

New Developments in the Diagnostics and Treatment of Adolescent Eating Disorders



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Disclosure ESCAP Madrid 2015

Since 2012:

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German Research Society (DFG)

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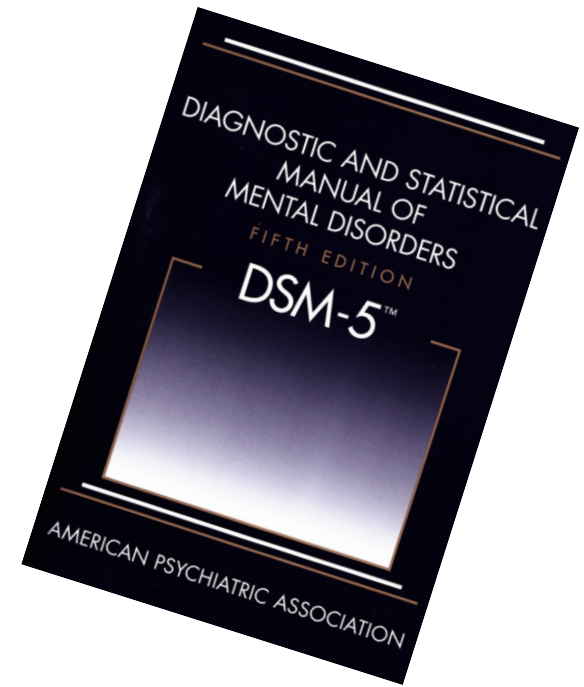


Outline of the talk (with emphasis on adolescent AN)

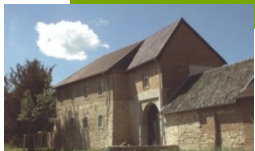
- Definition und Classification
- Epidemiology
- Etiology
- Assessment

- Treatment Setting
- Treatment Modalities
- Outcome





Definition und Classification of Eating Disorders





Diagnostic criteria according to DSM-5

Anorexia nervosa

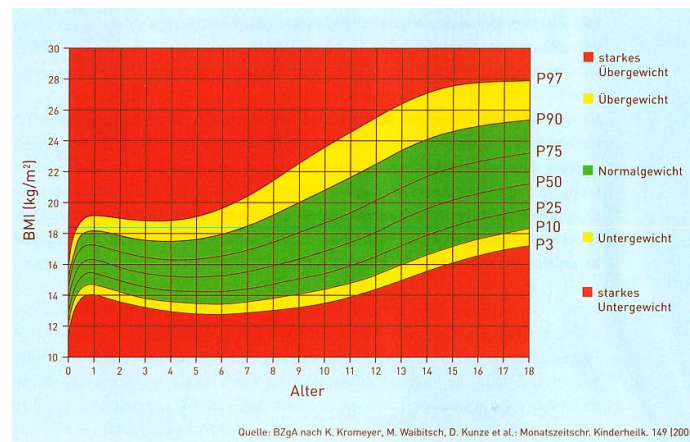
1. Restriction of energy intake relative to requirements, **leading to a significantly low body weight** in the context of age, sex, developmental trajectory, and physical health. Significantly low body weight is defined as a weight that is less than minimally normal or, for children and adolescents, less than minimally expected (instead of **refusal** to maintain body weight at a minimally normal weight).
2. Intense fear of gaining weight or of becoming fat, or **persistent behavior** that interferes with weight gain, even though at a significantly low weight.
3. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight (instead of **denial**).
4. Omission of the **amenorrhea-criterion**
5. Specify: **Restricting OR Binge-eating/Purging type**



Weight criterion – anorexia nervosa

For children and adolescents

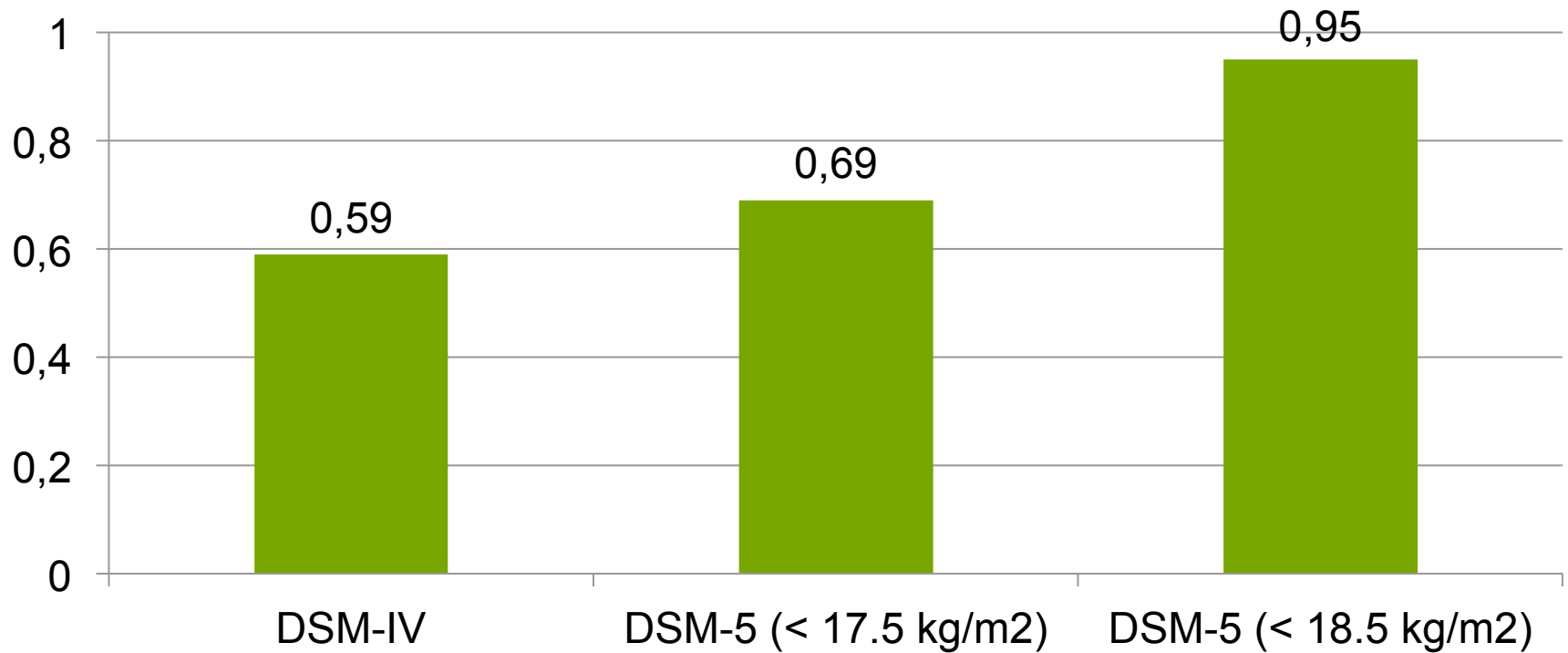
- DSM-5: „BMI percentiles should be used“.
- Proposed threshold: 10th BMI-percentile corresponding to a BMI of 18.5 in adults.
- However: proposal by ICD-11 (draft version): 5th percentile



Prevalence of AN (%) in relationship to classification and weight threshold

%

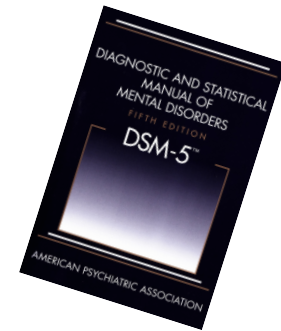
- Age: 16.29 y. (12-23 y.) High school and university students
- n=3048



(Machado et al. 2013)



Diagnostic criteria according to DSM-5 Bulimia nervosa (abbreviated form)

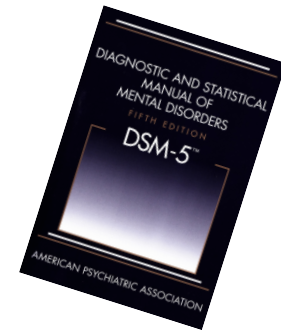


- a. Recurrent episodes of binge eating.
- b. Recurrent inappropriate compensatory behaviors, e.g. self-induced vomiting, laxative or diuretics abuse, or fasting or excessive exercise.
- c. Frequency of binge eating at least **once a week** for 3 months.
- d. Self-confidence is contingent on weight and shape.
- e. Symptoms do not only occur during the context of AN.



