td>4.5</td>
<td>2.7-7.4</td>
</tr>
<tr>
<td>Sibling</td>
<td>2.7</td>
<td>1.9-3.8</td>
<td>2.4</td>
<td>1.4-4.1</td>
</tr>
<tr>
<td>Adoptive relationships</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biological parent</td>
<td>13.7</td>
<td>6.1-30.8</td>
<td>4.3</td>
<td>2.0-9.5</td>
</tr>
<tr>
<td>Sibling</td>
<td>7.6</td>
<td>0.7-87.8</td>
<td>3.9</td>
<td>0.2-63.3</td>
</tr>
<tr>
<td>Adoptive parent</td>
<td>Adoptee</td>
<td></td>
<td>1.3</td>
<td>0.5-3.6</td>
</tr>
<tr>
<td>Sibling</td>
<td>Non-biological sibling</td>
<td></td>
<td>1.3</td>
<td>0.1-15.1</td>
</tr>
</tbody>
</table>

RR=relative risk. *Adopted children whose biological parents have disease.

Table 2: Recurrence risks for schizophrenia and bipolar disorders
What’s the phenotype?

Lichtenstein, Yip. Bijork, Pawitan, Cannon, Sullivan & Hultman (2009) - linked multigeneration registers containing information on all children and parents in Sweden with hospital discharge registers - 2 million families with 9 million participants!

- 36,000 schizophrenia and 40,000 bipolar patients

*Figure: Variance accounted for by genetic, shared environmental and non-shared environmental effects for schizophrenia and bipolar disorder. Red indicates genetic effects, with dark red for genetic effects in common with the other disorder and light red for unique genetic effects. Blue indicates environmental effects, with dark blue for shared environmental effects and light blue for non-shared environmental effects.*
Many genes with very small effects?

International Schizophrenia Consortium (2009)

Relaxed statistical rules to identify genes with very modest associations with schizophrenia (more than 1000, usually associated with an increased risk of < .02%). Created sum scores for polygenic association:

- Accounted for about 30% of the variance in liability to schizophrenia
- Accounted for a similar liability to bipolar disorder
What does 70% heritable mean?

• Heritability is defined as the percentage of the variance in a trait that is attributable to genes =

\[
\frac{\text{variance with genes}}{\text{variance with genes} + \text{variance with environment}}
\]

• It is often assumed that high levels of heritability preclude environmental influences (i.e. \text{variance due to genes} + \text{variance due to environment} = 100\% )
What does 70% heritable mean?

- Heritability is defined as the percentage of the variance in a trait that is attributable to genes =

\[
\text{variance with genes} \\
\text{variance with genes + variance with environment}
\]

BUT - if variance in the environment is low, heritability will always be high: In a world in which everyone smokes 20 cigarettes a day, the heritability of lung cancer will approach 100% (but the cause will still be smoking)!

Turkheimer et al (2003), in a large twin study, found that 60% of variance in IQ in impoverished environment is attributable to shared environmental effects with close to zero genetic effects. The reverse was true in middle class families.
Trauma and psychosis: Meta-analysis

Initial database search found 27,572 hits- after excluding studies based on inspection of the papers' titles and abstracts, the 763 remaining papers were examined for inclusion.

The analysis refers to studies focusing on EARLY adversity (exposure to trauma, bullying, parental death etc before the age of 18) and psychosis (both diagnostic and dimensional outcomes) with the following designs:

- epidemiological cross-sectional studies
- prospective studies (and quasi prospective studies)
- patient control studies
### Association between trauma and psychosis

