

DEE-P Webinar on Growth Attenuation, May 2022

Short-ening stature: when grown up is too tall:

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Disclosures

- ▶ I disclose my belief that parents are the only ones who know what is best for their children and their families

A.D.

- ▶ 7 year 8-month-old male with severe developmental delay, seizure disorder, cortical blindness following a neonatal stroke
- ▶ Family read about and was interested in growth attenuation therapy, but were unable to identify a willing provider at their regional Children's Hospital
- ▶ AD requires full care. Diapered, drinks from a sippy cup if it is held for him and eats pureed food. Unable to help with transfers - will lift his leg up to be in lap.
- ▶ Unable to communicate but will reach for sippy cup or mom's hands. No response to questions, no sign language
- ▶ Goes to MR/DD program and has 40 hour a week nurse and home health assistant 35 hours a week. Family has hooyer lift and wheelchair van
- ▶ Lives with mom, dad, two daughters - 10 and 5
- ▶ He likes to "cuddle, bathe and eat"

A.D.

- ▶ Family concerned he will be restricted from participating in regular activities if he grows to his expected height. He enjoys activities such as hiking etc. Mom can still carry him on her back, but doesn't know how much longer.
- ▶ Two nanny's have had fractures from lifting him and he has had multiple falls when he has been lifted and carried. He has fallen on mom when she is carrying him and has fallen on her in the bathtub
- ▶ "The hoyer lift doesn't go into the bathtub" and "You can't take a hoyer lift with you when you leave the house"
- ▶ When he was younger, they were unsure where he would be functionally and would not have intervened, but they are now more aware of what he will probably do and won't do.
- ▶ Pulmonary supportive of attenuation due to marginal respiratory status as he is getting bigger.



A.D.

- ▶ Family goal to make it possible for him to stay with his family
- ▶ He recognizes family faces and voices and is calmer at home. The family does not feel that he would do well in another residential setting or an institution, even if quality institutions existed
 - ▶ When mom was growing up she had a great uncle that her grandmother cared for until she got too old. Then he was put into a family home but the host family was into drugs and the great uncle was poorly cared for – the family finally got him out.
- ▶ They do not feel that stature has any meaning to him and they believe that he would choose to stay with the family over any other choice if he could make this decision.
- ▶ "Options are never good you have to pick the best one for the family."