Diagnostic criteria according to DSM-5

Binge Eating Disorder (BED) (abbreviated form)



- a. Recurrent episodes of binge eating.
- b. Binge eating is associated with eating faster until feeling uncomfortably full, eating when not feeling hungry, eating alone due to being embarrassed, or feeling disgusted or depressed.
- c. Marked distress because of the symptoms.
- d. Frequency at least once a week for 3 months.
- e. Symptoms are not followed by compensatory behavior and do not occur in the context of BN or AN.

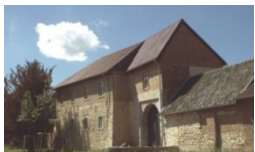


Loss of control of eating

- Loss of control of eating (LOC) and **not overeating** seems to be predictive of later overweight and obesity and depression” (Tanovsky-Kraff et al. 2009).
- “When I start to eat I just can’t stop“.

| | % Partic. | SCOFF Follow-up | overweight Follow-up | Low weight Follow-up | Depression Follow-up PHQ |
|-----------------------------|--------------|--------------------|-------------------------|-------------------------|--------------------------------|
| Deliberate vomiting | 4.5 | 0.06 | 0.05 | 0.02 | 0.003 |
| Loss of control over eating | 23.3 | < 0.0001 | 0.03 | 0.42 | 0.0006 |
| Weight loss | 4.8 | 0.05 | 0.11 | 0.28 | 0.48 |
| Body image distortion | 19.3 | < 0.0001 | 0.02 | 0.40 | 0.31 |
| High impact of food on life | 21.1 | 0.0004 | 0.22 | 0.07 | 0.25 |

BELLA-study, n=771, Herpertz-Dahlmann et al. ECAP 2015; Session M 7-01 today!





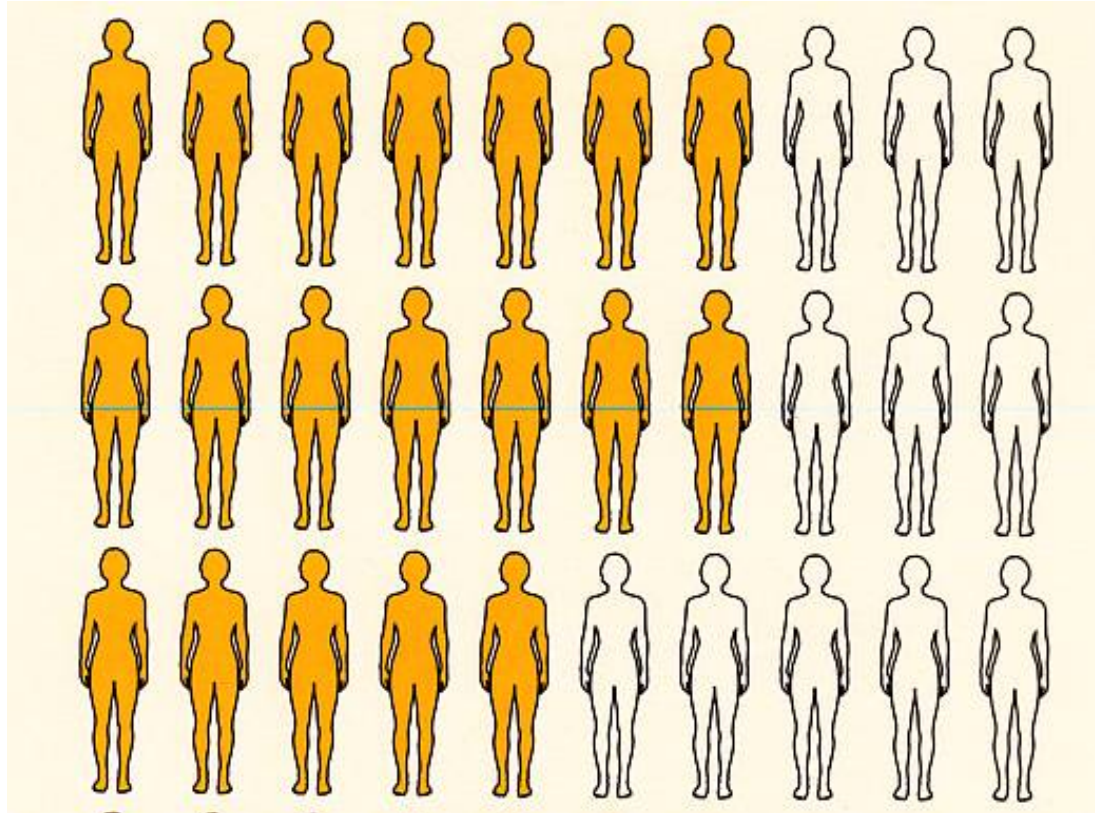
Summary (1)

- classification and definition

- a. AN: Removal of items in DSM-5 that imply a deliberate attitude and willful actions of the patient;
- b. - but lack of a weight criterion for children and adolescents;
- c. Reduction of the residual diagnosis of EDNOS by lowering the thresholds for AN and BN and introducing the new specific diagnostic criteria for BED;
- d. Feeling of loss of control in childhood seems to be more important for outcome than overeating.



Epidemiology

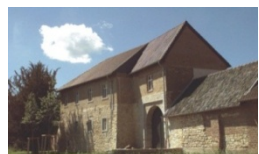


Epidemiology: Incidence of ED per 100 000 population for the year 2009 by age and gender

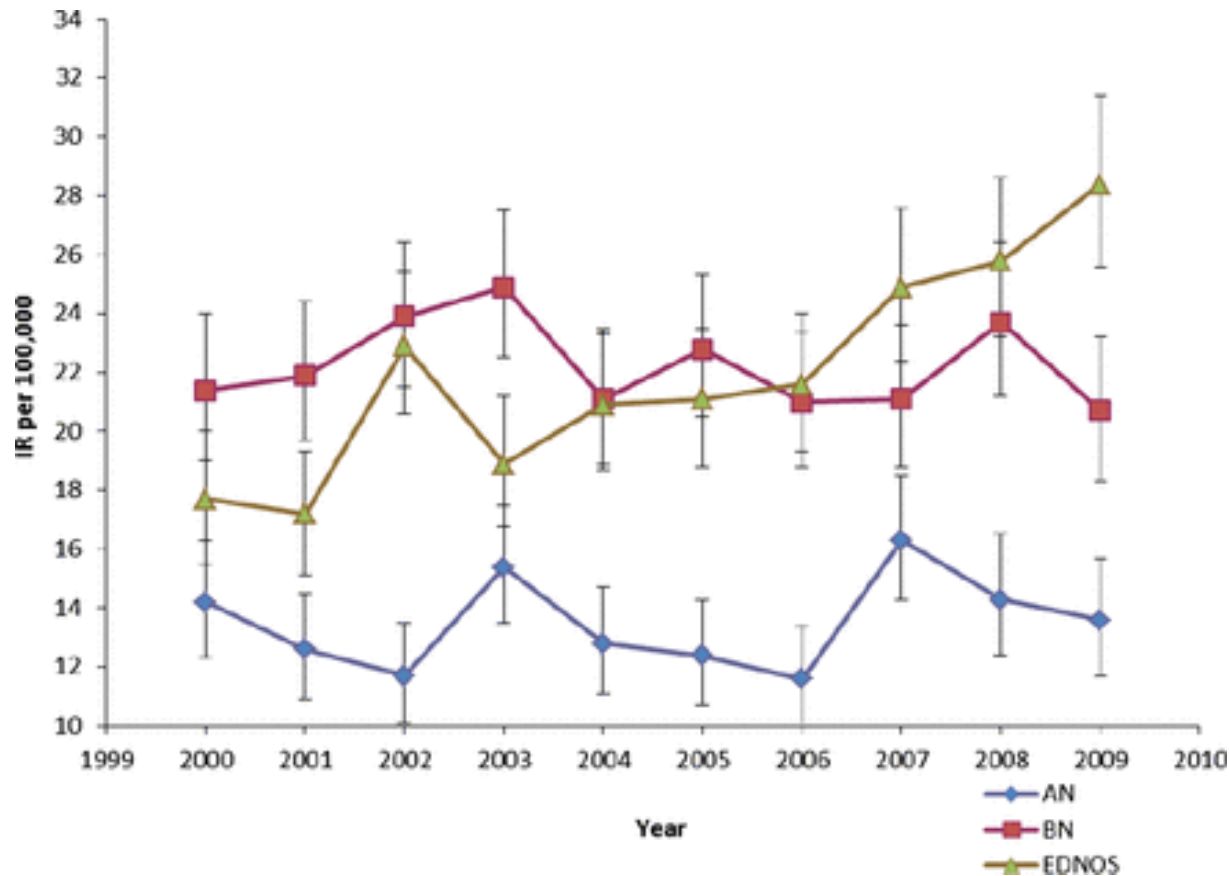


All eating disorders

| Age (years) | Females | | | Males | | |
|-------------|-----------|----------------|------------------------|-----------|----------------|---------------------|
| | Cases (N) | Population (N) | Incidence (95% CI) | Cases (N) | Population (N) | Incidence (95% CI) |
| 10–14 | 74 | 116.476 | 63.5 (50.2 to 79.3) | 21 | 120.219 | 17.5 (11.1 to 26.2) |
| 15–19 | 239 | 145.279 | 164.5 (144.6 to 186.4) | 23 | 132.375 | 17.4 (11.3 to 25.6) |
| 20–29 | 309 | 349.163 | 88.5 (79.4 to 98.8) | 28 | 277.454 | 10.1 (6.8 to 14.4) |
| 30–39 | 138 | 338.255 | 40.8 (34.4 to 48.0) | 6 | 288.468 | 2.1 (0.8 to 4.3) |
| 40–49 | 56 | 352.843 | 15.9 (12.1 to 20.5) | 3 | 319.724 | 0.9 (0.2 to 2.5) |



