



PWS GH Submission to Special Drugs Program

Jill Hamilton, MD, FRCPC
Pediatric Endocrinologist
Hospital for Sick Children

GH treatment indications for Prader-Willi Syndrome

- 2002 UK and Europe ; 2009 Australia
- 2000 then 2009 US

Canada:

Not approved – Why??

Submission: letter of support signed by Endocrinologists from across Canada

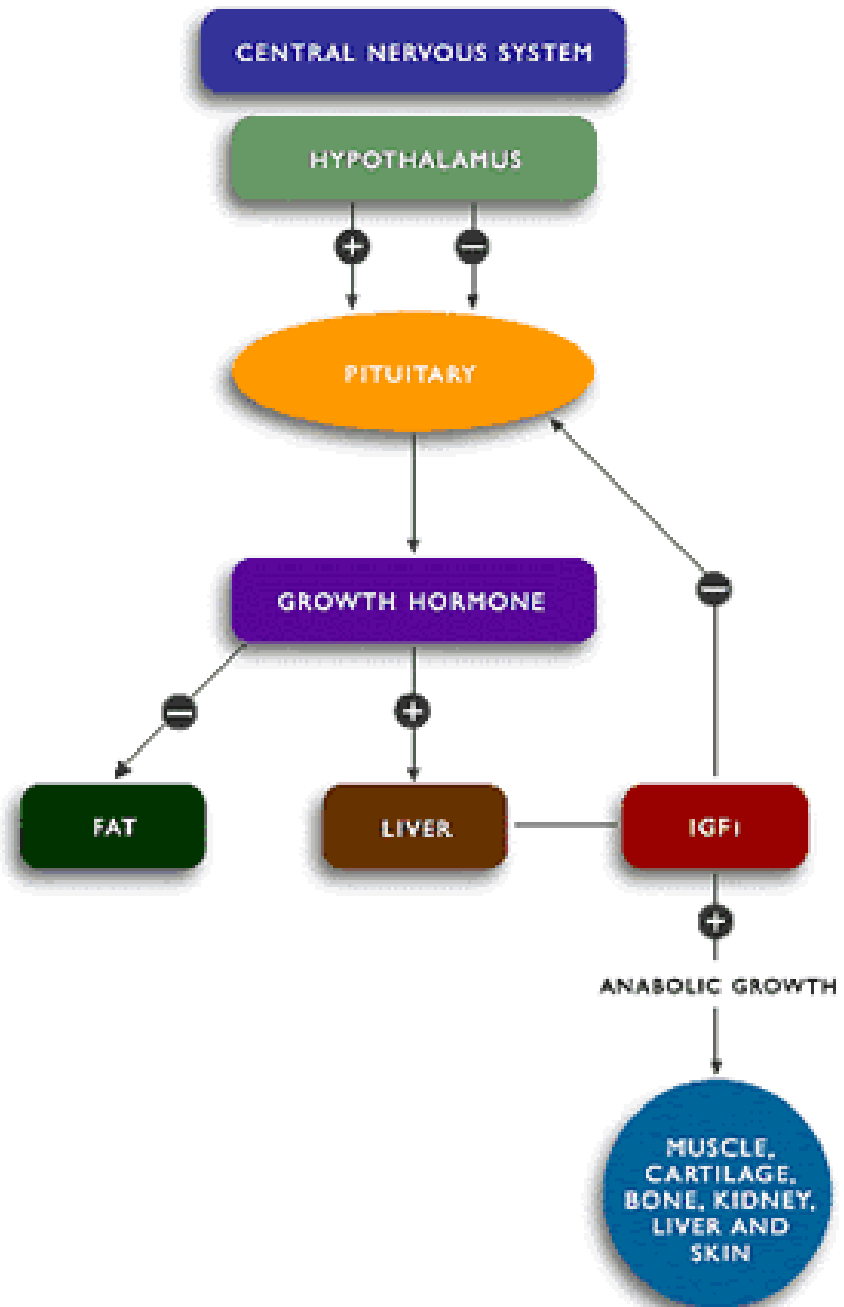
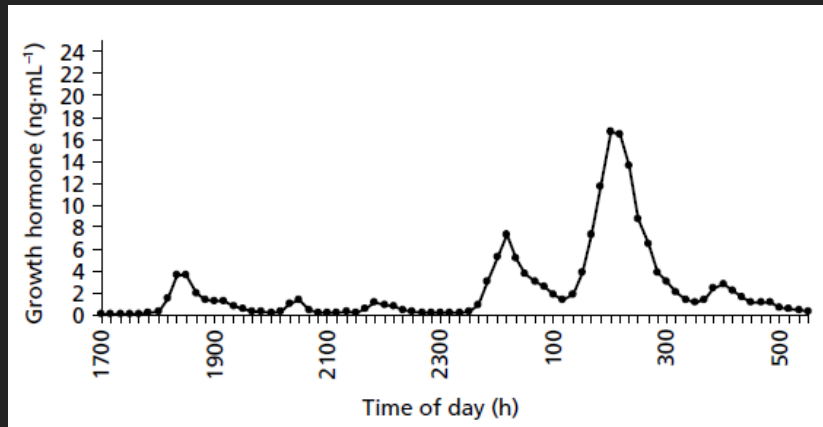
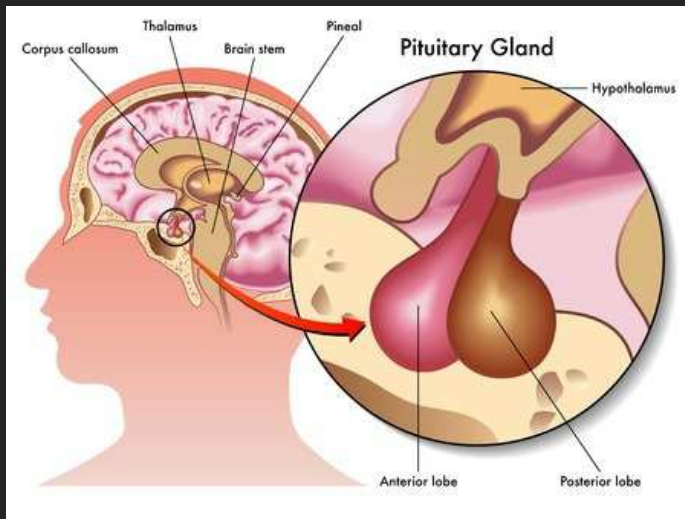
The Benefits

