Day Patient Treatment after Short Inpatient Care vs. Inpatient Treatment in Adolescent Anorexia Nervosa:

results of a multicenter, randomized open-label, non-inferiority trial

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Beate Herpertz-Dahlmann, Aachen
Objectives I

1. With the exception of family therapy there is a dearth of studies on the treatment of adolescent AN;

2. In spite of insufficient research evidence inpatient setting (IP) is considered the treatment of choice especially for moderately to severely undernourished patients (APA 2006, German guidelines 2011);

3. High readmission rates have challenged this opinion (Gowers et al. 2007; Steinhausen et al. 2008)

4. Very few open studies on day patient treatment (DP) with small sample sizes exist, only one in adolescent AN. (e.g. Zipfel et al. 2002; Olmsted 2007, Goldstein et al. 2011)
Objectives II
Possible advantages of day patient in comparison to inpatient treatment

1. New skills might be better transferred to everyday life;

2. Maintaining contact to family and peers;

3. Better resumption of own responsibility;

Inclusion criteria for randomized trial – comparison of inpatient and day patient setting -

- AN according to DSM-IV criteria
- Body weight below 10th percentile
- First admission for AN
- Age: 11-18 years
- Female sex
- IQ > 85
- Distance from residence to hospital within a 60 minute commute
Precondition for participation:

Day patient \textit{and} inpatient treatment setting at the same department
Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa

Procedure:

1. Inpatient somatic stabilization period of three weeks
2. Randomization
3. Standardized identical multimodal treatment program in both settings till reaching target weight (15th -20th BMI percentile)
4. DP for 5 days a week (with few exceptions)
5. Followed by an outpatient individual and group therapy till 52nd week after admission

Hypothesis: DP is not inferior to IP
Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa
Day patient treatment
– arriving in the morning by taxi –
Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa

Assessed for eligibility (N=660)

approached to participate: (N=275)

Randomized (N=176)

Alotted to inpatient treatment (N=85)

Allocated to day patient treatment (N=87)

Post-randomization exclusions (N=4)

excluded (N=385)

Declined participation (N=95)

Discontinued (N=10)

Completed inpatient treatment (N=75)

Completed day patient treatment (N=62)

Included in ITT-analysis (N=75)

Lost for follow up (N=10)

Included in ITT-Analysis (N=86)

Lost to follow-up) (N=1)
Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa

**Demographic and Clinical Characteristics at Admission**

<table>
<thead>
<tr>
<th>(mean ± sd)</th>
<th>AN Inpatient treatment N=85</th>
<th>AN Daypatient treatment N=87</th>
<th>p =</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>15.2 ± 1.5</td>
<td>15.3 ± 1.5</td>
<td>0.599</td>
</tr>
<tr>
<td>Duration of illness (weeks)</td>
<td>53.7 ± 39.6</td>
<td>42.4 ± 33.1</td>
<td>0.044</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>15.1 ± 1.2</td>
<td>14.9 ± 1.5</td>
<td>0.439</td>
</tr>
<tr>
<td>BMI-percentile for age and sex</td>
<td>2.1 ± 4.9</td>
<td>1.7 ± 3.0</td>
<td>0.536</td>
</tr>
<tr>
<td>Binge/purging type* n (%)</td>
<td>14 (16.5)</td>
<td>17 (19.8)</td>
<td>0.692</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>33 (44.0)</td>
<td>28 (38.4)</td>
<td>0.508</td>
</tr>
</tbody>
</table>
### Demographic and Clinical Characteristics at Discharge

<table>
<thead>
<tr>
<th>(mean ± sd)</th>
<th>AN Inpatient treatment N=84</th>
<th>AN Daypatient treatment N=87</th>
<th>p =</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of treatment (days)</td>
<td>103 ± 41</td>
<td>116 ± 49</td>
<td>0.072</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>17.9 ± 1.1</td>
<td>18.1 ± 0.9</td>
<td>0.20</td>
</tr>
<tr>
<td>BMI-percentile for age and sex</td>
<td>17.5 ± 8.3</td>
<td>18.6 ± 8.5</td>
<td>0.40</td>
</tr>
<tr>
<td>BMI-SDS</td>
<td>-1.0 ± 0.5</td>
<td>-1.0 ± 0.4</td>
<td>0.26</td>
</tr>
</tbody>
</table>
Demographic and Clinical Characteristics at 52nd-week-follow up

<table>
<thead>
<tr>
<th>(mean ± sd)</th>
<th>AN Inpatient treatment N=85</th>
<th>AN Daypatient treatment N=87</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI [kg/m²]</td>
<td>17.8 ± 1.7</td>
<td>18.1 ± 2.0</td>
</tr>
<tr>
<td>BMI-percentile for age and sex</td>
<td>16.7 ± 17.0</td>
<td>18.6 ± 19.7</td>
</tr>
<tr>
<td>BMI-SDS</td>
<td>-1.3 ± 0.9</td>
<td>- 1.2 ± 0.9</td>
</tr>
</tbody>
</table>
Intention-to-treat analysis
day patient (n=86) compared to inpatient (n=75) treatment

Method

► **Statistical Method:** linear Model (ANCOVA) adjusting for
  - BMI
  - duration of eating disorder
  - age

  at admission

► **Primary Endpoint:** weight gain (delta BMI) at week 52
  or at relapse

► **Main Results:**
  - Estimate Difference: 0.46 kg/m²
  - 95% confidence interval: (-0.12 kg/m² to 1.02 kg/m²)
Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa

Results: Intention-to-treat (ITT) and per-protocol analysis (PP)

Test for Non-Inferiority
\[ p = 0.0001 \]

