The Findings of GLADS

Group for Longitudinal Affective Disorders Study

and Their Clinical Relevance in Japan

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Learn, compare, collect the facts!

Pavlov 1849-1936

WHAT WE KNOW ABOUT

"OUR" DEPRESSION
Know What?
Epistemology of Illness

- Symptomatology → Cross-sectional studies
  - Paper & pencil, SPSS
- Etiology → Lab, arm chair theories
  - Animals and coffee
- Therapeutics → Clinical Trials
  - Drug companies
- Course → Cohort studies
  - Years of dedication
- Epidemiology → Community studies
  - Government commitment
GLADS

- Group for Longitudinal Affective Disorders
  - Started 1991
  - A cohort study by “us”

- Naturalistic prospective cohort study
  - Representative inception cohort of unipolar major depressive episodes
  - Recruited at the time of their treatment commencement
  - Followed up prospectively and serially with a semi-structured interview for 10 years
Methods make Facts

- Unbiased samples
  - Various 23 institutions in Japan
  - Quasi randomly sampled new patients were screened by PISA

- Unbiased measurements
  - Semi-structured Interview for this purpose
    - COALA Comprehensive Assessment List for Affective disorders
    - Developed and validated

- Dedication to continue
  - Monthly for two years, annually thereafter
Size of the study

- 1992/12 – 1995/12
- New patients: 1965
- Enrolled patients: 126
<table>
<thead>
<tr>
<th>Variable</th>
<th>Major depressive disorder, single episode (n=66)</th>
<th>Major depressive disorder, recurrent (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>44.1 (15.1)</td>
<td>44.3 (15.6)</td>
</tr>
<tr>
<td>Gender, n (%) female</td>
<td>36 (55%)</td>
<td>19 (68%)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single, n (%)</td>
<td>19 (29%)</td>
<td>8 (29%)</td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>47 (71%)</td>
<td>20 (71%)</td>
</tr>
<tr>
<td>Treatment settings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University n (%)</td>
<td>46 (70%)</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>General, n (%)</td>
<td>14 (21%)</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>Mental, n (%)</td>
<td>6 (9%)</td>
<td>6 (21%)</td>
</tr>
</tbody>
</table>
10 years later

<table>
<thead>
<tr>
<th>Missing due to:</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; year</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; year</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; year</th>
<th>4&lt;sup&gt;th&lt;/sup&gt; year</th>
<th>5&lt;sup&gt;th&lt;/sup&gt; year</th>
<th>6&lt;sup&gt;th&lt;/sup&gt; year</th>
<th>7&lt;sup&gt;th&lt;/sup&gt; year</th>
<th>8&lt;sup&gt;th&lt;/sup&gt; year</th>
<th>9&lt;sup&gt;th&lt;/sup&gt; year</th>
<th>10&lt;sup&gt;th&lt;/sup&gt; year</th>
</tr>
</thead>
<tbody>
<tr>
<td>dropouts</td>
<td>4%</td>
<td>6%</td>
<td>25%</td>
<td>28%</td>
<td>29%</td>
<td>34%</td>
<td>43%</td>
<td>40%</td>
<td>44%</td>
<td>41%</td>
</tr>
<tr>
<td>natural deaths</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
<td>3%</td>
<td>5%</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>suicides</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>3%</td>
<td>3%</td>
<td>4%</td>
</tr>
</tbody>
</table>
TREATMENT IN JAPAN
Treatment received by depressed patients in Japan and its determinants: naturalistic observation from a multi-center collaborative follow-up study

Dose of antidepressant

- Imipramine equivalent
  - At 1 month
    - 85.2mg (SD = 73.2)
    - 69% patients prescribed less than 125mg
  - At 6 months
    - 67% patients prescribed less than 125mg
Class of medications prescribed

For patients with major depressive disorder in Japan

<table>
<thead>
<tr>
<th></th>
<th>Antidepressants</th>
<th>Benzodiazepines</th>
<th>Antipsychotics</th>
<th>Lithium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upon entry</td>
<td>81%</td>
<td>60%</td>
<td>11%</td>
<td>5%</td>
</tr>
<tr>
<td>1 month</td>
<td>82%</td>
<td>53%</td>
<td>14%</td>
<td>6%</td>
</tr>
<tr>
<td>6 month</td>
<td>81%</td>
<td>48%</td>
<td>12%</td>
<td>12%</td>
</tr>
</tbody>
</table>
Adequacy of continuation and maintenance treatments for major depression in Japan

22 2 153-156
Dose of antidepressant

- **Imipramine equivalent**
  - **Continuation phase**
    - 45.1mg (SD = 64.7)
    - 74% patients prescribed less than 75mg
  - **Maintenance phase**
    - 42.0 (SD = 74.7)
    - 83% patients prescribed less than 75mg
OUTCOMES
Time to recovery of an inception cohort with hitherto untreated unipolar major depressive episodes

Furukawa TA, 2000, British Journal of Psychiatry
177: 331-335
Time to recovery without antidepressants

- Median time to recovery of the index episode after treatment commencement
  - 3 months (95% CI 2.5-3.6)

- Median time to recovery from the onset of the index episode
  - 7.0 months (95% CI 5.2-8.8)
Cumulative probability of remaining in the index episode after treatment commencement for the 90 probands with DSM-IV major depressive disorder not superimposed on dysthymia. Patients who recovered within a few days after treatment commencement were regarded as attaining recovery at 0 month.
Clinical Implications

- Median time to recovery: 3.0 months
  - 26% reached minimally symptomatic by 1 month,
  - 63% by 3 months,
- Better than suggested by the literature
- 12% remain an episode 24 months after
Time to recurrence after recovery from major depressive episodes and its predictors

Recurrence

1yr  2yrs  6yrs

84  Recover

48  Remain

39  Remain

32  Remain

95  Inception

19 m

>6yrs

50  Subthreshold relapse

31  Full Relapse
How many well vs. unwell days can you expect over 10 years, once you become depressed?

10 Years

- After starting treatment of their major depression
- 77% in euthymia,
- 16% in subthreshold depression
- 7% in major depression
<table>
<thead>
<tr>
<th></th>
<th>GLADS (n=94)</th>
<th>NIMH (n=431)</th>
<th>Cambridge (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remitted</td>
<td>77%</td>
<td>58%</td>
<td>67%</td>
</tr>
<tr>
<td>Subthreshold depression</td>
<td>16%</td>
<td>27%</td>
<td>20%</td>
</tr>
<tr>
<td>Major depression</td>
<td>7%</td>
<td>15%</td>
<td>13%</td>
</tr>
</tbody>
</table>
Major contributions

1. Furukawa TA, Time to recovery of an inception cohort with hitherto untreated unipolar major depressive episodes. Br J Psychiatry
2. Kanai T, Time to recurrence after recovery from major depressive episodes and its predictors. Psychol Med
5. Furukawa TA, Treatment received by depressed patients in Japan and its determinants: naturalistic observation from a multi-center collaborative follow-up study. J Affect Disord
6. Fujita A, Adequacy of continuation and maintenance treatments for major depression in Japan. J Psychopharmacol
Acknowledgements

Group: GLADS

Principle Investigators
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- Prof. Furukawa, TA

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Declaration of interest
- The speaker has/had research contracts with Fujimoto, GSK, Janssen, Lily, Mochida, Shinogi, Solvey, Suntory, UCB, and Wyth, for last 5 years.
Final note

Any questions?

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