- GH improves height in PWS
- GH has additional benefits in PWS in muscle tone, development

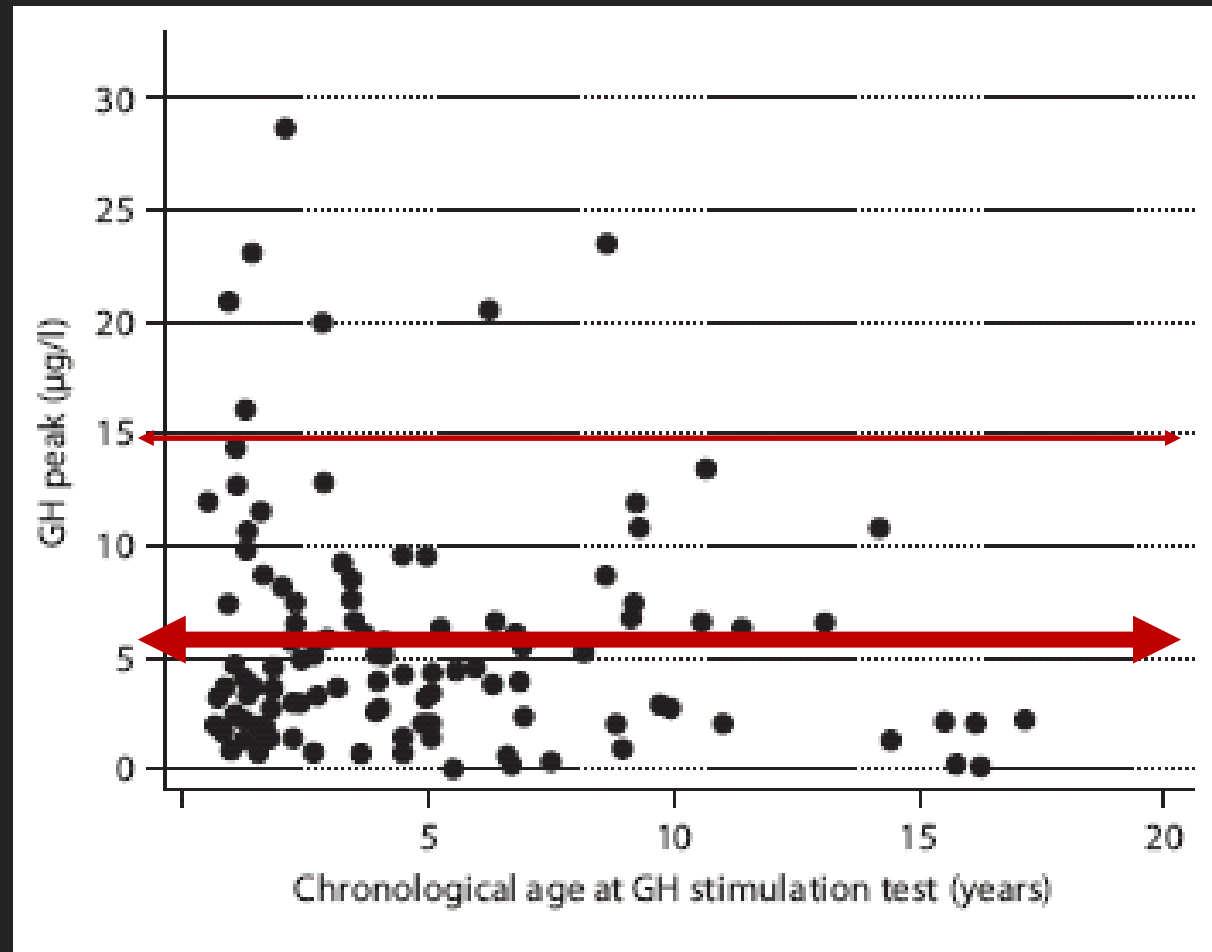
Growth Hormone Deficiency in PWS

- **Clinical features:** short stature and low growth rate, altered body composition *(Tauber Horm Res 2000)*
- **Radiologic and Biochemical:** delayed BA, low IGF-1 *(Eiholtzer Eur J Endo 1998, Diene Horm Res Pediatr 2010)*