Epidemiology : Incidence rates of anorexia nervosa, bulimia nervosa and EDNOS for females aged 10- 49 y., primary care.



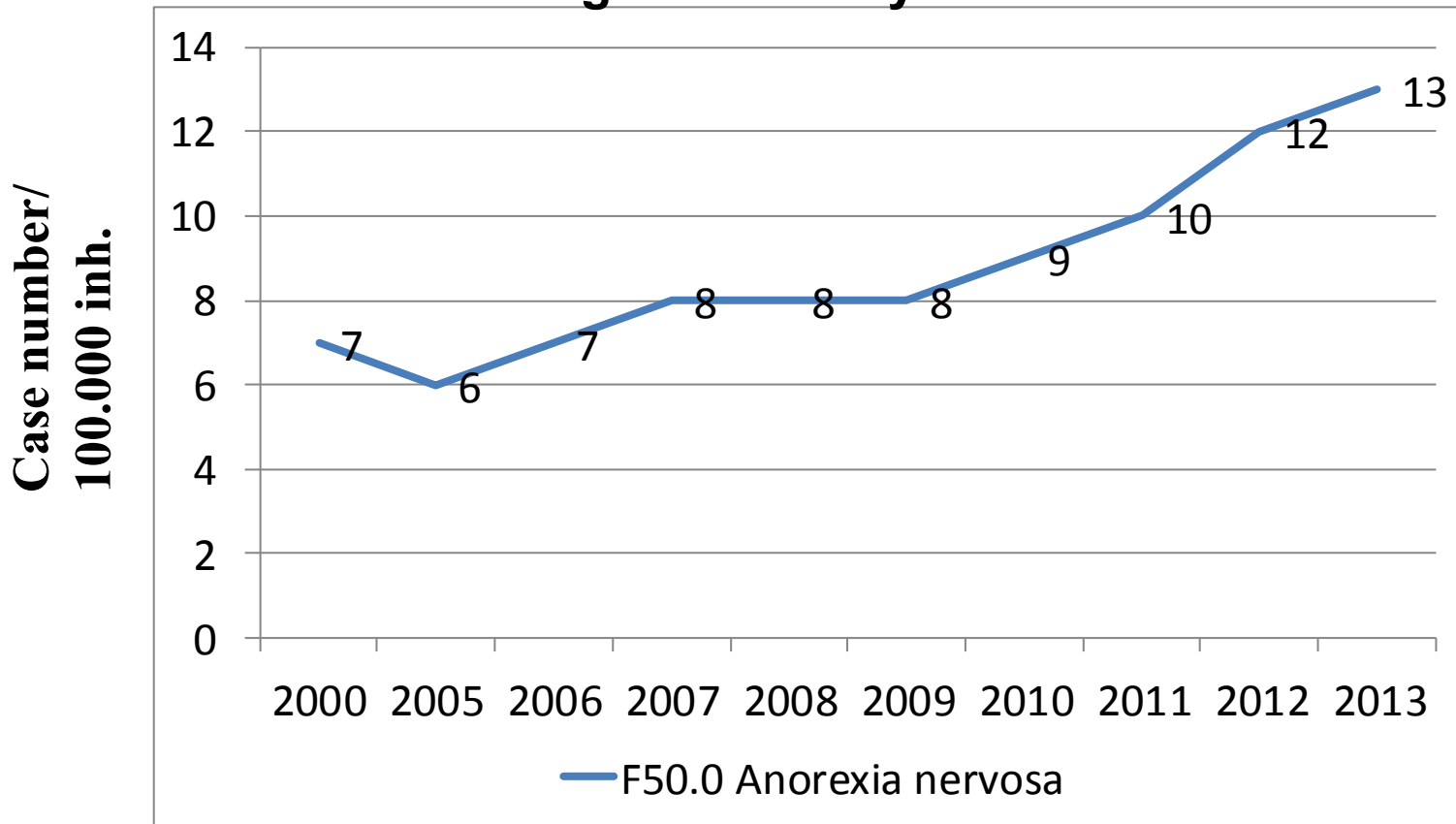
(Micali et al. 2013)
! Session M 7-01
today!



Increase of admissions to inpatient treatment for childhood AN in Germany



Age below 15 years



(German Institute for Federal Statistics, www.gbe-bund.de, 18.6.15)

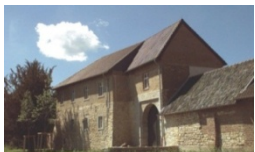


Incidence and prevalence rates of AN, BN and EDNOS in adolescence

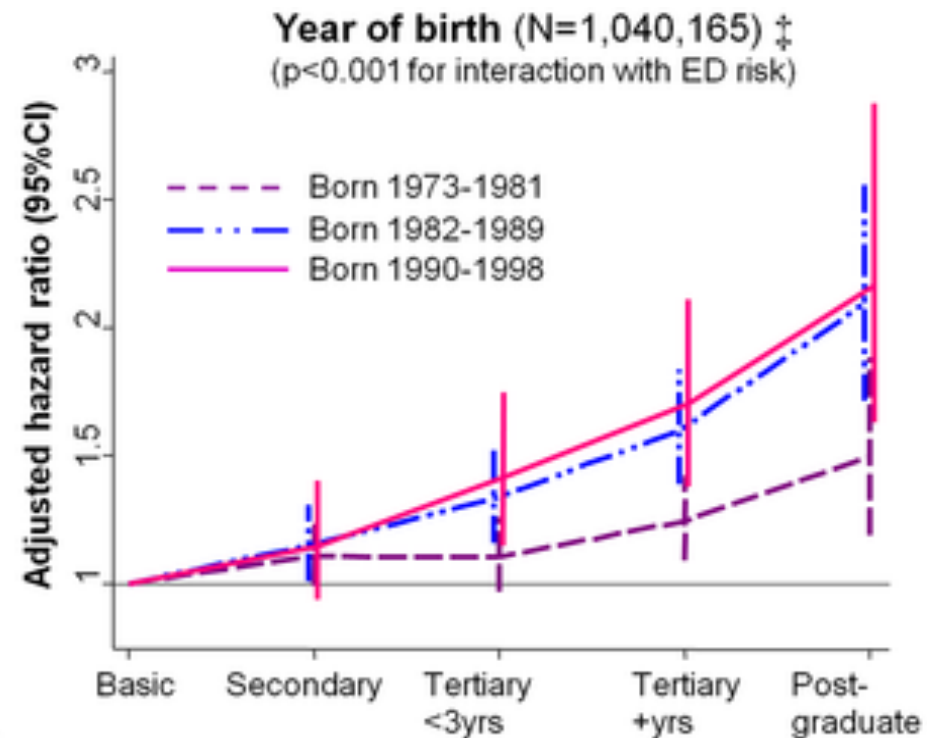
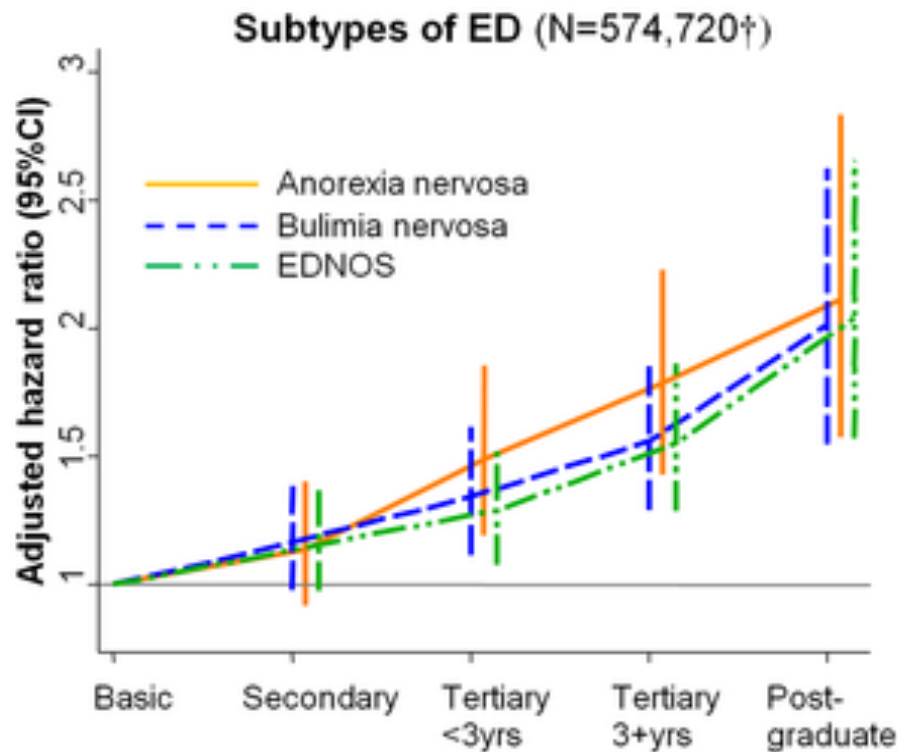