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio and 95% CI</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bebbington et al., 2011</td>
<td></td>
<td>Epidemiological cross-sectional</td>
</tr>
<tr>
<td>Harley et al., 2010</td>
<td></td>
<td>Epidemiological cross-sectional</td>
</tr>
<tr>
<td>McAloney et al., 2009</td>
<td></td>
<td>Epidemiological cross-sectional</td>
</tr>
<tr>
<td>Nishida et al., 2008</td>
<td></td>
<td>Epidemiological cross-sectional</td>
</tr>
<tr>
<td>Shevlin et al., 2008</td>
<td></td>
<td>Epidemiological cross-sectional</td>
</tr>
<tr>
<td>Whitfield et al., 2005</td>
<td></td>
<td>Epidemiological cross-sectional</td>
</tr>
<tr>
<td>Evans, 2011</td>
<td></td>
<td>Patient-control</td>
</tr>
<tr>
<td>Fisher et al., 2010</td>
<td></td>
<td>Patient-control</td>
</tr>
<tr>
<td>Habets et al., 2011</td>
<td></td>
<td>Patient-control</td>
</tr>
<tr>
<td>Husted et al., 2010</td>
<td></td>
<td>Patient-control</td>
</tr>
<tr>
<td>Rubino et al., 2009</td>
<td></td>
<td>Patient-control</td>
</tr>
<tr>
<td>Sommer et al., 2010</td>
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<td>Stompe et al., 2006</td>
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<td>Patient-control</td>
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<td>Varese et al., 2011</td>
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<td>Patient-control</td>
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<td>Weber et al., 2008</td>
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<td>Patient-control</td>
</tr>
<tr>
<td>Arseneault et al., 2010</td>
<td></td>
<td>Prospective (and quasi-prospective)</td>
</tr>
<tr>
<td>Cutjar et al., 2010 (M)</td>
<td></td>
<td>Prospective (and quasi-prospective)</td>
</tr>
<tr>
<td>Cutjar et al., 2010 (F)</td>
<td></td>
<td>Prospective (and quasi-prospective)</td>
</tr>
<tr>
<td>De Loore et al., 2007</td>
<td></td>
<td>Prospective (and quasi-prospective)</td>
</tr>
<tr>
<td>Schreier et al., 2009</td>
<td></td>
<td>Prospective (and quasi-prospective)</td>
</tr>
<tr>
<td>Spauwen et al., 2006</td>
<td></td>
<td>Prospective (and quasi-prospective)</td>
</tr>
</tbody>
</table>

Increased likelihood

0.01  0.1  1  10  100
5: Do diagnoses guide treatment?
In clinical practice

Diagnostic disputes, or at least changes in diagnoses, are quite common. This does not matter too much if the clinicians do not take the diagnoses too seriously.

However, if they are taken too seriously, the result may be confusion and distress by both patients and carers.
Prediction of outcome

Outcome of psychosis has been consistently shown to be enormously variable.


Similar findings have been reported by more recent investigators (e.g. Harrison et al. 2001)
Doubts about utility

Different illnesses should respond to different treatments:

- Schizophrenia - antipsychotics
- Manic depression - lithium carbonate

As Tamminga & David (2007) note, this does not seem to be the case. Johnstone et al. (1986) randomly assigned patients to pimozide (a neuroleptic), lithium carbonate, both or neither. Drug response was symptom-specific but not diagnosis-specific:

- Delusions and hallucinations - neuroleptics
- Abnormal mood - lithium carbonate
An alternative approach

In the light of the limited success of aetiological research based on neoKraepelinian diagnoses, some researchers have begun to look for alternatives.

One approach is to look for transdiagnostic processes that give rise to particular complaints or symptoms.

Once we have figured out how to explain hallucinations, delusions, thought disorder, negative symptoms, mania etc. maybe there will be no schizophrenia or bipolar disorder left to explain.
6: The example of hallucinations
Hallucinations in ‘normal people’

Even in “developed” countries, hallucinations are reported by a surprising number of the ‘normal’ population (Sidgewick et al., 1894; West, 1948; Posey & Losch, 1983; Romme & Escher, 1989).

**US Epidemiological Catchment Area Study (Tien, 1991)**
- Prevalence rate: 10-15%
- Annual incidence rate: 4-5%

**Dutch NEMESIS study (van Os et al., 2000) - 7.9%**

**New Zealand Dunedin cohort study (Poulton et al. 2000) - 13.2%**

**US National Comorbidity Study (Shelvin et al. 2007)**
- 8.5% auditory, 7% visual, and 7% tactile, with decreasing numbers reporting one type of hallucination (11.4%), two types of hallucination (3.9%) and all three types (1.6%).
Some key facts about hallucinations:

1. Hallucinations are influenced by - beliefs, stress, environmental noise.

2. Auditory hallucinations are associated with ‘subvocalization’.

3. Auditory hallucinations are associated with a history of trauma.
Trauma and psychosis: Meta-analysis

The findings suggest a significant association between trauma and psychosis across all different research designs (patient-control studies:

- patient-control studies: OR = 3.3
- epidemiological cross-sectional: OR = 2.5
- prospective: OR = 2.6
Transdiagnostic effect of trauma

Read et al. (2003) – chart review of 200 schizophrenia patients in New Zealand: strong association between hallucinations and CSA.