However: Provocative GH stimulation testing may be normal



Published rates of GH deficiency: 70-80%



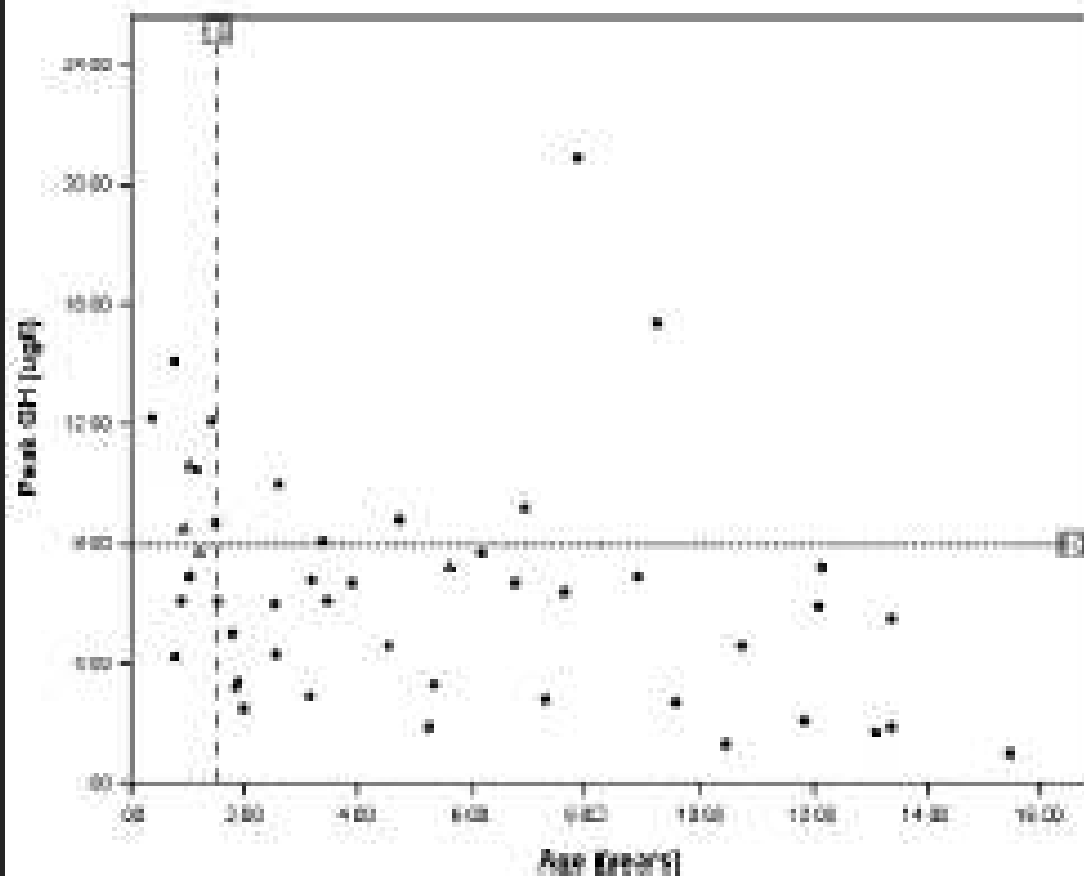
Diene et al. Horm Res 2010

ORIGINAL ARTICLE

Growth hormone secretion decreases with age in paediatric Prader-Willi syndrome

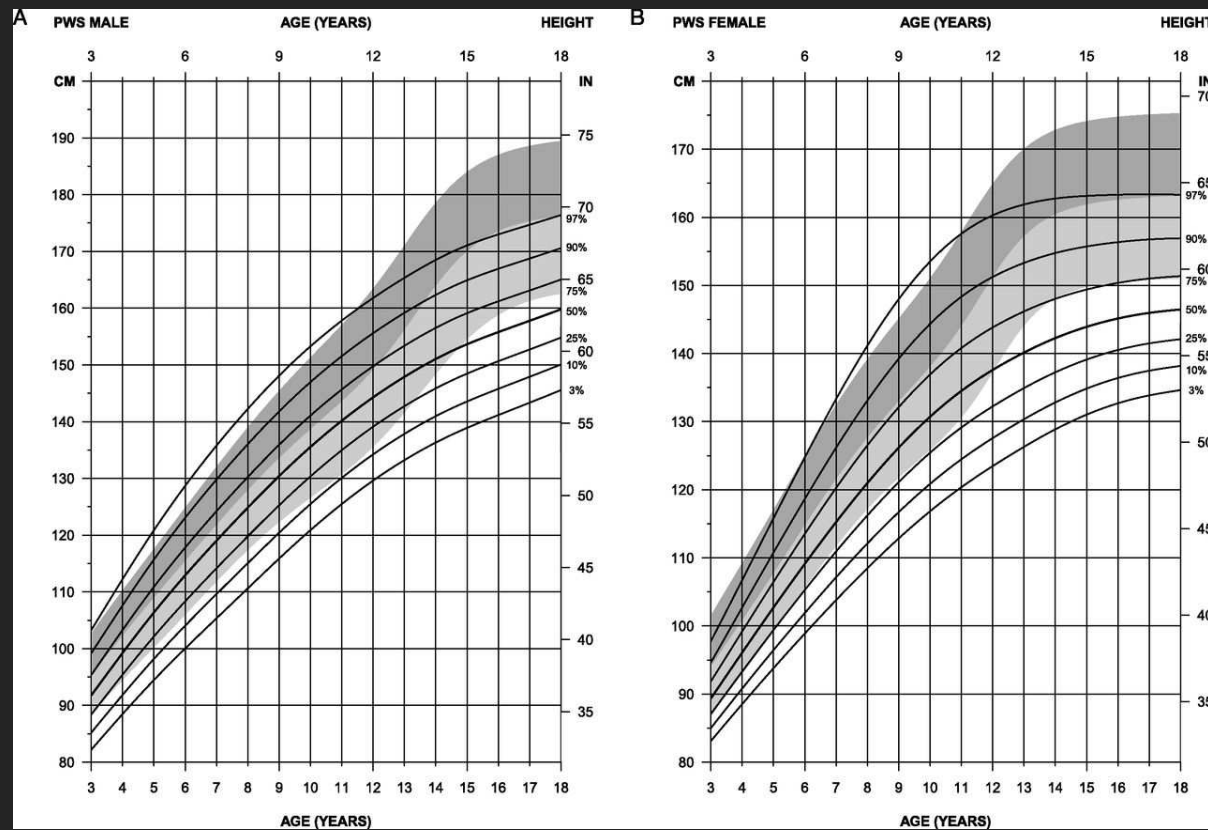
M. Cohen*, J. Harrington*, I. Narang† and J. Hamilton*