| | AN | | BN | | BED | |
|--|---------|---------|--------|---------|-------------|---------|
| | Female | Male | Female | Male | Female | Male |
| Incidence 100.000 15-19-year-olds in primary care | 40-100 | 1-4 | 40-50 | 2-3 | 70 EDNOS | 10 |
| 1 2 - m o n t h - prevalence (%) | 0.3-0.9 | 0.1-0.3 | 1-2.0 | 0.3-0.5 | 1.5-2.0 | 0.4-0.8 |

According to Currin et al. 2005, Swanson et al. 2011, Micali et al. 2013; reviews by Smink et al. 2012; 2013



Association between SOS and the development of an ED: Parental Educational Level and ED of their Daughter in Sweden across ED subtypes and year of birth



(Goodman et al. 2014)



Summary (2) - Epidemiology



- Incidence rates of AN are stable in Western countries in the adult group, probably increasing in childhood and adolescence;

- No significant increase of male to female ED ratio

(Micali et al. 2013);

- Increasing rates of ED in Asia and the Arab region

(Pike et al. 2014) ;

- Constant associations with SES and education

(e.g. Goodman et al. 2014);

- Highest incidence rate for AN and BN between 15-19 y.

- Increasing incidence in childhood?

(Smink et al. 2013; Nicholls et al. 2011);

- Increasing admissions of children in many European countries.



Comorbidity of AN with other psychiatric disorders

| | Prevalence |
|-------------------------------|-------------------|
| ▶ Anxiety disorders | 20-60 % |
| • Social phobia | 20-55 % |
| • Separation anxiety disorder | 17-66 % |
| ▶ Affective disorders | 15-60 % |
| ▶ OCD | 20-40 % |
| ▶ Substance abuse | 8-18 % |

Substance abuse and suicidality is more prevalent in the binge/purge subtype of AN and in BN.

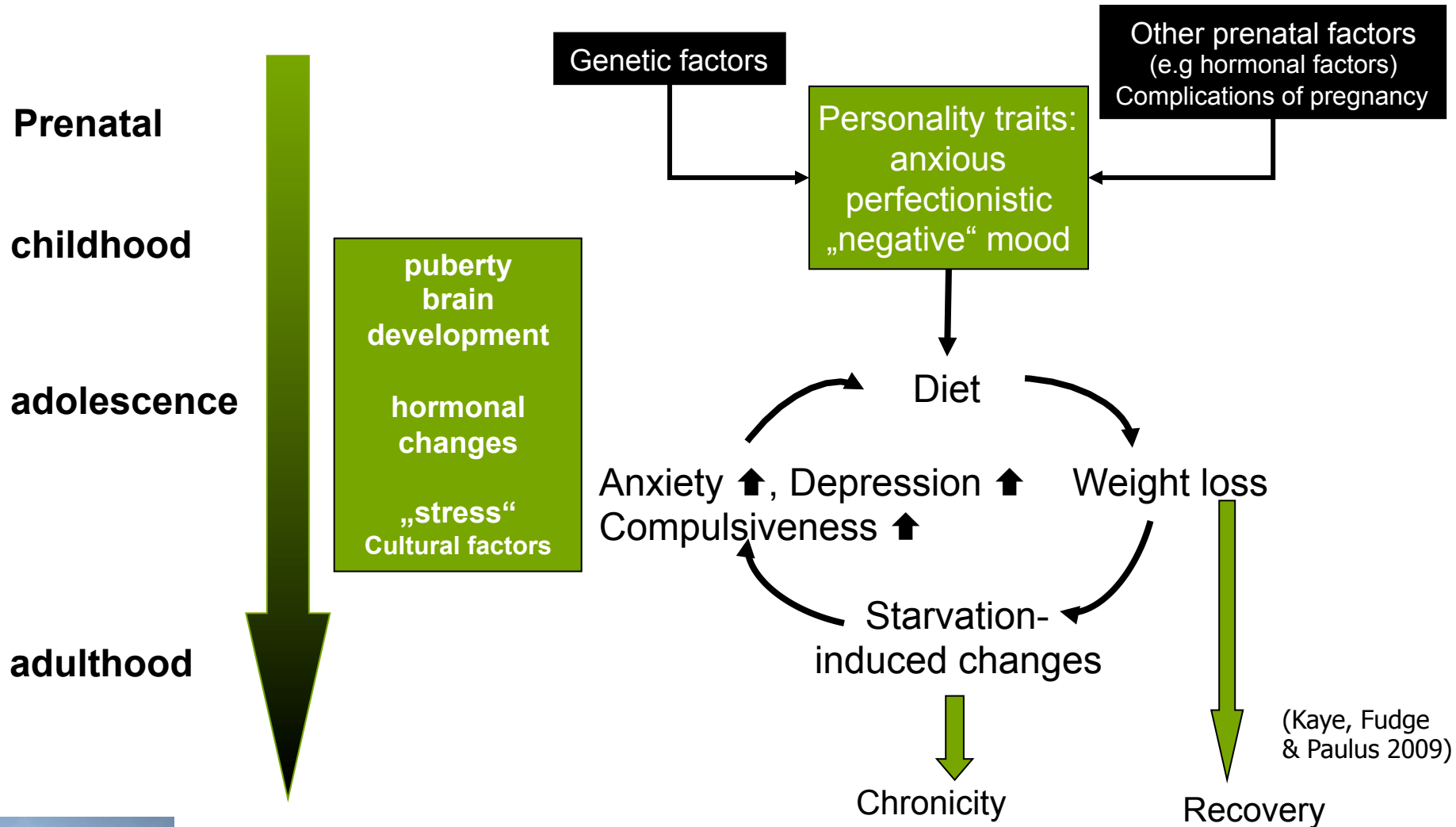
It is not yet clear, whether the restrictive type of AN protects against substance



Etiology



Etiology of AN





Assessment

Somatic changes and problems in AN

Medical assessment of eating disorders

- 1. Physical assessment** (heart rate, blood pressure, body temperature, dehydration, pubertal development)
- 2. Complete blood count**
- 3. Biochemical profile** (electrolytes, magnesium, phosphate, creatinine, urea, serum proteins, glucose, liver enzymes, amylase, lipase)
- 4. ECG** (bradycardia, prolonged QT-interval, pericardial effusion, edema)
- 5. EEG, MRI, CT** (in case of atypical eating disorder, e.g. boys, children, or manifestation of seizures)



Important Endocrine Dysregulations in AN

| | |
|------------------------------|------------------------------|
| Thyroid axis | ↓ fT3, n (↓) fT4 |
| Gonadal axis | ↓ LH pulsatility |
| | ↓ Estrogens |
| | ↓ Androgens |
| Adrenal axis | ↑ Cortisol |
| | ↔ DHEAS |
| Growth hormone | GH resistance (↑ GH/↓ IGF-1) |
| Appetite-regulating hormones | ↓ Leptin |
| | ↑ Ghrelin |
| | ↑ PYY |