Hammersley, Dias, Todd, Bowen-Jones, Reilly & Bentall (2004) – 96 patients receiving psychological treatment for bipolar disorder:

<table>
<thead>
<tr>
<th></th>
<th>No Auditory Hallucinations</th>
<th>Auditory Hallucinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSA</td>
<td>4 (27%)</td>
<td>11 (73%)</td>
</tr>
<tr>
<td>No CSA</td>
<td>62 (76%)</td>
<td>19 (23%)</td>
</tr>
</tbody>
</table>

P < .001
Specificity of adversities for symptoms

Data from the 2007 Adult Psychiatric Morbidity Survey (N = 7000+), which has measures of psychotic symptoms, and different kinds of childhood adversity.

Table 1: Odds ratios and their associated 95% CI for the effects of childhood sexual abuse, victimization and separation variables on auditory verbal hallucinations (AVHs) and paranoid delusions.

<table>
<thead>
<tr>
<th></th>
<th>Demographics adjusted</th>
<th>Comorbidity adjusted</th>
<th>Adjusted for trauma types</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AVHs</td>
<td>Paranoia</td>
<td>AVHs</td>
</tr>
<tr>
<td>Rape</td>
<td>10.6 [4.9, 23.1]</td>
<td>3.2 [1.2, 8.5]</td>
<td>9.0 [3.4, 24.2]</td>
</tr>
<tr>
<td>Sexual touch</td>
<td>4.7 [2.5, 8.7]</td>
<td>3.0 [1.5, 5.7]</td>
<td>4.3 [2.1, 9.0]</td>
</tr>
<tr>
<td>Sexual talk</td>
<td>4.1 [2.2, 7.8]</td>
<td>3.1 [1.7, 5.5]</td>
<td>3.7 [1.8, 7.9]</td>
</tr>
<tr>
<td>Physical abuse</td>
<td>3.9 [1.6, 9.3]</td>
<td>5.9 [3.3, 10.7]</td>
<td>2.9 [1.1, 7.1]</td>
</tr>
<tr>
<td>Bullying</td>
<td>1.9 [0.9, 3.9]</td>
<td>1.6 [0.9, 2.9]</td>
<td>1.9 [0.8, 4.2]</td>
</tr>
<tr>
<td>Institutionalized</td>
<td>3.9 [1.5, 10.0]</td>
<td>6.0 [3.0, 11.7]</td>
<td>2.7 [0.9, 8.3]</td>
</tr>
<tr>
<td>LA care</td>
<td>3.1 [1.0, 9.2]</td>
<td>2.2 [1.3, 3.8]</td>
<td>2.5 [0.7, 9.2]</td>
</tr>
</tbody>
</table>

Note: *Demographic confounds included age, gender, IQ, social class, education and ethnicity; *AVHs analyses were adjusted for concurrent paranoia (in addition to demographic confounds); †Paranoia analyses were adjusted for concurrent AVHs (in addition to demographic confounds); ‡AVHs analyses adjusted for other early adversity predictors (in addition to demographic factors and paranoia); §Paranoia analyses adjusted for other early adversity predictors (in addition to demographic factors and AVHs).
7: Psychological mechanisms
A consensus scientific model

Hearing voices:

occurs when inner speech is misattributed to a source that is alien and/or external to the self.
What is inner speech?

Vygotsky (1962): intrapsychic processes are formed by the internalisation of inter-psychic processes.

- Dialogue (esp commands) between caregiver and child
- Private, self-directed speech (ages 2-4 years)
- Internalization to inner Speech (aged 4+ years)
What is inner speech?

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- **Dialogue (esp commands) between caregiver and child**
- **Private, self-directed speech (ages 2-4 years)**
- **Internalization to inner Speech (aged 4+ years)**
- **Accompanied by Subvocalisation in adults (e.g. McGuigan, 1978)**
What is inner speech?

Fernyhough (2004) points out that Vygotsky’s final stage can be subdivided:

- **Dialogue (esp commands) between caregiver and child**
- **Private, self-directed speech** (ages 2-4 years)
- **Dialogic ‘expanded’ Inner speech**
- **Condensed Inner speech**
- Accompanied by **Subvocalisation in adults** (e.g. McGuigan, 1978)

Stress, cognitive demands
The source monitoring model of hallucinations

- Stimulus (Internal or External)
- Beliefs and Expectations
- Environmental Noise
- Source monitoring
- Classification: ‘Real’ or ‘Imaginary’
- Reinforcement?

