De effecten van interpersoonlijke psychotherapie bij depressie: een overzicht

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Overview

- Research on psychotherapy for depression: A comprehensive database
- The effects of IPT: A meta-analysis
- Results on IPT from other meta-analyses
- Challenges
- Conclusions
Database of randomized trials of psychotherapy for adult depression
315 included studies

- 180 studies comparing psychotherapy with control groups
- 81 studies comparing 7 major types of psychotherapy with other psychotherapies
- 42 studies comparing psychotherapy with pharmacotherapy
- 20 studies comparing psychotherapy with combined treatment
- 37 studies comparing pharmacotherapy with combined treatment
- 17 studies comparing psychotherapy + pharmacotherapy versus psychotherapy + placebo
- 13 controlled studies on psychotherapy for inpatients
- 12 studies comparing individual and group therapy
- 6 studies comparing face-to-face therapy with guided self-help
- 10 studies on self-guided therapy for depression
Methods

- Extensive literature searches (January 2012)
- Heterogeneity: Q and $I^2$
- Analyses: random effects model
- Subgroup analyses: mixed effects model
- Metaregression analyses
- 25 published/in press papers
- Validation of results with 42 other meta-analyses
- More information in Open Access paper: Cuijpers et al., BMC Psychiatry 2008; 8: 36.
- Data can be downloaded by other researchers: www.evidencebasedpsychotherapies.org
- Overview in: Cuijpers et al., Nord J Psychiatry 2011
Methods continued

- Excluded studies:
  - Adolescents
  - Maintenance treatments
- Only short-term effects
- Calculate effect sizes: difference between treatment and control at post-test
- Independent of instrument
- Not only significance, but also size of effect:
  - Small: $d=0.20$  $\text{NNT}=8.93$
  - Moderate: $d=0.50$  $\text{NNT}=3.62$
  - Large: $d=0.80$  $\text{NNT}=2.34$
International collaboration

• Prof. Pim Cuijpers (project leader)
• Prof. Steve Hollon, USA
• Prof. Gerhard Andersson, Sweden

• EMGO/Department of Clinical Psychology: Annemieke van Straten, Lisanne Warmerdam, Tara Donker, Ellen Driessen, Josien Schuurmans, Anna Geraedts, Jack Dekker, Filip Smit, Niels Smits.

• EMGO/Department of Psychiatry: Patricia van Oppen, Anneke van Schaik

• Others: Prof. Juan Li, prof. John Markowitz, prof. Stephan Hofmann, Dr. Jürgen Barth, Prof. David Mohr, Prof. Ernst Bohlmeijer
Trials on psychotherapy for depression (N=315)

2011-2015 are estimations based on 2011 only
The effects of IPT
Interpersonal Psychotherapy for Depression: A Meta-Analysis

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Objective: Interpersonal psychotherapy (IPT), a structured and time-limited therapy, has been studied in many controlled trials. Numerous practice guidelines have recommended IPT as a treatment of choice for unipolar depressive disorders. The authors conducted a meta-analysis to integrate research on the effects of IPT.

Method: The authors searched bibliographical databases for randomized controlled trials comparing IPT with no treatment, usual care, other psychological treatments, and pharmacotherapy as well as studies comparing combination treatment using pharmacotherapy and IPT. Maintenance studies were also included.

Results: Thirty-eight studies including 4,356 patients met all inclusion criteria. The overall effect size (Cohen's d) of the 16 studies that compared IPT and a control group was 0.63 (95% confidence interval [CI]=0.36 to 0.90), corresponding to a number needed to treat of 2.91. Ten studies comparing IPT and other psychological treatments showed a nonsignificant differential effect size of 0.04 (95% CI=−0.14 to 0.21; number needed to treat=45.45) favoring IPT. Pharmacotherapy (after removal of one outlier) was more effective than IPT (d=−0.19, 95% CI=−0.38 to −0.01; number needed to treat=9.43), and combination treatment was not more effective than IPT alone, although the paucity of studies precluded drawing definite conclusions. Combination maintenance treatment with pharmacotherapy and IPT was more effective in preventing relapse than pharmacotherapy alone (odds ratio=0.37; 95% CI=0.19 to 0.73; number needed to treat=7.63).