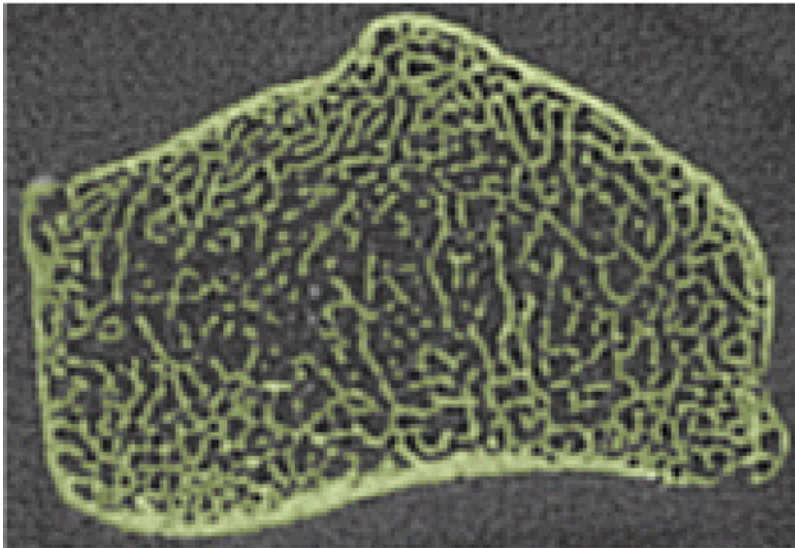


Abnormal bone microarchitecture in women with AN

(computed tomography, distale radius)

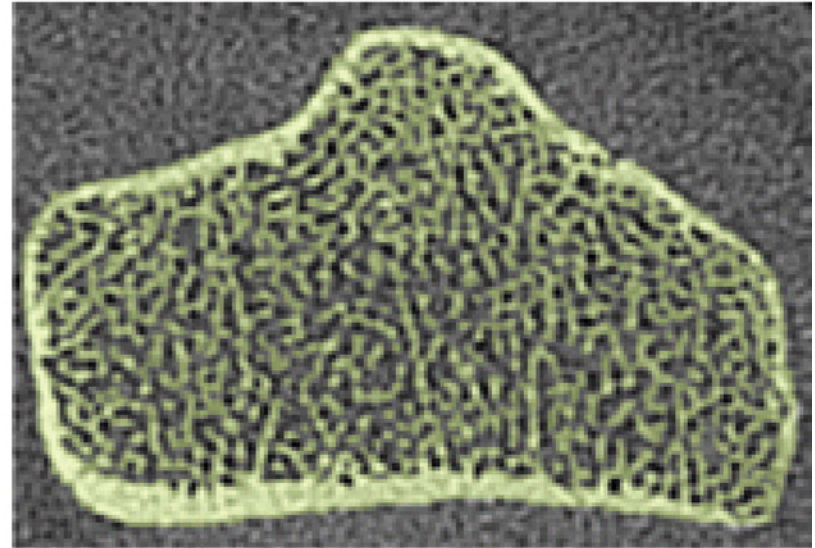
AN

A



Healthy control

B



(Miller K K JCEM 2011;96:2939-2949)



Estrogen supplementation in AN??

1. No benefit of estrogen in oral contraceptives for bone mineral density in AN, however, probably harmful (Misra et al. 2011; Starr & Kreipe 2014, review by Lebow et al. 2014)
-> suppression of IGF-1 and androgen production by the liver
2. *Withdrawal bleeding often misunderstood as normalisation of menstrual cycle*
3. Transdermal physiologic estrogen replacement !

(Misra et al. 2011)

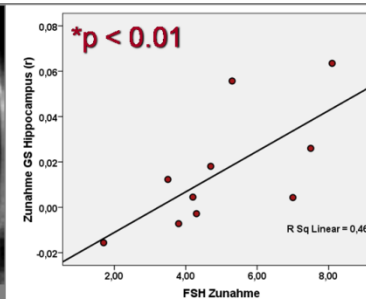
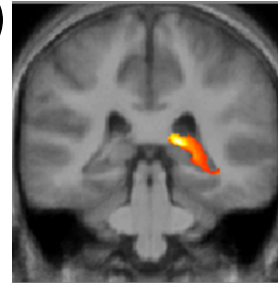


Hormonal Changes and Brain Structure in Adolescent AN

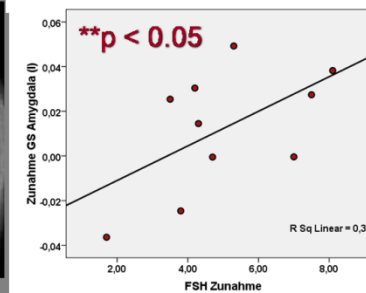


Association with gonadal axis (FSH)

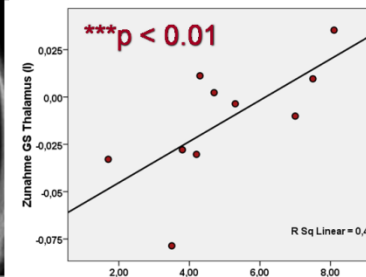
ROI Hippocampus (uncorr)
Spearman`s Rho: 0.733



ROI Amygdala (uncorr)
Spearman`s Rho: 0.564



Roi Thalamus (uncorr)
Spearman`s Rho: 0.687



(Mainz ,...Herpertz-Dahlmann, Konrad 2012)

M6-04 today!





Summary(3) - Assessment

- Physical including laboratory assessment is very important in moderately to severely starved AN patients;
- Testing of electrolytes, especially potassium, necessary in patients who vomit or practise laxative abuse (purging type or BN);
- Highly increased risk of osteoporosis in later life periods
- No benefit of oral contraceptives.
- Do not forget psychological assessment (EDI, EDE, K-SADS, etc.)