GH secretion in paediatric PWS 213

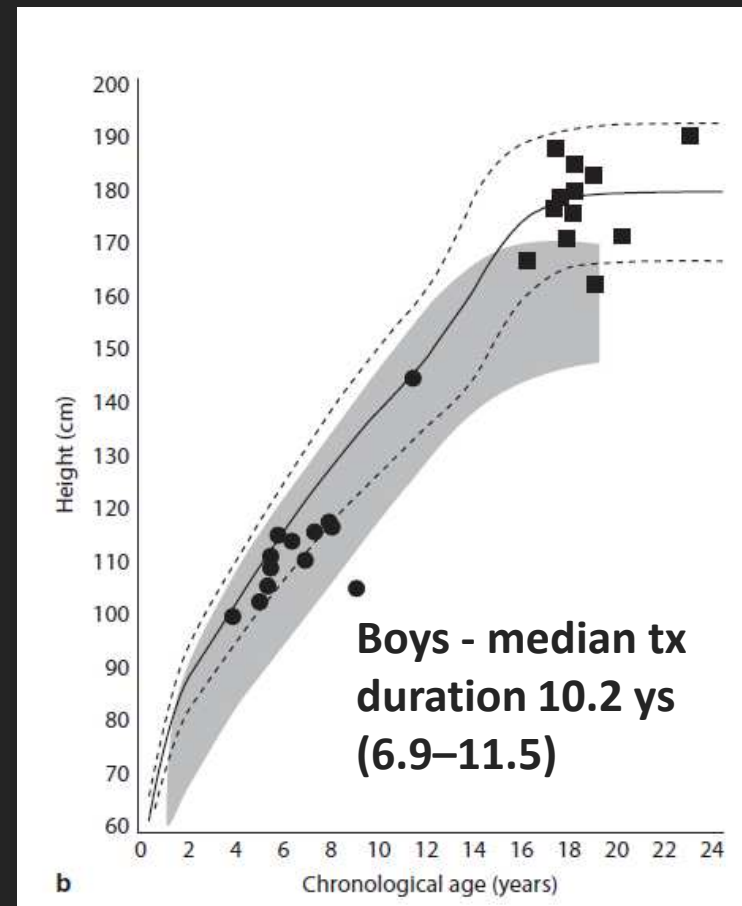
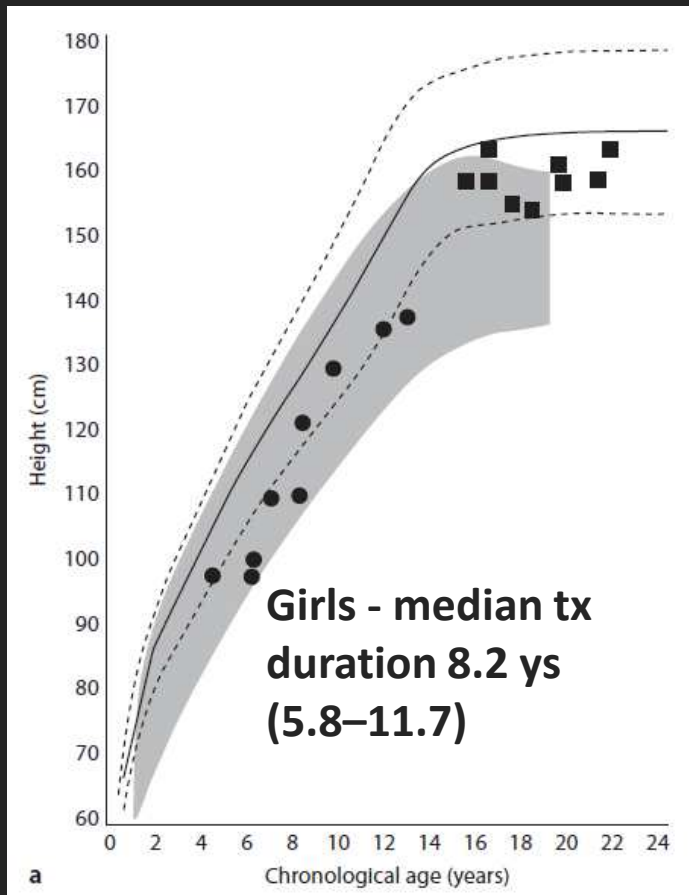


Biochemical GH deficiency
≤ 18 mo of age (3/11; 27%)
> 18 mo of age (29/36 ;81%)

CHILDREN WITH PWS BENEFIT FROM GH THERAPY



GH increases final height in PWS



- Solid line - growth of a normal population ± 2 SDS
- shaded area – PWS specific growth

Growth Hormone Treatment in Children With Prader-Willi Syndrome: Three Years of Longitudinal Data in Prepubertal Children and Adult Height Data From the KIGS Database

Nienke E. Bakker,^{1,2} Anders Lindberg,³ Joseph Heissler,⁴ Hartmut A. Wollmann,⁴ Cecilia Camacho-Hübner,⁴ and Anita C. Hokken-Koelega,^{1,2} on behalf of the KIGS Steering Committee

- GH registry
- Height outcomes:
 - (i) prepubertal children tx for 3 yrs (n=522)
 - (ii) final height in adolescents (173)
- Safety outcomes (n=2233)