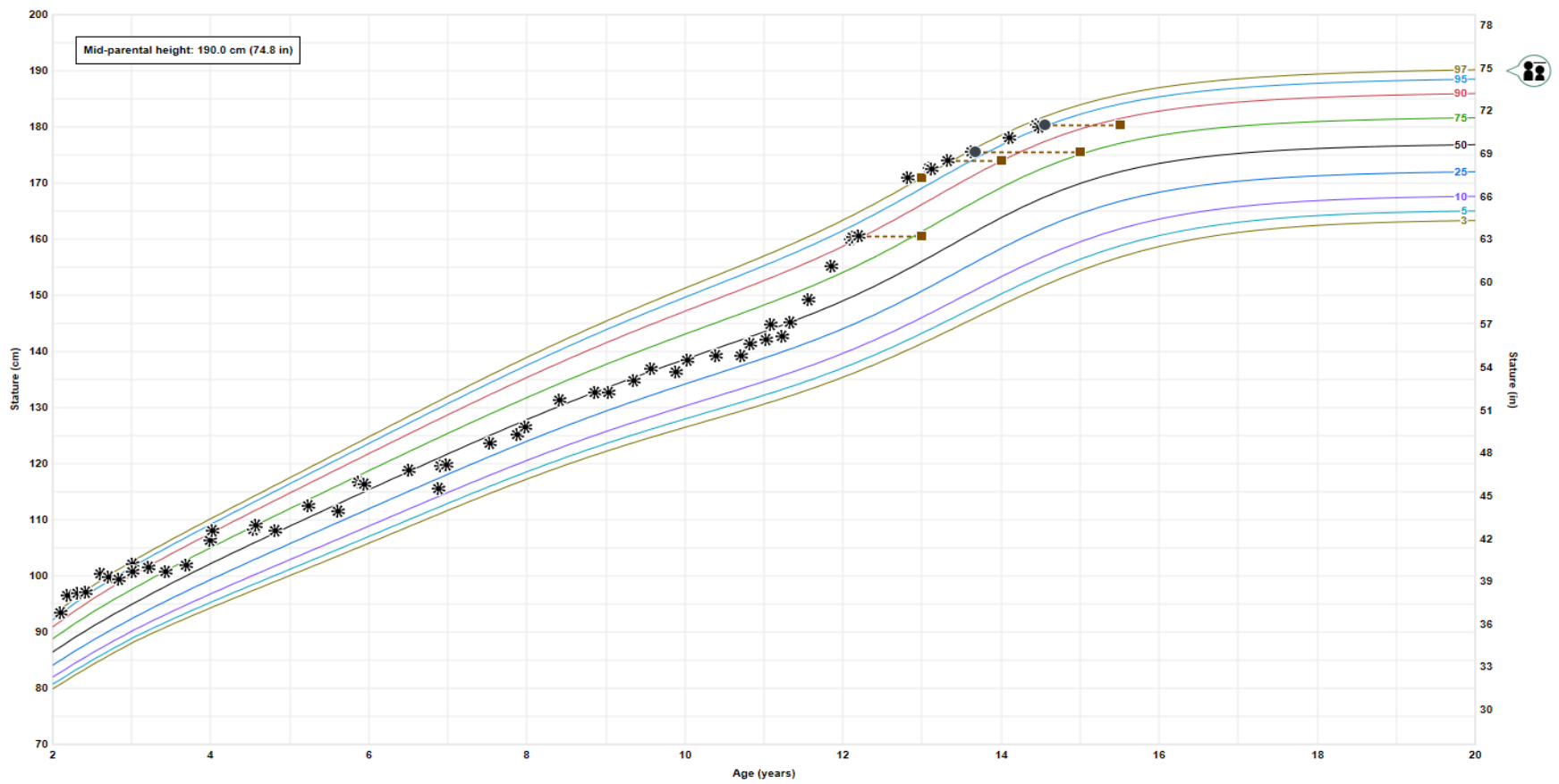
A.D.

- ▶ Reviewed potential risks and unknown benefits
- ▶ CHCO ethics committee previously determined that
 - ▶ There are no fundamental ethical issues in promoting shorter stature in individuals in whom height is not beneficial
 - ▶ Medical interventions to facilitate care (G-tube, trach etc) are common in medically complex children
 - ▶ Parents generally know what is best for their child and family
 - ▶ The wishes of the family should be followed if they are acting according to their perception of the best interests of the child
- ▶ Baseline laboratory evaluation obtained to exclude contraindications
- ▶ Family elected to proceed

What does growth attenuation look like?

- ▶ Evaluation of growth chart

Interpretation of the growth chart



Bone age

- ▶ A means to determine degree of development
- ▶ Puberty generally starts at a bone age of 12 in boys
- ▶ Bone age is a better predictor of puberty than chronological age
- ▶ Bone age indicates the remaining growth potential