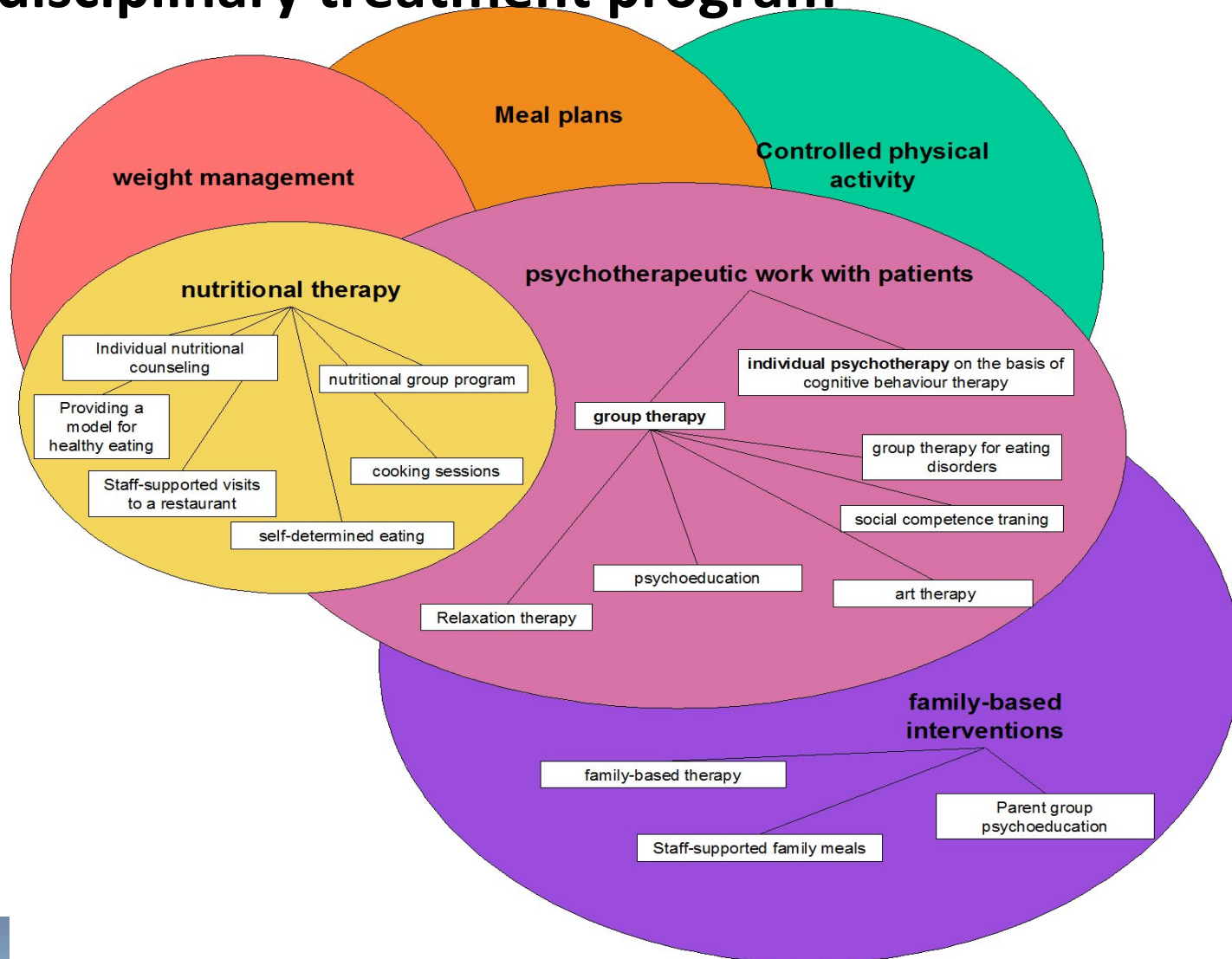
Major aspects of treatment in AN

„major points in treatment of AN“

- a. **Nutritional rehabilitation**, treatment of medical problems
- b. **Nutritional counseling**, normalisation of eating habits
- c. **Individual therapy** (and, whenever possible, additional group sessions) to correct dysfunctional thoughts concerning weight and shape and self-confidence
- d. **Intensive involvement of parents**
- e. **Treatment of additional mental disorders**



Multidisciplinary treatment program



Major treatment goals in AN

Nutritional rehabilitation

- Weight gain and **BMI at discharge**: important prognostic factor for short-term and long-term course of AN

(Steinhausen et al. 2009; Kaplan et al. 2009; Lock et al. 2013)



Target weight

- very diverging definitions of target weight in Europe from 10th to 75th age-adjusted BMI-percentile

(Roots et al. 2006)

Our proposal:

- 20th to 25th BMI-percentile because of resumption of menses in most adolescent patients (Golden et al. 2008; Faust et al. 2013; Dempfle et al. 2013)
- **Recommendation:** weight range instead of strictly defined body weight.
- **Note:** importance of premorbid body weight! (Föcker et al. 2015)
- **Note:** premenarchal AN tends to need more time to start menstruation (Dempfle et al. 2013).



Major treatment goals in AN

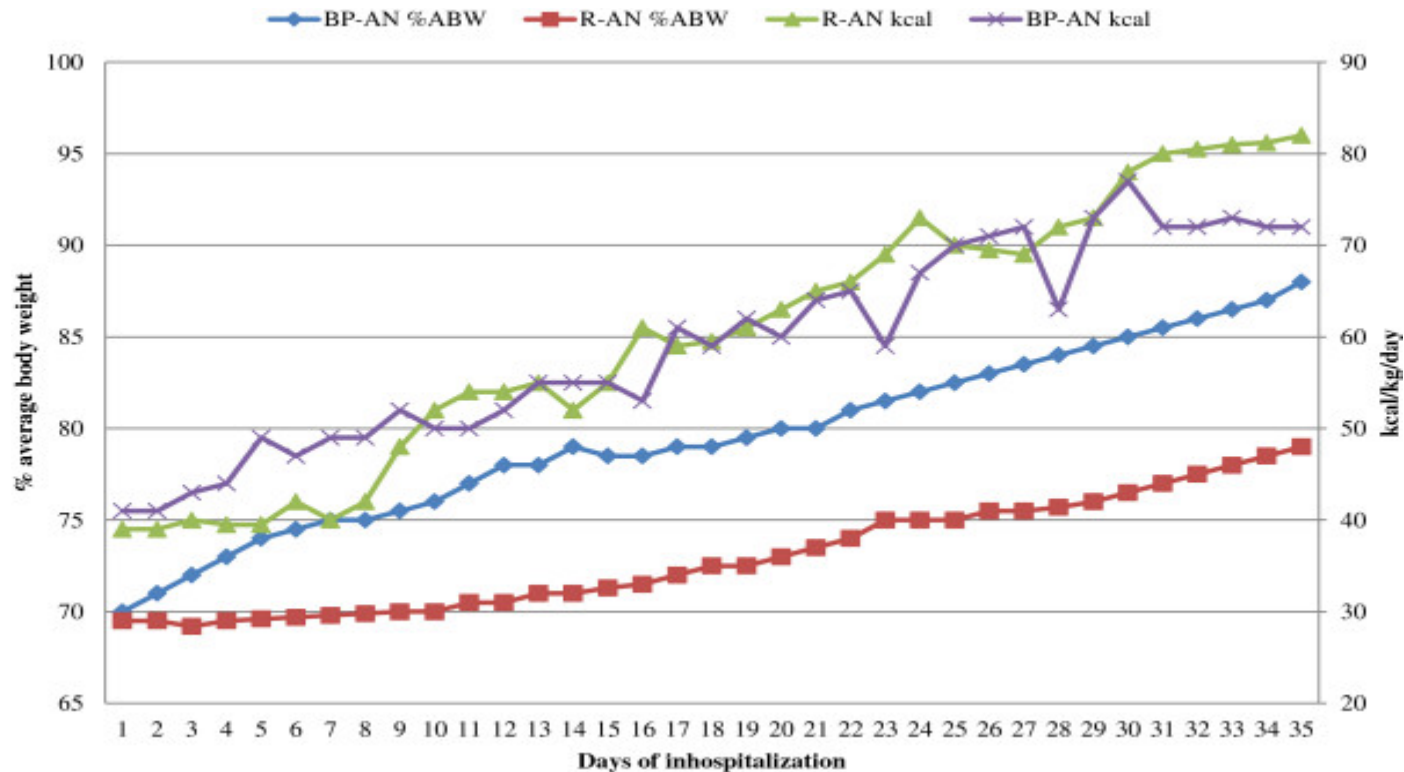
Expected rate of weight gain

- European recommendations: 0.5 – 1 kg/week during inpatient treatment
- US recommendations: 1 kg – 2 kg/week (Marzola et al. 2013)
- **Refeeding or underfeeding?**
- **Refeeding syndrome**
- No difference between those on a high-calorie diet in comparison to those on a low-calorie diet (Golden et al. 2013).
- Refeeding syndrome mostly occurs during the first fortnight after starting refeeding (Robinson & Nicholls 2015).
- Refeeding syndrome more dependent on low BMI at intake (O'Connor & Nicholls 2013).



Nutritional rehabilitation

- Restricting-type AN patients need more kcal than binge-purging-type AN



(Marzola...Kaye 2013)