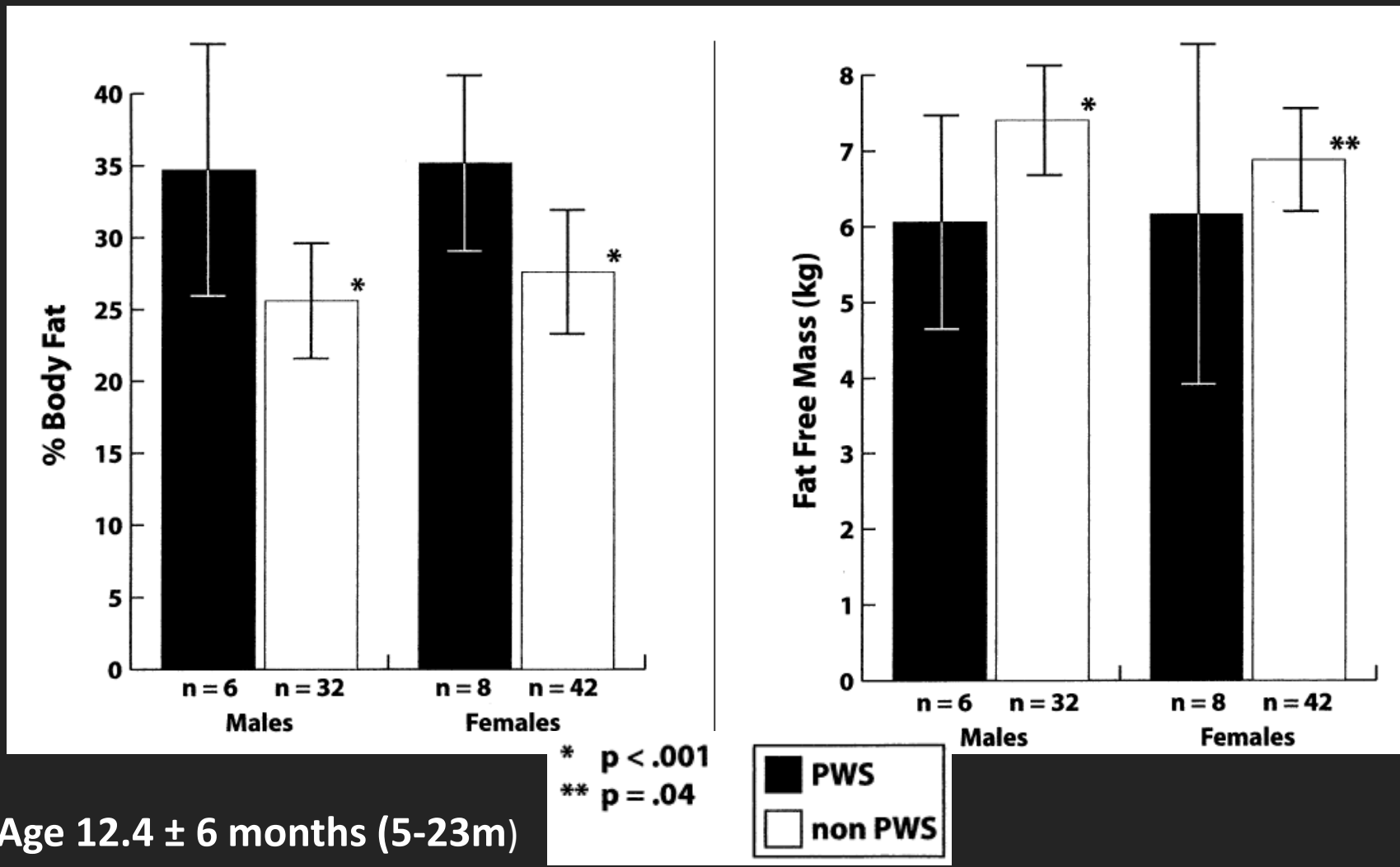
Main Findings: Height

- Prepubertal height SDS increased significantly over 3 years of GH Tx
- Some height SDS lost during adolescence
 - ? Pubertal growth spurt inadequate
 - ? compliance with GH
 - ? Scoliosis