Bentall (1990, 2000); Ditman & Kuperberg (2005); Laroi (2006)
The hunting analogy..... Imagine that you have to hunt for a rhinoceros

I MUSTN'T SHOOT AN ELEPHANT...
OH SHIT!
The source monitoring model

- Stimulus (elephant of rhino)
- Beliefs and Expectations
- Environmental Noise
- Discriminative decision
- "Shoot" or "Don't shoot"
- Motivational factors

Did this elephant look particularly like a rhino?
The source monitoring model

**Was there a lot of foliage in the area?**
The source monitoring model

Beliefs and Expectations

Environmental Noise

Stimulus (elephant of rhino)

Discriminative decision

“Shoot” or “Don’t shoot”

Motivational factors

Did you believe there are no elephants in the area?
Hanna

**Early Experiences**
Strict Catholic upbringing
Married man with daughter

**Beliefs Formed**
Must be good Catholic

**Critical Incidents**
Husband demands termination of 4th pregnancy
Husband guilty – unsupportive
Distressed – sees psychologist
Rejected by psychologist

Hear voice of psychologist saying comforting things
**Signal detection analysis:**

Possible relationships between types of actually present stimuli (external or internal) and whether or not an external stimulus is reported to be present can be understood as a contingency table:

<table>
<thead>
<tr>
<th>External Stimulus Present</th>
<th>Stimulus Reported</th>
<th>Stimulus Not Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Real&quot;</td>
<td>&quot;Real&quot;</td>
<td>MISS</td>
</tr>
<tr>
<td>HALLUCINATION</td>
<td>&quot;It’s imaginary&quot;</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>External Stimulus Absent</th>
<th>Stimulus Reported</th>
<th>Stimulus Not Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;It’s imaginary&quot;</td>
<td></td>
<td>&quot;It’s imaginary&quot;</td>
</tr>
</tbody>
</table>
Signal detection analysis:

Signal Detection Theory suggests that the ratio of these outcomes can be understood in terms of two processes:

- **Stimulus Reported**
  - External Stimulus Present: HIT
  - External Stimulus Absent: FALSE ALARM

- **Stimulus Not Reported**
  - External Stimulus Present: MISS
  - External Stimulus Absent: CORRECT REJECTION

**Perceptual sensitivity** and **response bias**
Signal detection studies

Bentall and Slade (1985)
1. Hallucinating schizophrenic patients vs non-hallucinating schizophrenic patients
2. ‘Hallucinating’ students (high-scoring on Launay-Slade Hallucinations Scale) vs non-hallucinating patients
   Both studies found differences between hallucinators and controls on bias but not sensitivity.

Rankin & O’Carroll (1999)
Hallucinating students vs non-hallucinating students - difference in bias, not sensitivity

Li et al. (2002)
No differences between hallucinating and non-hallucinating patients, both showed more bias and less sensitivity than controls.

Brebian et al. (2005)
SDT analysis of immediate source monitoring.
Hallucination scores in patients correlated with false recognition bias.

Barkus et al. (2007)
Highly hallucination-prone students compared to controls showed more bias to detecting signals on a SDT task similar to that used by Bentall and Slade (1985)
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Why the link with trauma? The role of dissociation

Varese, Udachina, Myin-Germeys, Oorshott & Bentall (2011)

42 schizophrenia-spectrum patients (21 hallucinated during assessment) vs 23 controls

Dissociation assessed using 3 statements:

“Since the last beep I’ve found it difficult to focus on what was happening around me”
“Since the last beep I’ve been easily distracted”
“Since the last beep I’ve found myself doing things without paying attention” (Cronbach’s $\alpha = .92$).

Cronbach’s alpha=.92), rated on 7-point Likert scales. PCA identified one factor (eigenvalue >1) explaining 88% of the variance.
Why the link with trauma? The role of dissociation

- Increased dissociation significantly predicted the occurrence of auditory hallucinations, especially under conditions of elevated stress. (True even when controlling for paranoia).

- Hallucinating patients also reported a significantly larger increase in dissociation following minor daily life stressors compared to clinical and non-clinical controls.
Varese & Bentall (2011)

46 patients with psychosis (15 with current hallucinations, 14 with remitted hallucinations, 17 never hallucinated) plus 20 controls.