Summary (4) – nutritional therapy

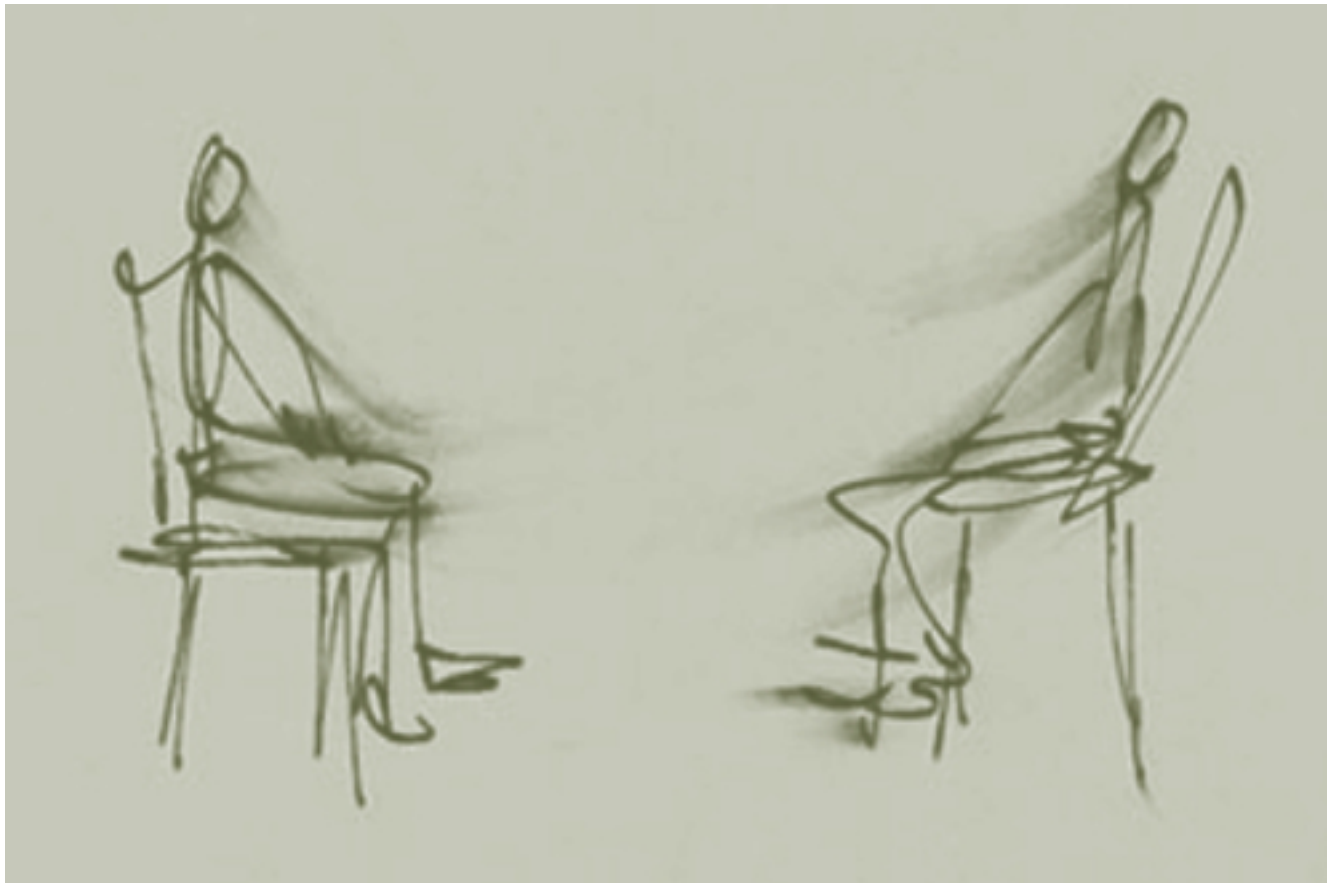


1. weight gain is inevitable;
2. higher calorie-diets for restrictive AN vs. binge-purging AN?
3. adaptation of target weight for increases in age and height;
4. target weight range around 20th – to 25th BMI percentile;
5. individualized meal plan;
6. regular weight control;
7. readmission contract depending on body weight.



Major aspects of treatment in AN

Individual psychotherapy



Individual psychotherapy

- **Cognitive- behavioral psychotherapy – enhanced (CBT-E)**
 - thinking afresh about the current state, analysis of pros and cons
 - modification of concerns surrounding weight and shape, cognitive restructuring
 - maintaining changes and developing strategies to handle setbacks
 - *development of an individual disturbance model (personal recommendation)*

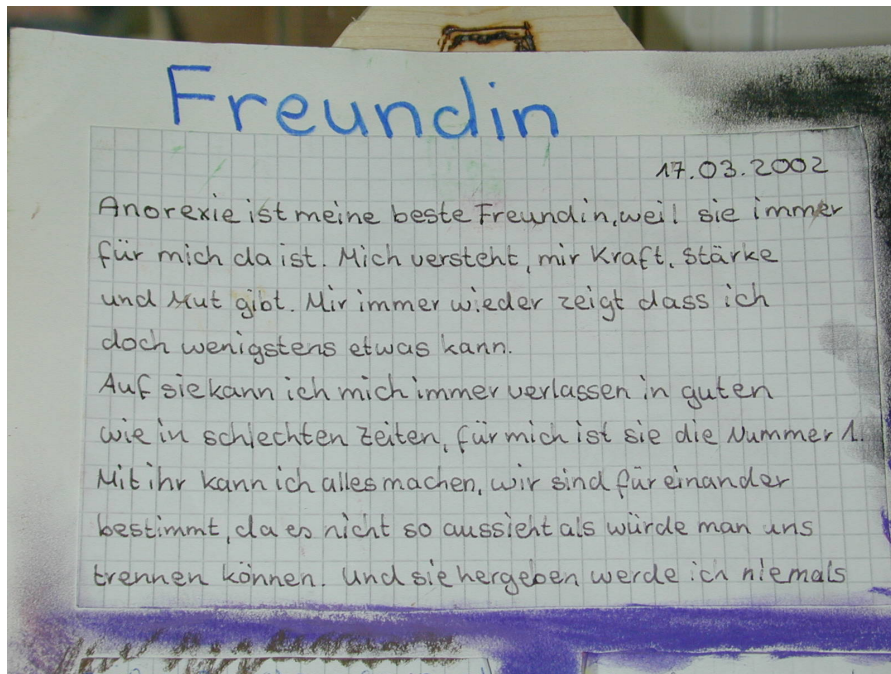
(Fairburn 2008; Dalle Grave et al. 2014)



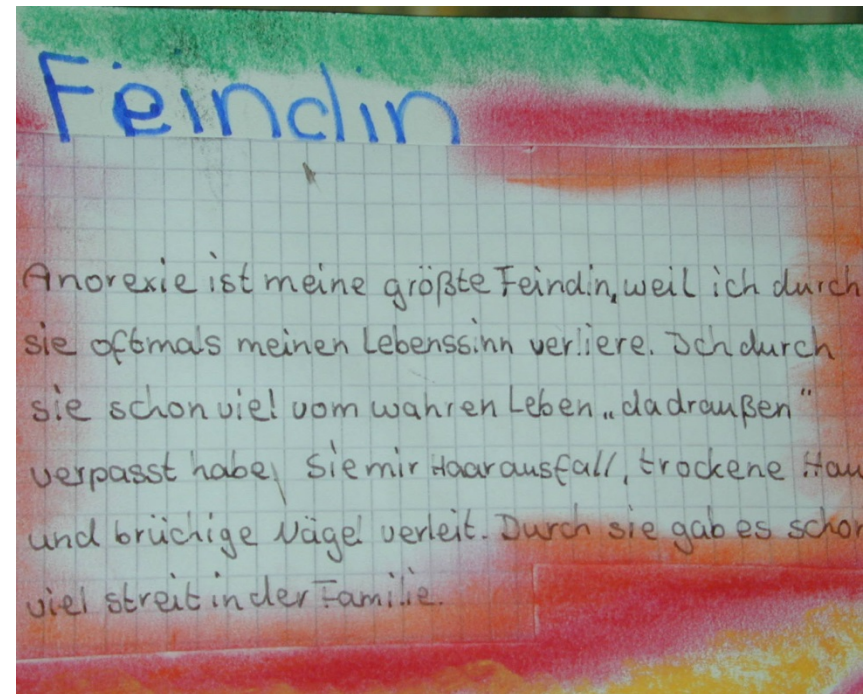
Individual Psychotherapy

Therapeutic writing tasks to explore pros and cons of AN in the adolescent's life

friend



foe



Role of the family



- “The AED (Academy of Eating Disorders) stands firmly against any etiologic model of eating disorders in which family influences are seen as the primary cause of anorexia nervosa or bulimia nervosa”.
- “No evidence exists supporting the concept of “anorexogenic” parents or families.”
- “The AED recommends that families be included in the treatment of younger patients...”

Family-based therapy is the only evidence based treatment in (adolescent) AN (NICE guidelines, grade B).



Main principles of Family-Based Therapy

Outpatient therapy for medically stable non-chronic adolescent AN in three phases:

- 1) parents take care of their child`s weight rehabilitation and normalization of eating and restrict physical activity;
- 2) the adolescent is encouraged to regain responsibility over food and eating – parents focus more on questions about age-appropriate life of an adolescent;
- 3) increasing autonomy of the adolescent, disturbing influence of the eating disorder on adolescent development; development of relapse prevention strategies.

(Lock et al.2010, Murray & Le Grange 2014)



Outcome of family-based therapy vs. individual therapy

- RCT comparing Family Based Therapy to Adolescent Focused Therapy (n=121):
- After 12-month-follow-up significantly more full remissions in FBT than in AFT (however no difference in BMI) (Lock et al. 2010) Note: patients had a higher BMI at intake than in most European studies.
- After 2-4 year-follow-up no difference in number of remissions or relapses between both treatments. (Le Grange et al. 2014)



Further involvement of parents in therapy

1. conjoint family meals
2. parent group psychoeducation
3. caregiver skills program



(Holtkamp et al. 2005)

(Schmidt & Treasure)





Summary (5) – psychotherapy in AN

- With the exception of family-based therapy there is no evidence-based treatment modality in AN;
- However, adolescents should be offered individual appointments with a healthcare professional separate from those with their family members or carers (NICE guidelines);
- Group therapy may provide support and understanding (not evidence-based);
- Specialist care services for AN are more effective than non-specialist care services (House et al. 2012).
- Psychotherapy without gaining weight does not make sense.