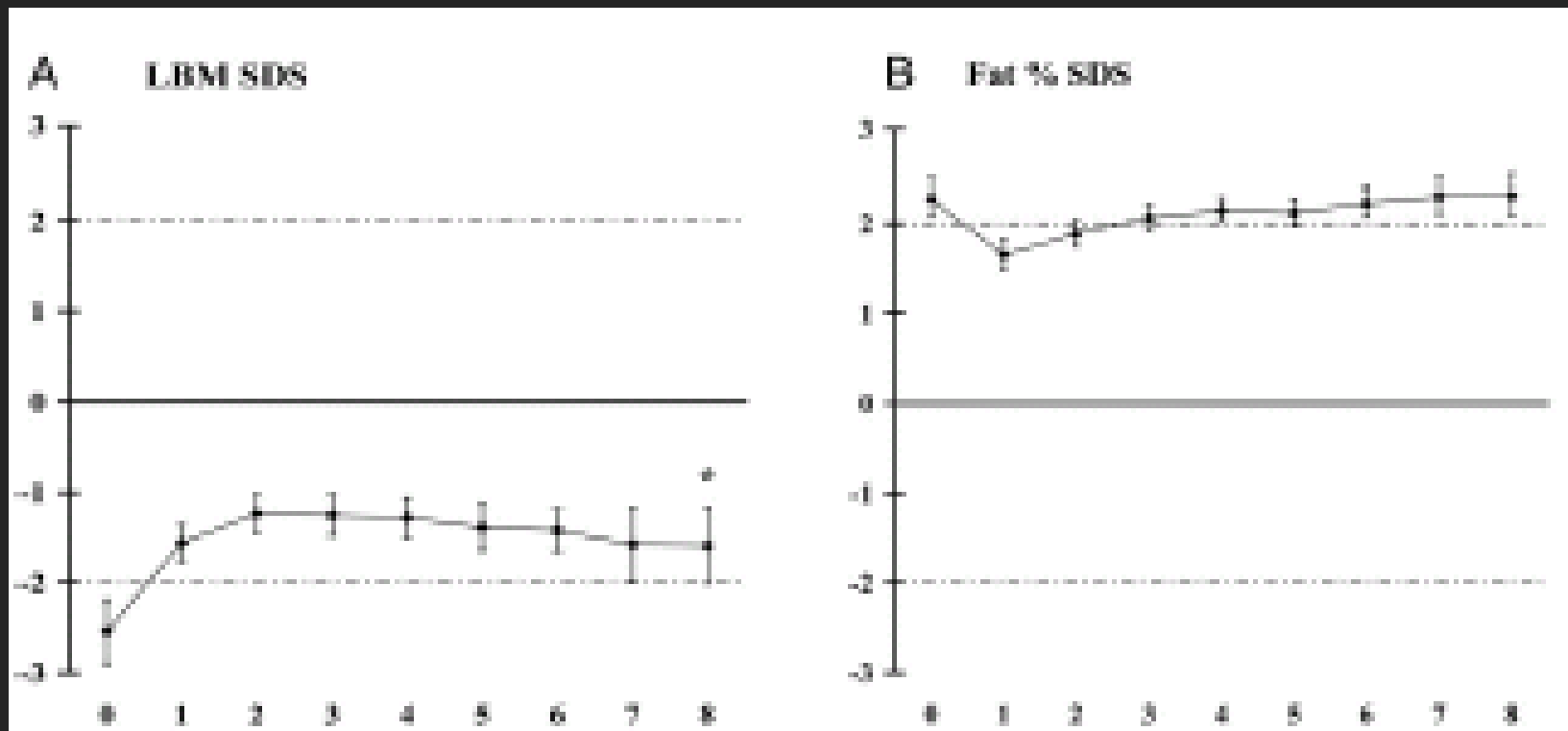
Body composition in PWS is altered



Infants with PWS have increased % fat and decreased muscle mass



GH Effect on Body Composition and BMI is Durable with Ongoing Tx



N = 60 (33 M/27 F); mean age at onset GH Tx: 5.4 yrs

Bakker et al. JCEM 2013

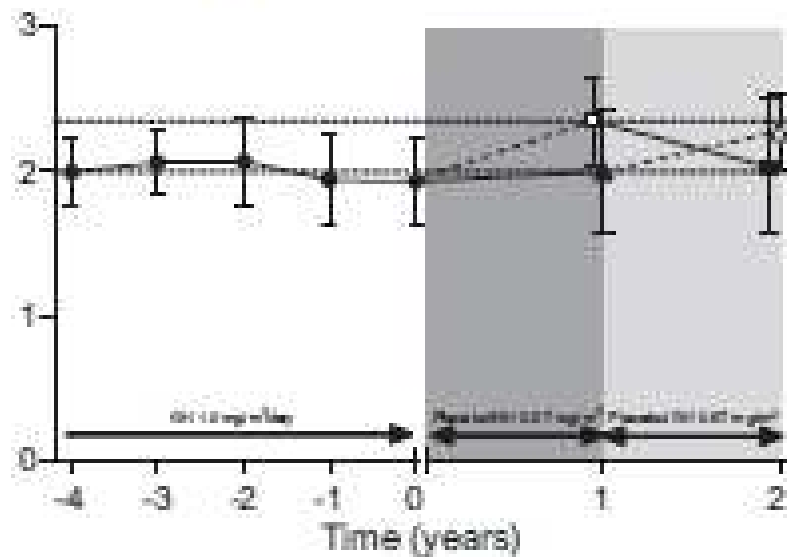
Beneficial effects of growth hormone in young adults with Prader-Willi syndrome: a 2-year cross-over trial

Dutch study group: Kuppens et al.