Genetic Potential

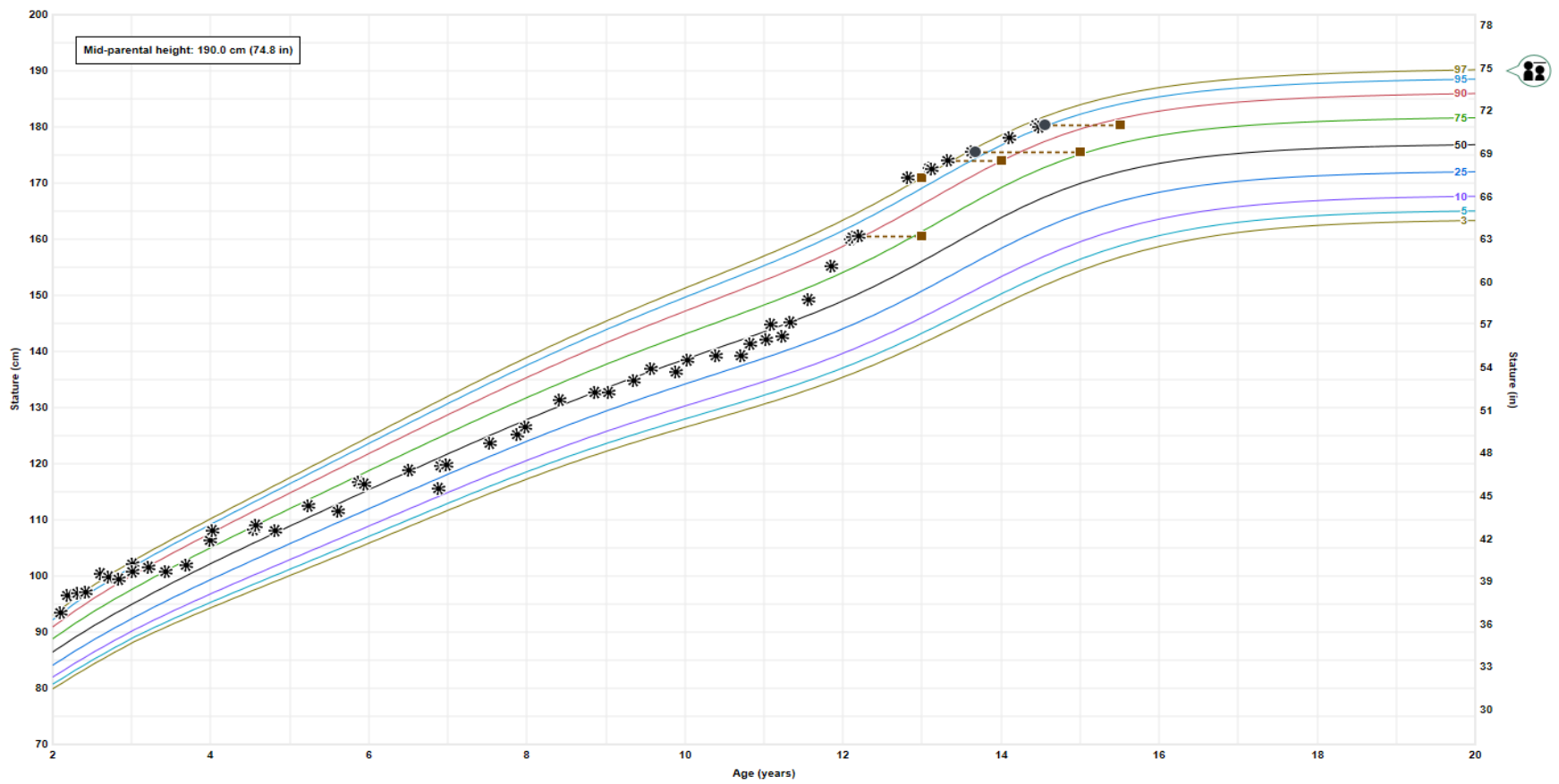
► For boys:

$$\frac{(\text{Mother's height} + 13 \text{ cm (5 in)} + (\text{Father's height}))}{2}$$

► For girls:

$$\frac{(\text{Father's height} - 13 \text{ cm (5 in)} + (\text{Mother's height}))}{2}$$

Interpretation of the growth chart



What does growth attenuation look like?