Day patient treatment is non-inferior to inpatient treatment

Test for Superiority
\[ p = 0.12 \]

Superiority could not be shown
Per protocol - Analysis
Day patient compared to inpatient treatment

Per protocol sample including „changers“: patients who completed treatment according to trial rules including those who had to change into inpatient treatment because of medical reasons or suicidality
- (IP: n=65; DP: n=70)

Estimator: 0.44 kg/m² (95%-CI: -0.17 kg/m² - 1.06 kg/m²)
Results: Intention-to-treat (ITT) and per-protocol analysis (PP)

Test for Non-Inferiority
\[ p = 0.0001 \]

Day patient treatment is non-inferior to inpatient treatment

Test for Superiority
\[ p = 0.12 \]

Superiority could not be shown
## Average Outcome Score 52nd week

### Average Morgan&Russell Score (MRAOS)

<table>
<thead>
<tr>
<th></th>
<th>IP</th>
<th>n=69</th>
<th>DP</th>
<th>n=71</th>
<th>CI</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MRAOS Subscales</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>scale A (food intake)</td>
<td>6.6</td>
<td>3.2</td>
<td>7.7</td>
<td>3.1</td>
<td>1.02 (-0.03 to 2.08)</td>
<td>0.06</td>
</tr>
<tr>
<td>scale B (menstruation)</td>
<td>4.2</td>
<td>4.9</td>
<td>4.1</td>
<td>5.0</td>
<td>-0.52 (-2.19 to 1.16)</td>
<td>0.54</td>
</tr>
<tr>
<td>scale C (mental state)</td>
<td>8.0</td>
<td>3.1</td>
<td>10.1</td>
<td>2.6</td>
<td>1.05 (0.09 to 2.02)</td>
<td>0.03</td>
</tr>
<tr>
<td>scale D (psychosexual adjustment)</td>
<td>7.5</td>
<td>3.5</td>
<td>9.1</td>
<td>2.7</td>
<td>1.29 (0.34 to 2.24)</td>
<td>0.008</td>
</tr>
<tr>
<td>scale E (socio-economic state)</td>
<td>9.8</td>
<td>2.1</td>
<td>10.5</td>
<td>1.5</td>
<td>0.46 (-0.12 to 1.04)</td>
<td>0.12</td>
</tr>
</tbody>
</table>
Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa

Drop out of treatment and drop out of study and Relapses in ITT-Sample

Drop out of treatment: 20%
- IP: 10 (out of 85): 12%
- DP: 25 (out of 87): 29%

Drop out of study at 52nd week follow-up: 7%
- IP: 10 (out of 85): 12%
- DP: 1 (out of 87): 1%  p<0.005

Relapses at 52nd week follow-up: 19%
- IP: 19 (out of 75): 25%
- DP: 13 (out of 86): 15%  p<0.12

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Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa

Day Patient Treatment after Short Inpatient Care vs. Inpatient Treatment in Adolescent Anorexia Nervosa

### Costs

<table>
<thead>
<tr>
<th>Costs (€)</th>
<th>IP Mean (sd)/number (%)</th>
<th>N</th>
<th>DP Mean (sd)/number (%)</th>
<th>N</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>39.481 € (± 16174)</td>
<td>85</td>
<td>31.114 € (± 16.246)</td>
<td>87</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>(33.788 ± 13.842 £)</td>
<td></td>
<td>(26.628 ± 13.903 £)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Serious Adverse Events

<table>
<thead>
<tr>
<th>Category</th>
<th>IP</th>
<th>DP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Intensive treatment because of complete refusal of eating</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Appendectomy</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td><strong>After discharge</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suicidal ideation</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>IP for depression</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Somatic problems (circulatory collapse)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Suicide attempt</td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>
Conclusion I

1. In a large randomized multisite trial after short medical stabilization DP was as effective as IP in young non-chronic AN;
2. superiority of day patient treatment just missed significance;
3. patients in the DP-group were more compliant;
4. Psychosocial outcome tended to be better in DP;
Conclusion II

► Stepped-care DP resulted in a mean insurance cost savings of 20%;

► Considering the developmental significance of adolescence, treatment options facilitating autonomy and self-confidence should be supported;

► Investigation of 2.5-year- follow-up is still going on.
And the parents and patients?

► „It is wonderful being at home in the evening together with my family and friends…“

► „Eating at home is much more comfortable and relaxing…“

► „It was so good that our daughter was at home – although it was hard for us…“

► „It was good that our daughter could keep her personal contacts and friends…she was never lonely…“

► „(During DP) she got much more independent and self-conscious than ever before…“

► „DP was the best that could happen to her – it was like getting six numbers right in the lottery…“
Comparison of inpatient and day-patient treatment in adolescent anorexia nervosa

Thanks to

► A. Dempfle, Statistician, Marburg

- Ch. Fleischhaker, MD, Freiburg
- Ch. Wewetzer, MD, Cologne
- A. Warnke, MD, Würzburg
- U. Lehmkuhl & E. Pfeiffer, MD, Berlin
- B. Müller, MD, Düren

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And to my team in Aachen

Thank you for your attention.

And of course to all the patients and parents!

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Results

Comparison of Intention-to-treat analysis (DP (n=86)/ IP (n=75) and per protocol analysis including changers (PPS1) and without changers (PPS2)

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And the parents and patients? Critical voices...

► “Everything at home remembers me of my old anorexia: the table, the fridge, it is a great effort…”

► “At the beginning I did not know whether to be happy or unhappy (about day patient treatment): it was so difficult at home…”

► “The disadvantage of day patient treatment is that you can do so much more in secret: running, exercising, skipping meals…”

► “We, the family, definitely had to realize that our daughter was so ill …”