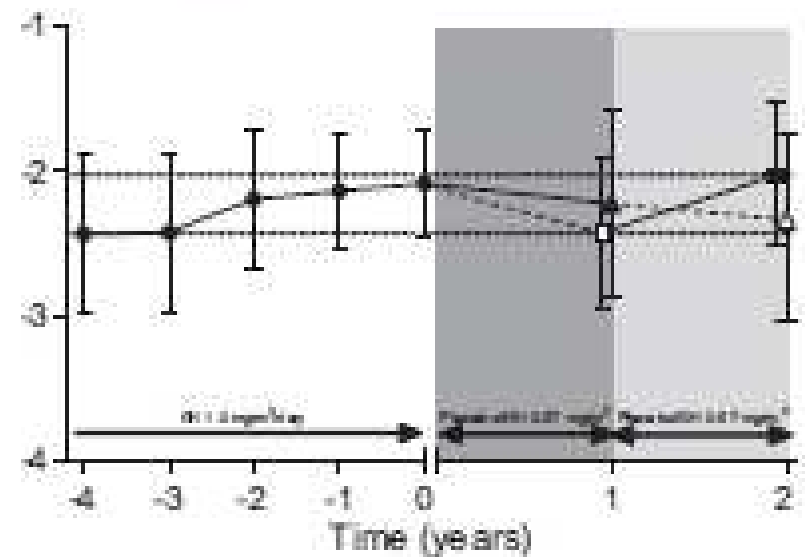
J Clin Endocrinol Metab

doi: 10.1210/jc.2016-2594

a FM% SDS



b LBM SDS



0.67 mg/m²/d GH

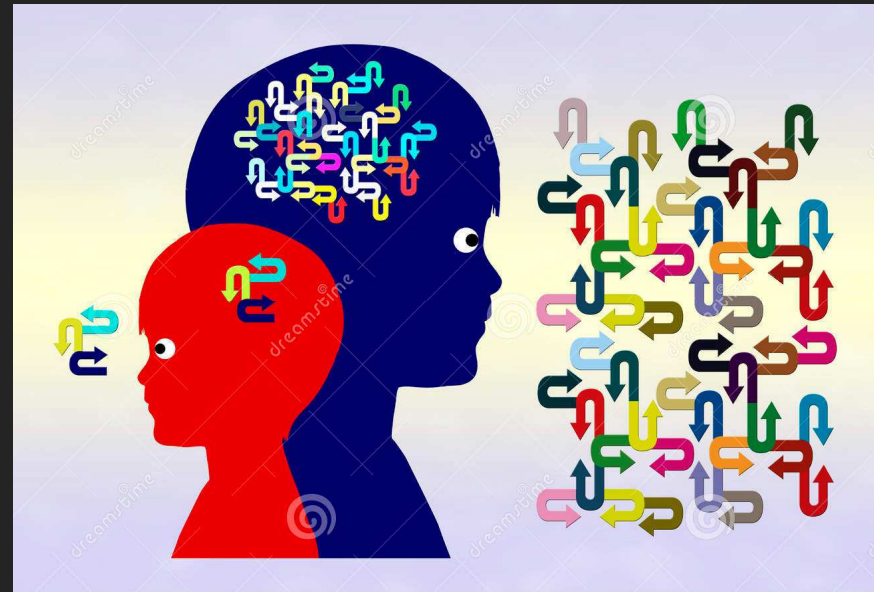
N=27; ----- no GH
_____ GH

GH therapy in PW syndrome and neuro-developmental benefits

Motor development



Cognition



GH Tx at early age onset and 6 years duration improves strength and agility

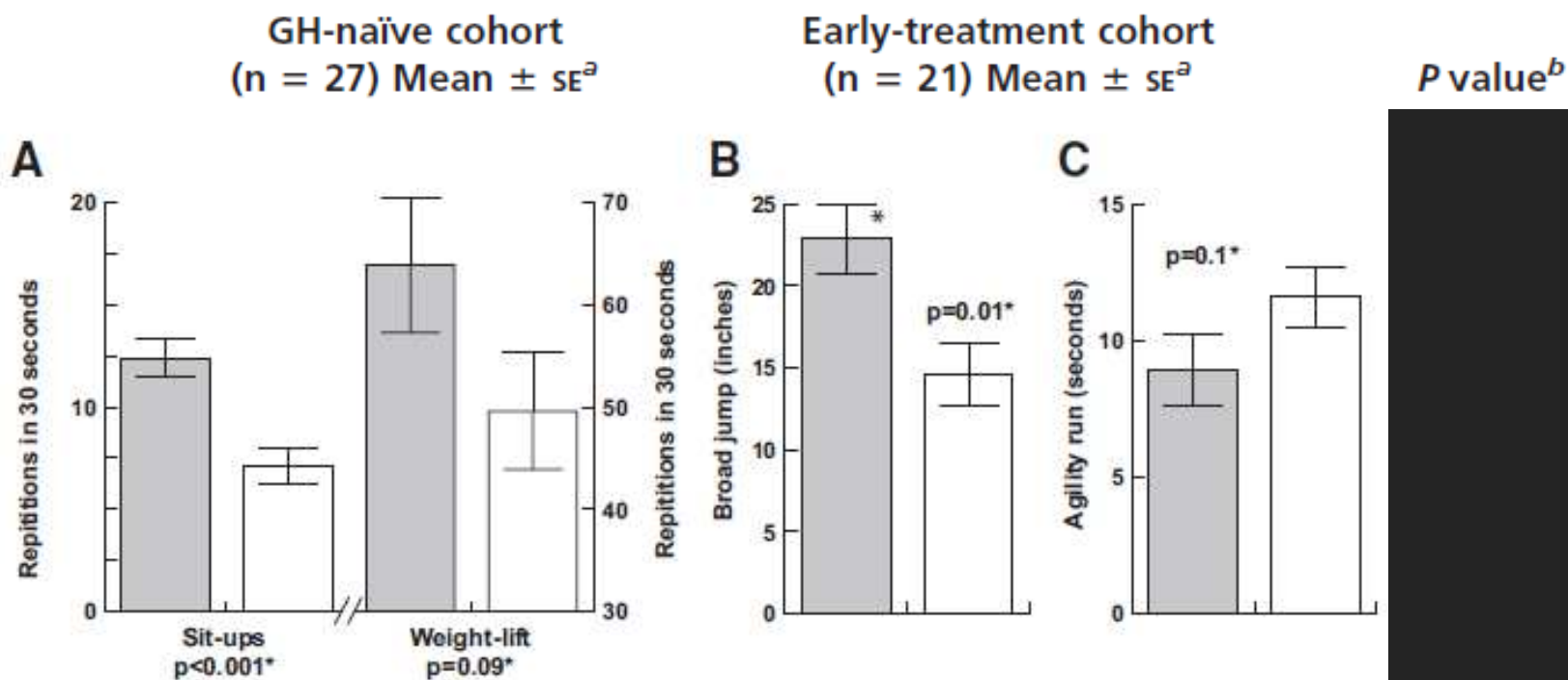


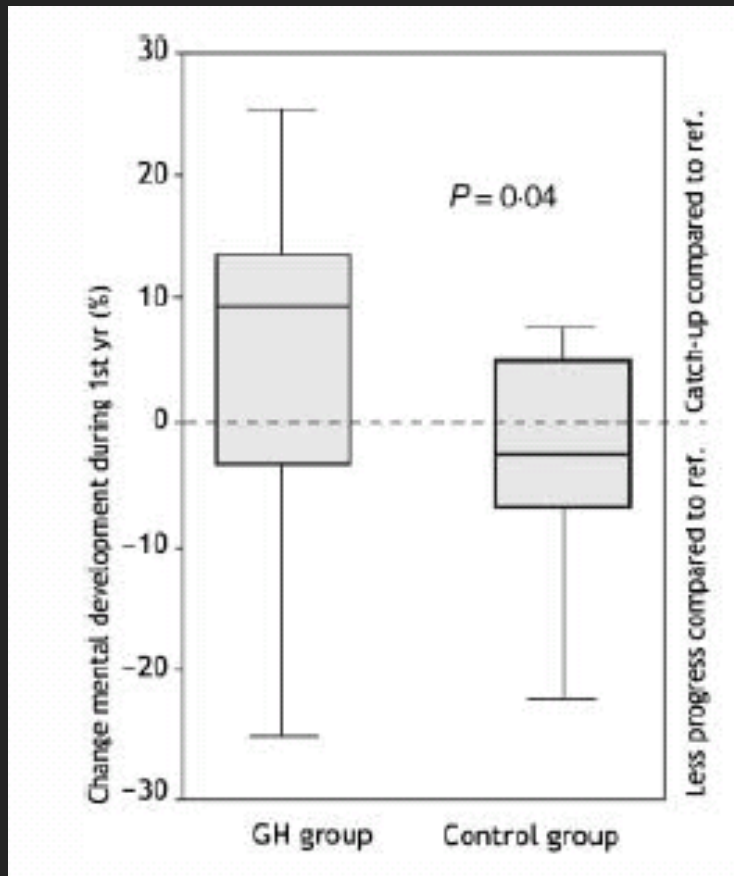
FIG. 3. Effect of GH on strength in PWS [GH treated (*shaded*) vs. untreated]. A, Repetitions in 30 sec. B, Broad jump. C, Agility. *, Age- and gender-matched analysis using ANCOVA.

Comparison of children
 Age 5-9 yrs
 Early Tx started mean 13 mo
 Dose 1 mg/m²/d X 6 yrs

J Clin Endocrinol Metab, March 2010, 95(3):1131-1136

Aaron L. Carrel, Susan E. Myers, Barbara Y. Whitman, Jens Eickhoff, and David B. Allen