- ▶ Evaluation of growth chart.
- ▶ Determination of appropriateness for growth attenuation
 - ▶ Will it benefit the child and the family
 - ▶ Will attenuation likely be significant
 - ▶ Is “optimal” height likely to be shorter than projected height
- ▶ Are there any contraindications
 - ▶ Baseline safety screening: clotting, liver function, prolactin
 - ▶ Family and other providers in alignment
- ▶ Initiation of therapy – dosing based on older protocols for decreasing stature in tall women in the 50s and 60s
 - ▶ Oral estradiol 2 mg a day (adult female replacement dose), increasing 2 mg a week until 10 mg a day
 - ▶ In girls, initiation of continuous progesterone to prevent endometrial hyperplasia and vaginal bleeding



Follow up

- ▶ Every 3 months: repeat laboratory testing
- ▶ Every 6 months: repeat bone age
- ▶ Continue treatment until bone age 15 in girls, 16 in boys
- ▶ Wean estradiol back down again to minimize “menopausal” symptoms

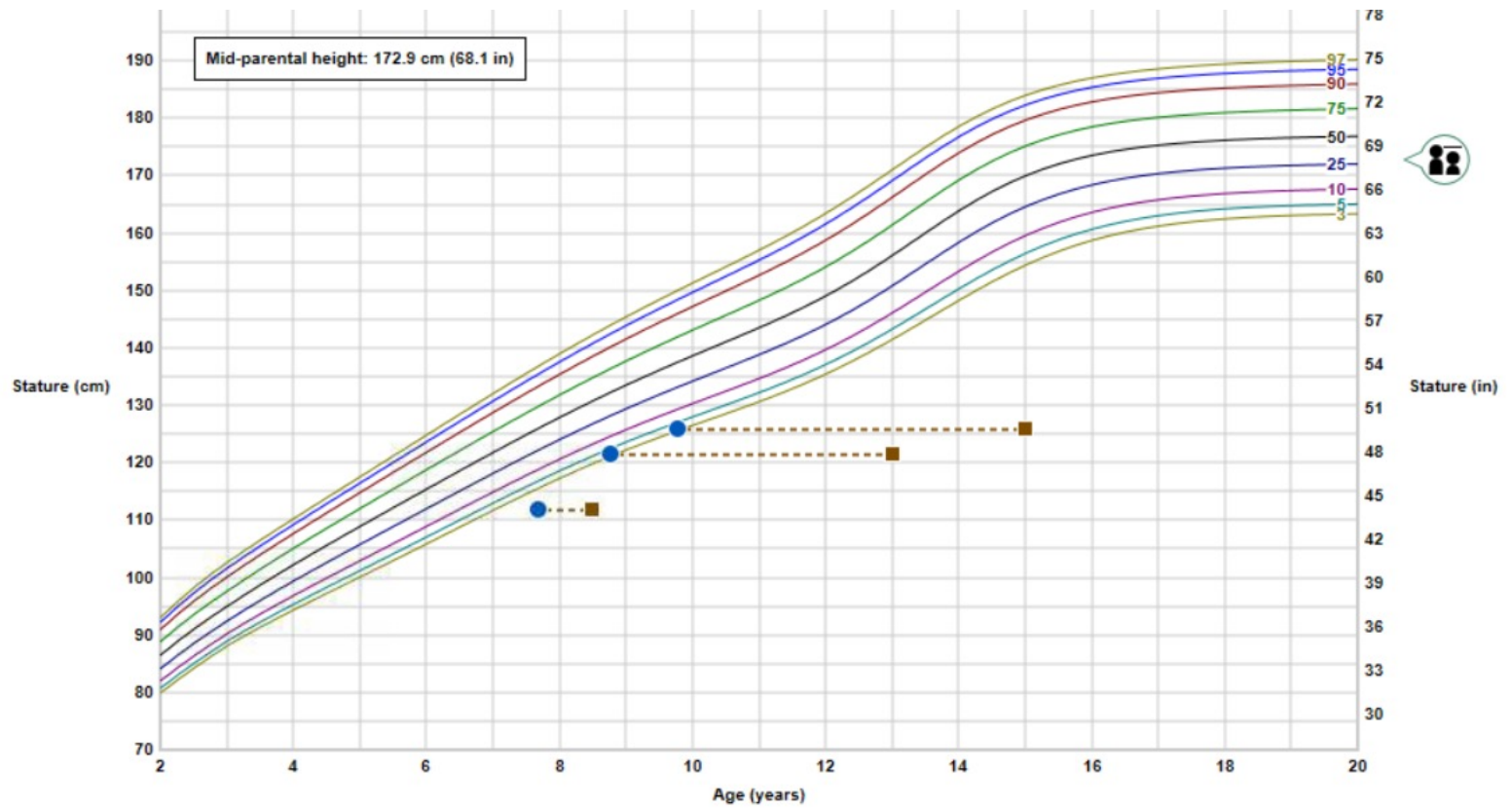
Our first case: March 2016

The New York Times Magazine

Should Parents of Children With Severe Disabilities Be Allowed to Stop Their Growth?