Conclusions: There is no doubt that IPT efficaciously treats depression, both as an independent treatment and in combination with pharmacotherapy. IPT deserves its place in treatment guidelines as one of the most empirically validated treatments for depression.
The effects of IPT: included studies

- Studies on adolescents were included
- Studies on maintenance therapy were included
- Number of included studies: 38, with 4,356 patients
- Comparisons - Acute:
  - IPT vs. Control: 16
  - IPT vs. other psychotherapy: 13
  - IPT vs. pharmacotherapy: 10
  - Pharmacotherapy vs combined: 10
- Comparisons - Maintenance:
  - Pharmacotherapy vs combined: 4
  - IPT+placebo vs placebo: 4
## Effects of IPT - Acute

<table>
<thead>
<tr>
<th>Comparison</th>
<th>N</th>
<th>d</th>
<th>95% CI</th>
<th>$I^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>• IPT vs control</td>
<td>16</td>
<td>0.63</td>
<td>0.36~0.90 ***</td>
<td>82.96 ***</td>
</tr>
<tr>
<td>• IPT vs control (1 outlier removed)</td>
<td>15</td>
<td>0.52</td>
<td>0.36~0.68 ***</td>
<td>42.84 *</td>
</tr>
<tr>
<td>• IPT vs other psychotherapy</td>
<td>13</td>
<td>0.04</td>
<td>-0.14~0.21</td>
<td>39.81</td>
</tr>
<tr>
<td>• IPT vs pharmacotherapy</td>
<td>10</td>
<td>-0.12</td>
<td>-0.36~0.12</td>
<td>61.98 **</td>
</tr>
<tr>
<td>• IPT vs PHA (1 outlier removed)</td>
<td>9</td>
<td>-0.19</td>
<td>-0.38~-0.01 *</td>
<td>30.95</td>
</tr>
<tr>
<td>• Pharmacotherapy vs combined</td>
<td>10</td>
<td>0.16</td>
<td>-0.03~0.36</td>
<td>39.26</td>
</tr>
</tbody>
</table>
## Effects of IPT vs control

<table>
<thead>
<tr>
<th>Study name</th>
<th>Outcome</th>
<th>Statistics for each study</th>
<th>Std diff in means and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolton 2003</td>
<td>other</td>
<td>1.86, 1.54, 2.17</td>
<td>0.00</td>
</tr>
<tr>
<td>Bolton 2007</td>
<td>other</td>
<td>0.57, 0.30, 0.85</td>
<td>0.00</td>
</tr>
<tr>
<td>Elkin, 1989</td>
<td>Combined</td>
<td>0.24, -0.12, 0.60</td>
<td>0.19</td>
</tr>
<tr>
<td>Mufson 1999</td>
<td>Combined</td>
<td>0.66, 0.08, 1.24</td>
<td>0.03</td>
</tr>
<tr>
<td>Mufson 2004</td>
<td>Combined</td>
<td>0.44, -0.06, 0.94</td>
<td>0.09</td>
</tr>
<tr>
<td>Mulcahy, 2009</td>
<td>Combined</td>
<td>0.61, 0.04, 1.18</td>
<td>0.04</td>
</tr>
<tr>
<td>O’Hara 2000</td>
<td>Combined</td>
<td>1.15, 0.72, 1.58</td>
<td>0.00</td>
</tr>
<tr>
<td>Ransom 2008</td>
<td>BDI</td>
<td>0.16, -0.28, 0.60</td>
<td>0.47</td>
</tr>
<tr>
<td>Rossello 1999</td>
<td>CDI</td>
<td>0.76, 0.09, 1.42</td>
<td>0.03</td>
</tr>
<tr>
<td>Schulberg 1996</td>
<td>HRSD</td>
<td>0.44, 0.15, 0.73</td>
<td>0.00</td>
</tr>
<tr>
<td>Sloane 1985</td>
<td>HRSD</td>
<td>0.00, -0.69, 0.69</td>
<td>1.00</td>
</tr>
<tr>
<td>Spinelli 2003</td>
<td>HRSD</td>
<td>0.76, 0.10, 1.42</td>
<td>0.02</td>
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<tr>
<td>Swartz 2008</td>
<td>Combined</td>
<td>0.87, 0.22, 1.51</td>
<td>0.01</td>
</tr>
<tr>
<td>Tang, 2009</td>
<td>BDI</td>
<td>0.87, 0.39, 1.35</td>
<td>0.00</td>
</tr>
<tr>
<td>Van Schaik 2006</td>
<td>PRIME-MD</td>
<td>0.18, -0.15, 0.51</td>
<td>0.28</td>
</tr>
<tr>
<td>Weissman 1979</td>
<td>RTADS</td>
<td>0.42, -0.23, 1.07</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.63, 0.36, 0.90</td>
<td>0.00</td>
</tr>
</tbody>
</table>
Effects of IPT vs control

