Mood Disorders: Conceptual Issues

• Basic mood disorder is **depression**
• Some patients with depression also have episodes of mania (bipolar-I) or hypomania (bipolar-II). These patients have **bipolar disorder**
• The course of the illness and its response to treatment varies between depression and bipolar disorder.
Heritability Estimates for Psychiatric Disorder

Bipolar disorder: Heritability 0.9
Schizophrenia: Heritability 0.8
Alzheimer's disease: Heritability 0.7
Cocaine use disorder: Heritability 0.6
Anorexia nervosa: Heritability 0.5
Alcohol dependence: Heritability 0.4
Cannabis use disorder: Heritability 0.3
Panic disorder: Heritability 0.2
Stimulant use disorder: Heritability 0.1
Major depressive disorder: Heritability 0.0
Generalized anxiety disorder: Heritability 0.0

Bienvenu et al 2011
DSM-5 Criteria for Mania

• Must have; Elevated or irritable mood for at least one week and 3 of:
  • Inflated self-esteem or grandiosity
  • Decreased need for sleep
  • Pressure of speech
  • Pressure of thought
  • Distractibility
  • Increase in goal-directed activity (may be fruitless)
  • Harmful activities (buying sprees, sexual indiscretions)

Must have marked impairment in social/occupational function. Not due to a substance. Changes observable to others
DSM-5 Criteria for Hypomania

- Must have; Elevated or irritable mood for at least four days and 3 of:
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep
  - Pressure of speech
  - Pressure of thought
  - Distractibility
  - Increase in goal-directed activity (may be fruitless)
  - Harmful activities (buying sprees, sexual indiscretions)

*Not* severe enough to cause marked impairment in social/occupational function. *Not due to a substance. Changes observable to others.*
Pharmacological Treatment of Bipolar Disorder

• Acute Mania
• Acute Depression
• Maintenance Treatment
Best Treatment for Mania - Network Meta-Analysis

Cipriani et al, 2011
“He's bipolar.”
Problems with Antidepressants in Bipolar Depression

- Conventional antidepressants seem rather ineffective
- May produce mania and rapid cycling
- Not recommended as first-line in guidelines
- Should be used with a mood stabiliser
- Therefore important to try to identify depressed patients who might be bipolar. Use history, family history and Mood Disorder Questionnaire (MDQ- available online)
Quetiapine Monotherapy in Bipolar Depression
Lamotrigine compared with placebo: meta-analysis of randomised trials. (>50% reduction on Montgomery-Asberg Depression Rating Scale)

Network Meta-Analysis of Pharmacological Treatments in Bipolar Depression

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DRUG/PLACEBO RESPONSE RATIO</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine</td>
<td>1.84</td>
<td>1.44-2.36</td>
</tr>
<tr>
<td>+fluoxetine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lurasidone</td>
<td>1.72</td>
<td>1.33-2.22</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>1.36</td>
<td>1.24-1.49</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>1.25</td>
<td>1.07-1.46</td>
</tr>
<tr>
<td>Lithium</td>
<td>1.12</td>
<td>0.92-1.44</td>
</tr>
</tbody>
</table>

From Vázquez et al, 2014
NICE Guideline for Pharmacological Treatment of Bipolar Depression

• If a person develops moderate or severe bipolar depression offer fluoxetine combined with olanzapine, or quetiapine on its own, depending on the person's preference and previous response to treatment.

• If the person prefers, consider lamotrigine on its own.
Maintenance Treatment in Bipolar Disorder

• Lithium has best evidence for long-term mood stability. However, problems with tolerance and safety (drug interactions, renal impairment)
• Valproate some efficacy, though less than lithium- terratogenic
• Carbamazepine less effective than lithium
• Lamotrigine effective in prevention of depression, not mania
• Some evidence for a maintenance role of quetiapine and olanzapine either by themselves or combined with lithium/valproate
## Risk of Admission to hospital in 35,000 bipolar patients in Sweden

<table>
<thead>
<tr>
<th>Drug</th>
<th>Relative Risk of Admission (hazard-ratio)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>0.66</td>
<td>(depression and mania)</td>
</tr>
<tr>
<td>Valproate</td>
<td>0.73</td>
<td>(depression and mania)</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>0.77</td>
<td>(depression and mania)</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>0.78</td>
<td>(depression only)</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>0.82</td>
<td>(depression and mania)</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>0.92</td>
<td>(mania only)</td>
</tr>
</tbody>
</table>

Joas et al, 2017
Lithium Decreases Suicidal Behaviour in Mood Disorder

Cipiriani et al, 2005
Lithium Monitoring (Shared Care Guideline)

- Lithium level every three months (aim for 0.6-0.8mmol/L, 12 hours post dose).
- Prescribe by brand name
- TSH, creatinine, eGFR, calcium every six months
- Weight annually

Also monitoring for bipolar disorder

- Annual metabolic status (lipids, HbA1c, LFTs)
- Annual cardiovascular status
Lithium Drug Interactions (Increased levels)

- Diuretics
- ACE Inhibitors
- Angiotensin II receptor antagonists
- Metronidazole, tetracycline
- NSAIDS

- BNF advises caution with serotonergic potentiating agents (triptans, SSRIs).
Conclusion

• It is useful to distinguish bipolar disorder from major depression because of differing prognosis and response to treatment.
• Hypomania can be difficult to detect from the history. The Mood Disorder Questionnaire (MDQ, available online) can be helpful.
• The best pharmacological treatments for acute mania are risperidone, quetiapine and olanzapine
• The best treatments for bipolar depression are olanzapine/fluoxetine combination and quetiapine.
• Sixty years on, lithium remains the best maintenance treatment for bipolar disorder