

*Treatment of ADHD: Stimulants: Growth*

- Height and weight:
  - Does not affect growth hormone
  - Less appetite in 14-22% vs. 2-6.4% with placebo
  - Height velocity, or yearly growth, typically slows for the first few years of stimulant therapy and then resumes at a nearly normal rate, and pubertal development is normal; adult height usually normal)
  - With long term (2-3 years+) treatment, slowing of growth is usually minimal, though more significant slowing may occur in a subset of patients (?10%?)
  - there are NO published studies which have reported the final adult height of patients treated continuously from childhood through adulthood
  - Pubertal development is normal
  - Slowing of growth appears to be related to decreased appetite and food intake
  - Slowing of growth may be greater in:
    - Pre-pubertal children (vs. adolescents)
    - Boys (vs. girls)
    - Children who are tall (vs. average or short)
    - Children are overweight (vs. average or underweight)
    - Children treated with sustained release formulations (vs. immediate release/shorter acting meds)
    - Children treated with higher drug doses (controversial)
  - Effect of methylphenidate on height and weight in Korean children and adolescents with attention-deficit/hyperactivity disorder: a retrospective chart review

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**OBJECTIVE:** The purpose of this study was to investigate the effect of methylphenidate (MPH) on growth in Korean children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

**METHODS:** The medical records of 157 subjects (mean age 8.9±2.2 years; 134 boys) with ADHD who received treatment with MPH for at least 1 year at the Department of Psychiatry at Asan Medical Center were retrospectively reviewed. Height and weight were prospectively obtained and retrospectively gathered. Height and weight were converted to age- and gender-corrected standard scores (z scores) using norms from the Korean population. Growth changes were analyzed from the starting to the end of treatment using random coefficients models with change in weight or height z score as the dependent variable.

**RESULTS:** Weight ( $\beta = -0.109$ ,  $p < 0.001$ ) and height ( $\beta = -0.072$ ,  $p < 0.001$ ) z scores significantly decreased during treatment. Weight z score decreased more in girls ( $\beta = -0.247$ ,  $p < 0.001$ ) than in boys ( $\beta = -0.090$ ,  $p < 0.001$ ). Weight z score decreased during the 1st year of medication ( $\beta = -0.327$ ,  $p < 0.001$  for boys;  $\beta = -0.646$ ,  $p < 0.001$  for girls), and did not change or increase after the 1st year. Height z score significantly decreased during treatment ( $\beta = -0.072$ ,  $p < 0.001$ ) after controlling for the effect of age at treatment, gender, mean daily mg/kg dose, and comorbid depressive disorder. Height z score also decreased during the 1st year of medication ( $\beta = -0.089$ ,  $p < 0.001$ ) but did not change after the 1st year.

**CONCLUSIONS:** These results suggest that MPH could be related to weight and height deficit in Korean children and adolescents, although the effects were minor, and disappeared after the 1st year. Because of the limitations of this study such as retrospective design, selection bias, and high attrition rate, further prospective studies are needed.
- Swanson et al, 2007, 2013:
  - growth deficit found to persist in future years in continuously treated children

- data from MTA study should eventually yield definitive information on youth treated continuously up to adulthood; so far, there is some data suggesting growth deficits of up to 1 inch persisting after 10-12 years of treatment (from age 8 to 18-20)
- JAACAP, 2006 (2 studies): confirmed that stimulant treatment in children with ADHD for up to 3 years has a negligible effect on adult height and weight (drug holidays had no impact).
  - Spencer, et al, 2006: 178 children 6-13 yo taking Concerta for 21 months or longer; an average of 0.23 cm less than expected heights at 21 months; an average of 1.23 kg less than expected at month 21 (after a 4 month period of no growth in weight); drug holidays made no difference
  - Plizka, et al, 2006: children on methylphenidate vs. Adderall for 3 years; both had virtually no effect on height; Adderall had slightly greater effect on weight
- MTA study, 2004: youth on stimulants grew an average of 1.4 cm less than those not on stimulants
  - for those children who took stimulant medications (immediate release) for 24 months, there appeared to be a modest growth suppression of 1.7 cm in height and 1 kg in weight
  - after 2 years, the differences widened to 3.7 cm in height and nearly 5 kg in weight.
  - data on folks treated continuously have had a growth deficit of about 1 inch which has persisted after 10-12 years of treatment (from about ages 8 to 18-20).

**Young Adult Outcomes in Follow Up of MTA: Symptom Persistence, Source Discrepancy and Height Suppression**  
*(Swanson, J. et al. J Child Psychol Psych; 58 (6); 2017; 663-678*

- ▶ **Results:** For adult height, ADHD group was 1.29 cm shorter than local control group ( $p < 0.01$ ).
- ▶ Treated group with **Consistent or Inconsistent pattern** was 2.55 cm shorter than the subgroup with negligible pattern ( $p < 0.005$ ).
- ▶ Within the treated group, the Consistent pattern was 2.36 cm shorter than inconsistent ( $p < 0.04$ )
- ▶ **Conclusion:** ADHD group showed persistence of symptoms compared to local norms. Within the naturalistic subgroups of ADHD cases, extended use of medication was associated with adult height suppression, but not reduction of symptom severity.

- With long-term stimulant treatment, final adult height is usually normal, though more significant slowing of growth may occur in a subset of patients (perhaps 10%)
- primarily within the first year of use
- usual loss of weight is 1 kg or less
- rebound in growth or habituation to this effect seems to occur with in time
- more prevalent with Dexedrine
- evidence indicates that children with ADHD may be somewhat smaller than their counterparts without ADHD prior to puberty and catch up with their peers during adolescence; this is not associated with stimulant use
- weight and height curves appear to return to normal when medicine stopped
- may have 0.2-3 cm decrement over the entire developmental period
- there appears to be no significant impairment of height attained in adulthood (Kramer, 2000; Mannuzza, 1991)
- pubertal development is normal; growth hormone secretion is normal
- monitor weight and height with pediatrician and psychiatrist
- to minimize:
  - closely monitor weight and height with psychiatrist and pediatrician
  - give with or after meals

- give high-protein, high calorie breakfast when possible
- give high calorie snacks, especially in early morning and late evening; encourage grazing
- use nutrient dense meals (e.g., yogurt, cottage cheese, peanut butter, turkey, granola)
- may want to enlist the expertise of a nutritionist
- try high-protein drinks/shakes/smoothies
- avoid soft drinks and overly refined foods; fruit juice (but not too much) and water is better
- schedule outdoor play before meals when possible (even a quick walk)
- give a daily multivitamin
- drug holidays; no evidence of working in clinical research, but anecdotal evidence
- possible medications to help with appetite problems
  - cyproheptadine, 4-8 mg/day (4-20 mg/day in adults), may also be helpful; adverse effects: sleepiness, dry nasal mucosa (with bloody nose), facial swelling
  - mirtazapine, 3.75-15 mg/pm