- Launay-Slade Hallucination Scale (trait measure of hallucination)
- Dissociative Experiences Scale (Bernstein & Putman, 1986)
- Childhood Abuse and Trauma Scale (CATS; Sanders & Becker-Launsen, 1995)
- Signal detection task (Barkus et al. 2004; 8 minute version)
Varese & Bentall (2011)

All differences at least $p < .05$
Varese & Bentall (2011)

CATS total: All clinical groups > controls
CATS CSA: Hall > Never Hall > Remitted > Controls
Varese & Bentall (2011)

Hall > Remitted Hall = Never Hall > Controls
Varese & Bentall (2011)

Hall = Remitted Hall > Never Hall = Controls
Varese & Bentall (2011): Mediation analysis

Conditions for mediation (Baron & Kenny, 1986):

Independent variable → Mediation factor → Dependent variable
Varese & Bentall (2011): Medialational analysis

Conditions for mediation (Baron & Kenny, 1986):

- Independent variable
- Mediator variable
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Varese & Bentall (2011): Mediation analysis

Conditions for mediation (Baron & Kenny, 1986):

- Independent variable
- Mediator variable
- Dependent variable
Varese & Bentall (2011): Mediational analysis

Conditions for mediation (Baron & Kenny, 1986):

- Dissociation (DES)
- CSA (CATS) → LSHS
**Varese & Bentall (in press): Mediational analysis**

Conditions for mediation (Baron & Kenny, 1986):

The mediational model works with history of hallucination, but the effect is less marked.

<table>
<thead>
<tr>
<th>Analysis of the total sample</th>
<th>Indirect effect</th>
<th>Direct effect</th>
<th>Total effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>CATS scores</td>
<td>0.12 [0.06, 0.19]</td>
<td>0.12 [0.02, 0.22]</td>
<td>0.24 [0.13, 0.35]</td>
</tr>
<tr>
<td>Sexual abuse</td>
<td><strong>0.65 [0.24, 1.07]</strong></td>
<td>0.58 [-0.02, 1.12]</td>
<td>1.23 [0.68, 1.76]</td>
</tr>
<tr>
<td>Physical abuse</td>
<td>0.30 [-0.03, 1.32]</td>
<td>0.45 [-0.50, 1.19]</td>
<td>1.00 [0.14, 1.92]</td>
</tr>
<tr>
<td>Neglect</td>
<td>0.26 [0.11, 0.42]</td>
<td>0.30 [0.09, 0.46]</td>
<td>0.56 [0.32, 0.78]</td>
</tr>
<tr>
<td>Emotional abuse</td>
<td>0.43 [0.17, 0.72]</td>
<td>0.36 [-0.05, 0.79]</td>
<td>0.79 [0.27, 1.32]</td>
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<table>
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</tr>
<tr>
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<td>0.01 [-0.80, 0.83]</td>
<td>0.21 [-0.83, 1.31]</td>
</tr>
<tr>
<td>Neglect</td>
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<td>0.22 [-0.02, 0.42]</td>
<td>0.35 [0.05, 0.61]</td>
</tr>
<tr>
<td>Emotional abuse</td>
<td>0.24 [-0.02, 0.54]</td>
<td>0.26 [-0.31, 0.73]</td>
<td>0.49 [-0.10, 1.08]</td>
</tr>
</tbody>
</table>
Varese & Bentall (2011): Signal detection

There was no evidence of mediation with respect to signal detection

• No significant difference between high DES and low DES participants

• Hence, we think the effects of poor source monitoring and dissociation may be additive

• Perhaps dissociation is related to the persistence of hallucinations
Transdiagnostic models

It is possible to construct convincing scientific accounts of symptoms which make no reference to diagnoses. Adding diagnoses to the models does not improve them!

Hallucinations:

- Impaired source monitoring
- Dissociation
- Trauma
- Hallucinations

Impaired communication between frontal and temporal brain regions
**Transdiagnostic models**

It is possible to construct convincing scientific accounts of symptoms which make no reference to diagnoses. Adding diagnoses to the models does not improve them!

**Paranoid delusions:**

- Insecure attachment
- Victimisation/powerlessness
- Abnormal cognitive style
- Threat anticipation
- Paranoia

might involve dopamine!
8: Conclusions
Conclusions and implications

Although many of the arguments I have made have focused on the psychoses, they can just as cogently be applied to the non-psychotic disorders, eg.:

- Comorbidity between anxiety and depression
- Non-specificity of drugs to particular depressive or anxiety disorders

An approach to psychiatry based on an analysis of patients’ symptoms is much more scientific than the Kraepelinian approach, which has failed to explain madness or help patients despite the expenditure of many millions of £s and $s

It is also much more humane.
That’s all folks!