Major aspects of treatment in AN

Medication/Second generation antipsychotics

- **Note:** No medication for AN has been approved today by the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA).

Second generation antipsychotics

(olanzapine, risperidone, pimozide, aripiprazole)

- Three recent metaanalyses of RCT's in adults and adolescents (a) n=220; b) n=197) could not demonstrate any superiority of the antipsychotic in comparison to placebo (Kishi et al. 2011; Lebow et al. 2013; Dold et al. 2015).

but : danger of ECG abnormalities and metabolic changes (Glucose ↑).

- However, use of medication (e.g. olanzapine) might be necessary intermittently in highly anxious and agitated patients.



Major aspects of treatment in AN

Antidepressive Medication/SSRI

SSRI (fluoxetine)

Acute AN

- No effect in the starved state;

Relapse prevention

- No effect of additional SSRI when administered together with CBT (Walsh et al. 2006).
- **Note:** After weight restoration SSRI treatment of comorbid depression, anxiety or OCD-symptoms may be helpful.



New treatment modalities in AN

Cognitive remediation therapy (CRT)

- Cognitive rigidity
 - „all or nothing“ type of thinking
 - strict attention to details
 - perfectionistic tendencies

Neuropsychological therapy

- consists of mental exercises aimed at improving cognitive strategies
- promotes reflection on thinking styles
- encourages thinking about thinking
- helps to explore new thinking strategies in everyday life



(Tchanturia et al. 2014, **symposium this afternoon**)
<http://onlinelibrary.wiley.com/doi/10.1002/erv.2326/pdf>

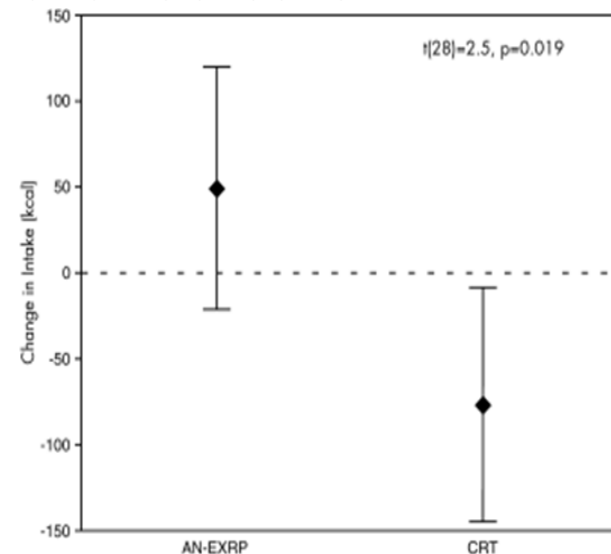
New treatment modalities in AN

Exposure and Response Prevention in AN

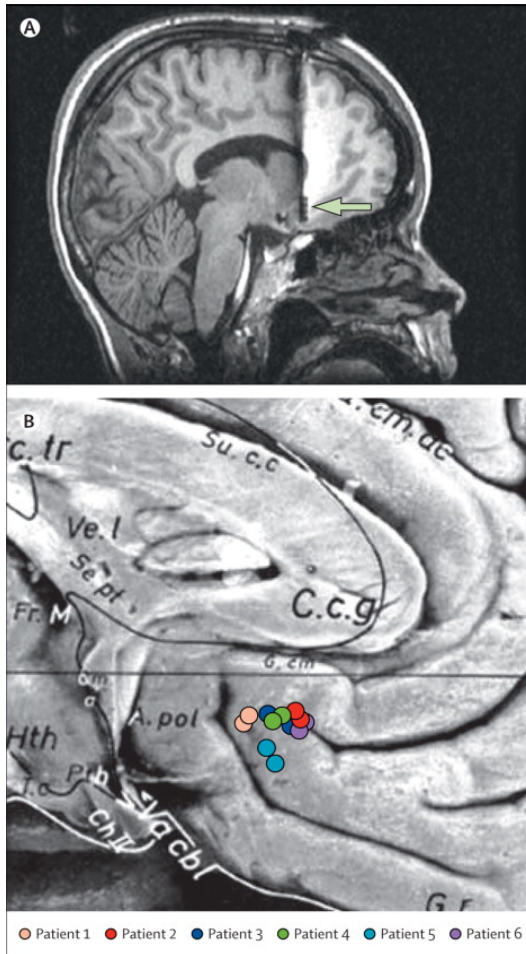
RCT: Weight-restored patients received 12 sessions of EXP-PREV (n=15) or CRT (n=15)

- Individual hierarchy list of feared eating situations
- exposition in-session to feared eating situations
- Moving from least anxiety provoking food to most
- Interventions increase awareness of anxiety and habituation
- Self-guided exposure between sessions.

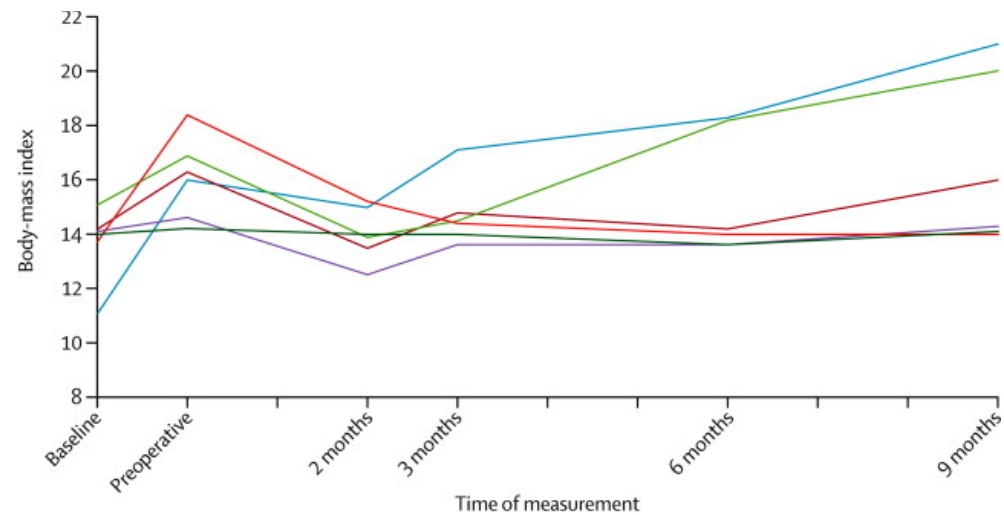
EXP-PREV was associated with higher caloric intake



Subcallosal cingulate deep brain stimulation in treatment-refractory AN (N=6)



Changes in BMI of each patient



| | Baseline | Preoperative | 2 months | 3 months | 6 months | 9 months |
|-----------|------------|--------------|------------|------------|------------|------------|
| Patient 1 | 11.1 | 16.0 | 15.0 | 17.1 | 18.3 | 21.0 |
| Patient 2 | 14.2 | 16.3 | 13.5 | 14.8 | 14.2 | 16.0 |
| Patient 3 | 14.1 | 14.6 | 12.5 | 13.6 | 13.6 | 14.3 |
| Patient 4 | 13.7 | 18.4 | 15.2 | 14.4 | 14.0 | 14.0 |
| Patient 5 | 15.1 | 16.9 | 13.9 | 14.5 | 18.2 | 20.0 |
| Patient 6 | 14.0 | 14.2 | 14.0 | 14.0 | 13.6 | 14.1 |
| Mean | 13.7 (1.4) | 16.1 (1.5) | 14.0 (1.0) | 14.7 (1.2) | 15.3 (2.3) | 16.6 (3.2) |

(Lipsman et al. 2013, The Lancet)

Positioning of electrode

Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital of the RWTH Aachen



18-year-outcome in adolescent AN (community-based study, n=51)

Outcome and psychiatric disorder (point prevalence)

| | | |
|--|-----------------------------|--|
| Mortality | 0 % | |
| Persistent eating disorder ▶ AN | 12 % 6 % | (n = 6) (n = 3) |
| Psychiatric disorders according to DSM-IV ▶ affective disorders ▶ OCD | 39 % 22 % 16 % | (n = 20) (n = 16) (n = 8) |
| No paid employment because of ED or any other psychiatric disorder | 25 % | (n = 13) |

(Wentz et al. 2009)

However, highest mortality of all mental disorders !



Eating Disorders in adolescence

Treatment is a marathon, not a sprint!

Thank you for your attention!

For further questions:
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