- N=16
- d=0.63 (NNT=3), after removal of outlier d=0.52 (NNT=4)
- Power to detect d=0.21
- No indication of publication bias
- Moderator analyses:
  - Adapted manual resulted in larger effects (d=0.67) than original manual (d=0.29)
  - No other significant moderators (adults vs specific target group; diagnostic interview vs self-report; usual vs waiting list vs other control; ITT vs per-protocol)
IPT vs other psychotherapies

- N=13; Power to detect d=0.25
- Resulting d=0.04
- No significant moderators
- Some publication bias (number of missing studies: 4; adjusted effect size: d=-0.11)
- Earlier meta-analysis found superior effects of IPT (Cuijpers et al., J Consul Clin Psychol 2008)
IPT vs pharmacotherapy

- N=10; Power to detect d=0.28
- Resulting d=-0.12, with significant heterogeneity ($I^2=61.98\%$).
- After removal of 1 outlier (Finkenzeller et al., 2009): d=-0.19 and significant (p<0.05)
- Moderator analyses: SSRIs had higher effect sizes (d=-0.39) than TCAs (d=-0.02); maybe due to studies on dysthymic patients
- No indications for publication bias
- Other meta-analyses show that psychotherapy = pharmacotherapy (Cuijpers et al., J Clin Psychiatry 2008; 2010)
IPT+PHA vs PHA alone

- $N=10$; Power to detect $d=0.28$
- Resulting $d=0.16$ (n.s.)
- No significant moderator analyses
- Some indications for publication bias (number of missing studies: 3; adjusted $d=0.07$)
- Combined treatment vs psychotherapy is effective in other meta-analyses (Cuijpers et al., Depress & Anx 2009) as is combined vs pharmacotherapy (Cuijpers et al., J Clin Psychiatry 2009)
IPT as maintenance treatment

- **M-PHA vs combined M-IPT+M-PHA (N=4):**
  - Recurrence rate: OR=0.37 (95% CI: 0.19~0.73); NNT=8

- **M-IPT+placebo vs placebo**
  - Recurrence rate: OR=0.47 (95% CI: 0.25~0.87); NNT=6
Conclusions from meta-analysis IPT

- IPT is effective as acute treatment of depression
- Not clear whether pharmacotherapy is better
- Not better than other psychotherapies
- M-IPT is effective in reducing relapse
- It is well-examined, and deserves its prominent place in treatment guidelines
Positive results on IPT from other meta-analyses
Prevention of depressive disorders

- A meta-analysis of preventing the onset of depressive disorders (not based on database)
- 19 studies, with 21 comparisons between prevention and care-as-usual control
- IRR = 0.78 (95% CI: 0.65 to 0.93)
- Subgroups of types of interventions:
  - Based on CBT: IRR = 0.84 (95% CI: 0.71~1.00)
  - Based on IPT: IRR = 0.14 (95% CI: 0.05~0.44)
  - Other: IRR = 0.76 (95% CI: 0.47~1.20)
- Difference is significant
- Caution: only 3 small studies

Cuijpers et al., Am J Psychiatry 2008
Publication bias

- Duvall & Tweedie’s trim & fill procedure:
  - Unadjusted effect size: $d=0.67$
  - Adjusted effect size: $d=0.42$ (p<0.001)
  - Imputed studies: 51

- Other tests: Begg & Mazumdar; Egger’s test

- For all psychotherapies together: Very significant results (p<0.001)

- Strong indications for publication bias in CBT

Cuijpers et al., Br J Psychiatry 2010
Publication bias? Unadjusted
Publication bias? Adjusted
Publication bias in IPT?

- No indication for publication bias in IPT
- Number of imputed studies: 0
- Unadjusted and adjusted effect sizes are exactly the same
- Caution: number of studies is much smaller than for CBT
53 studies directly comparing 7 major types of psychotherapy for depression

7 separate meta-analyses

IPT > others: N=8; d=0.21 (95% CI: 0.01~0.42), p<0.05

CBT vs IPT: N=5; d=0.12 (95% CI: 0.33~0.09)

Difference is significant, but small

Not replicated in AJP 2011 meta-analysis

Cuijpers et al., J Consult Clin Psychol 2008
Differences between types of psychotherapies?