A.D.



Completed
individuals



Demographics

Table 1. Patient Characteristics (N=29)		
	n	%
Sex: Female	13	45%
Race		
White	18	62%
Black	1	3%
Asian	3	10%
>1 race	4	14%
Not reported	3	10%
Ethnicity		
Hispanic	2	10%
Non-Hispanic	23	80%
Not reported	3	10%
Caregiver Language: English	28	98%
Primary Caregiver		
Biological Parents	25	86%
Adoptive Parents	3	11%
Other	1	3%
Home State		
Colorado	17	59%
Other	12	41%
Insurance Type		
Private	8	28%
Private + Medicaid	4	14%
Medicaid	16	55%
Other	1	3%
Neurodevelopmental Disability		
Genetic Diagnosis	13	45%
Prenatal/perinatal brain injury	12	41%
Acquired brain injury	6	21%
Respiratory Status		
Room air (RA)	15	52%
RA with O2 or NIPPV at night	10	34%
Day O2 with NIPPV at night	1	3%
NIPPV/trach dependent	3	9%
G-tube dependent	26	90%
Cerebral Palsy		
Quadriplegic	20	69%
Hemiplegic	2	7%
Diplegic	2	7%
None	3	10%
Unknown	2	7%
Seizure disorder	19	66%
Scoliosis	20	69%
Completely immobile	23	79%
No meaningful communication	22	76%

Outcomes

Figure 1. Change in Adult Predicted Height

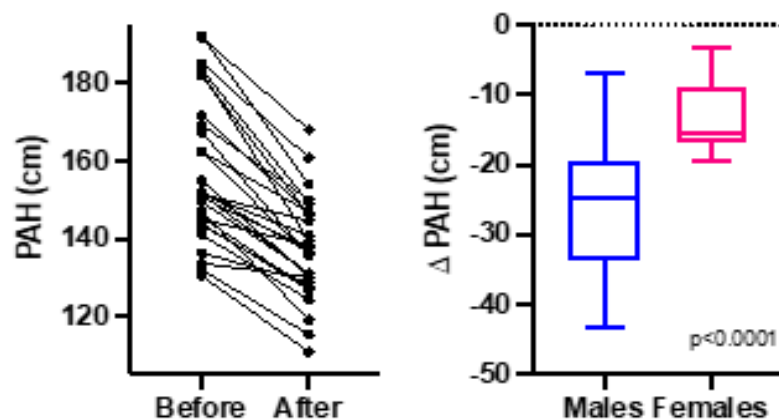
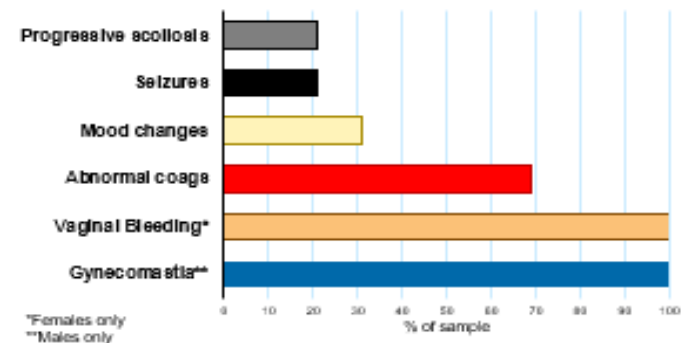


Table 2. GAT Outcomes

Age at initiation (yrs)	8.7 ± 3.3
range	(4.6-20.6)
Duration of GAT (yrs)	2.2 ± 0.7
Δ Bone age z-score (yrs)	$+3.5 \pm 2.5$
Δ Predicted Adult Height (cm)	-20.6 ± 9.9
Males	$-25.7 \pm 9.6^*$
Females	$-13.8 \pm 5.1^*$

Figure 2. Side Effects



- Dose reduction due to side effects in 3 patients: 1 increased seizures, 1 increased tremors, 1 decreased protein S level
- 1 hospitalization potentially attributable to GAT (status epilepticus)
- 1 surgery potentially attributable to GAT (progressive scoliosis)

Growth Attenuation Therapy: Practice & Perspectives of Pediatric Endocrinologists

Allison J Pollock, MD · Norman Fost MD MPH · David B Allen MD · Department of Pediatrics · University of Wisconsin School of Medicine & Public Health

Disclosure: the authors have nothing to disclose.



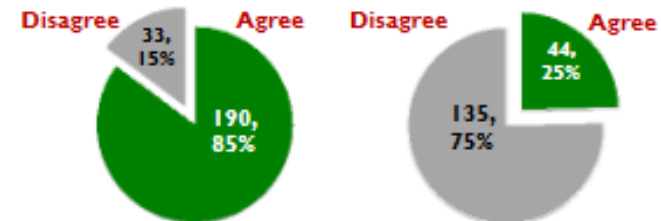
Key Findings

Number of respondents who have been asked about GAT for a child with SPCD:	98
Number of respondents who have prescribed GAT for a child with SPCD:	32
Number of children with SPCD treated (minimum calculation):	65
Number of respondents who have withheld treatment of precocious puberty to attenuate growth in a child with SPCD:	130
Percent of respondents who obtained ethics consultation for GAT of children with SPCD:	34%
Percent of respondents who obtained ethics consultation for withholding treatment of precocious puberty in order to attenuate growth in children with SPCD:	5%

RESPONDENTS' ATTITUDES ABOUT GAT

"Growth attenuation therapy is sometimes appropriate."

"GAT should be actively offered for cases of severe physical and cognitive disability, not just when raised by a parent."



REASONS RESPONDENTS DID NOT PRESCRIBE GAT IN CHILDREN WITH SEVERE PHYSICAL & COGNITIVE DISABILITY

1. Family decided against (63%)
2. Concern about side effects (43%)
3. Legal concerns (13%)
 - Concern about publicity (13%)
4. Personal conviction or beliefs (10%)
5. Ethics consultation recommendation (7%)

Summary

- ▶ As endocrinologists, we recognize that height is not a “good” in itself but can only be understood within the concept of functional height
- ▶ There is no *a priori* reason why optimal functional height would be the same for ambulatory and non-ambulatory individuals.
- ▶ We have the same duty to support functional height attainment in non-ambulatory as ambulatory patients.
- ▶ Limited data on outcomes suggest
 - ▶ Height loss with high dose estradiol is in the range of 5 inches, but with a large range
 - ▶ Interestingly, this is quite similar to outcomes of treatment of tall stature in girls in the past
 - ▶ The taller the MPH and initial PAH, the greater the height loss
 - ▶ The earlier the treatment, the greater the height loss.

Thank you!