<table>
<thead>
<tr>
<th>Methodology</th>
<th>$N$</th>
<th>$d$</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT vs all other</td>
<td>56</td>
<td>0.03</td>
<td>166.67</td>
</tr>
<tr>
<td>Supportive vs all other</td>
<td>30</td>
<td>-0.17*</td>
<td>10.42</td>
</tr>
<tr>
<td>Behavioral Activation vs all other</td>
<td>21</td>
<td>0.14</td>
<td>12.82</td>
</tr>
<tr>
<td>Psychodynamic vs all other</td>
<td>16</td>
<td>-0.07</td>
<td>25.00</td>
</tr>
<tr>
<td>PST vs all other</td>
<td>7</td>
<td>0.40</td>
<td>4.50</td>
</tr>
<tr>
<td>IPT vs all other</td>
<td>8</td>
<td>0.21*</td>
<td>8.47</td>
</tr>
<tr>
<td>Social Skills vs all other</td>
<td>7</td>
<td>0.05</td>
<td>35.71</td>
</tr>
</tbody>
</table>
Challenges...
Relation between effect size and study quality?

• 115 controlled studies
• Quality criteria (Chambless & Hollon, 1998; Cochrane)
  (1) diagnostic criteria for a depressive disorder
  (2) treatment manual
  (3) training of therapists
  (4) treatment integrity was checked
  (5) intention-to-treat analyses
  (6) minimal level of statistical power ($N \geq 50$)
  (7) randomization conducted by independent party
  (8) assessors of outcome were blinded
• Only 11 studies met all criteria!
• Only 2 on IPT (8 on CBT)!

Cuijpers et al., Psychol Med 2009
### Difference between high-quality and other studies

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>d</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All studies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- High-quality</td>
<td>16</td>
<td>0.22</td>
<td>8.06</td>
</tr>
<tr>
<td>- Other</td>
<td>162</td>
<td>0.75</td>
<td>2.48</td>
</tr>
<tr>
<td><strong>CAU</strong></td>
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<tr>
<td>- High-quality</td>
<td>9</td>
<td>0.22</td>
<td>8.06</td>
</tr>
<tr>
<td>- Other</td>
<td>34</td>
<td>0.51</td>
<td>3.55</td>
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<tr>
<td><strong>Placebo</strong></td>
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<td></td>
</tr>
<tr>
<td>- High-quality</td>
<td>7</td>
<td>0.23</td>
<td>7.14</td>
</tr>
<tr>
<td>- Other</td>
<td>27</td>
<td>0.55</td>
<td>3.31</td>
</tr>
</tbody>
</table>
How does psychotherapy work?

- Dismantling studies
- Studies on mediators
  - Change in mediator is associated with change in outcome
  - Causal association can not be proven
  - Results are not presented
Component and mediation studies

- 7 studies in which a component is removed: none on IPT
- 6 studies in which a component is added: none on IPT
- Differences between pooled studies are not significant
- All studies have far too little statistical power
- 6 studies on mediators, none on IPT
- Conclusion: We have very little knowledge on how psychotherapies work, none on IPT
Are specific therapies needed?

- Meta-analysis of 30 studies on non-directive supportive therapy (NDST)
- NDST vs control: $g=0.59$ (95% CI: 0.45~0.72)
- NDST vs other psychological treatments differential $g=-0.17$ (95% CI: -0.28~0.05; N=33)
- Not significant after controlling for researcher allegiance
- NDST vs CBT: $g=-0.06$ (95% CI: -0.20~0.07; N=23)
- NDST vs IPT: $g=-0.12$ (95% CI: -0.47~0.23; N=3)

Cuijpers et al., Clin Psychol Rev 2012
Summary

• Main meta-analysis
  – IPT is effective as acute treatment of depression
  – Not clear whether pharmacotherapy is better
  – Not better than other psychotherapies
  – M-IPT is effective in reducing relapse
  – It is well-examined, and deserves its prominent place in treatment guidelines

• Positive results on IPT from other meta-analyses:
  – Maybe effective as preventive intervention
  – No publication bias

• Challenges:
  – Few high-quality studies / lower effect sizes
  – Very little research on how it works
  – Contribution of specific effects may be limited
Conclusions

• IPT is effective and more than deserves its place in treatment guidelines

• More research is needed in how it works and for whom

• We need high-quality research

• One advantage of IPT is that there is one manual that is used in most studies: treatment integrity

• Translating IPT to routine practice

• Dissemination!
Thank you for your attention!

More information on: www.evidencebasedpsychotherapies.org

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