Cognitive Development with GH treatment



Tx group [n=15]
Mean age 2.3 yrs

Dose: 1 mg/m²/day
GH x 12 months

Control group [n=14]
Mean age 1.5 yrs

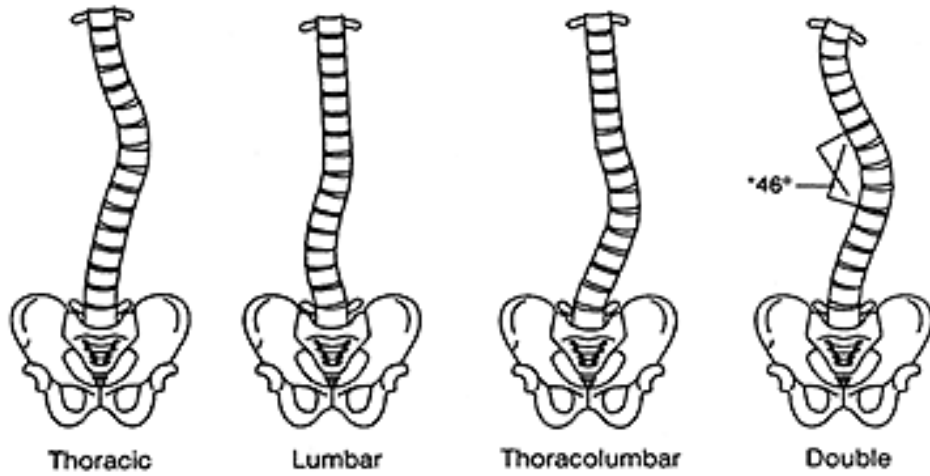
Bayley Scale of Infant
Development



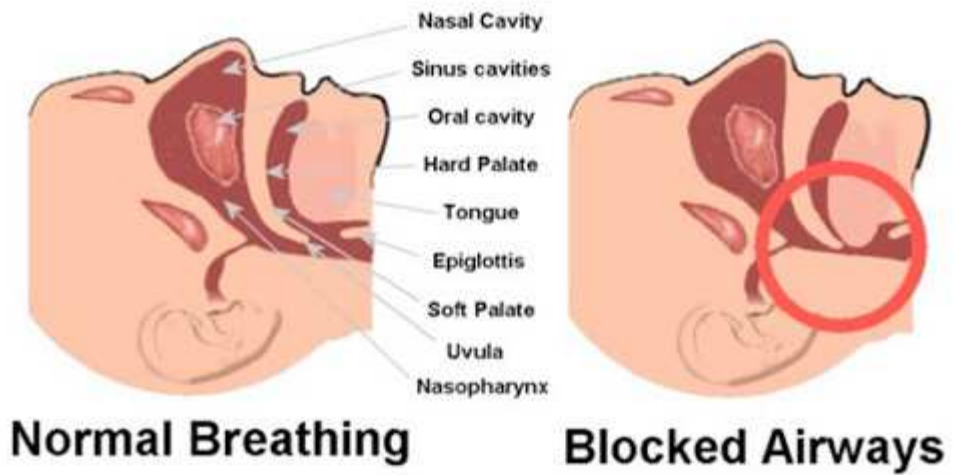
what's the harm?



Curve Patterns



Sleep Apnea

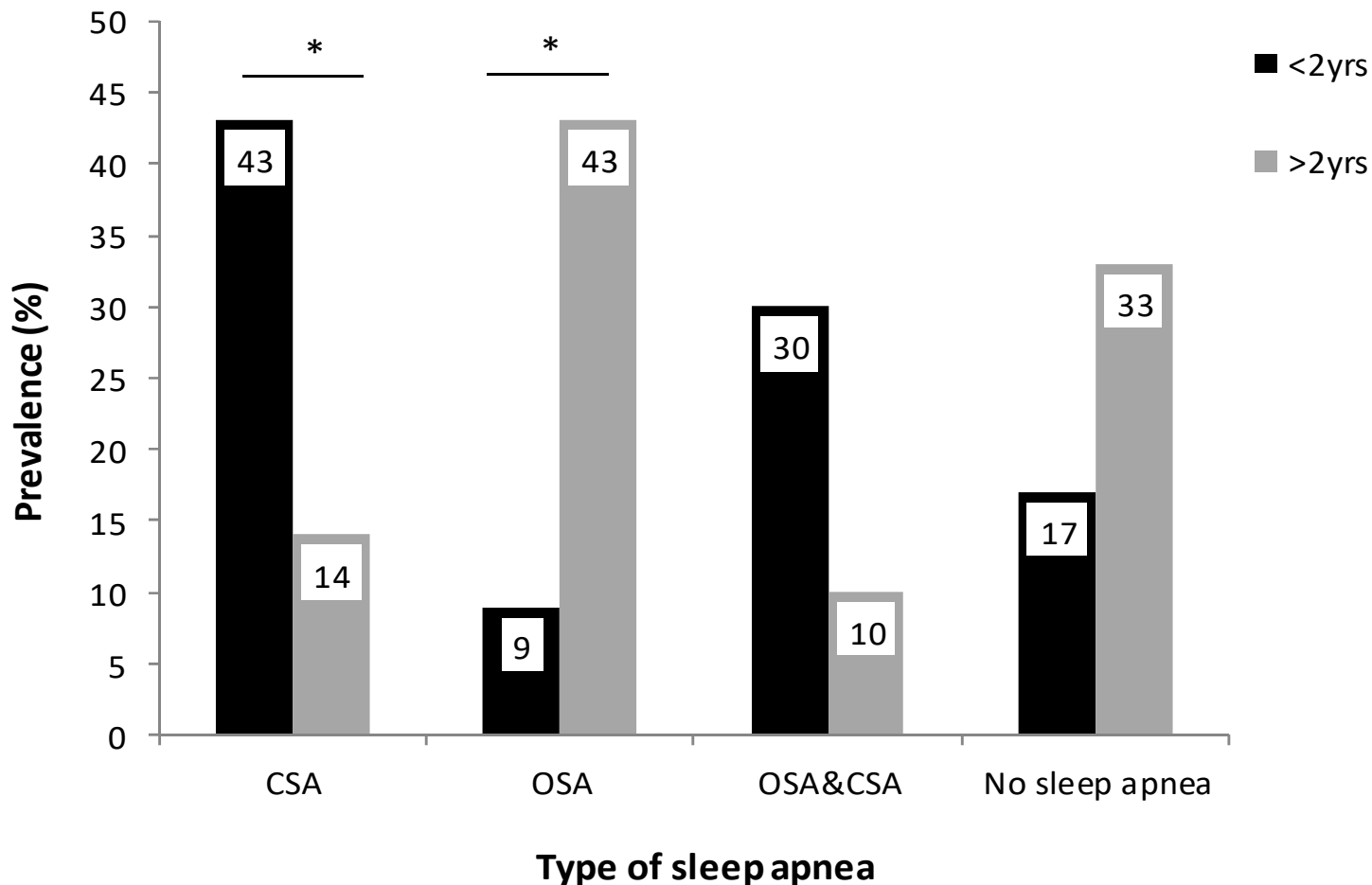


Clinically Important Age-Related Differences in Sleep Related Disordered Breathing in Infants and Children with Prader-Willi Syndrome

Michal Cohen^{1,2*}, Jill Hamilton^{1,2}, Indra Narang^{2,3}

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¹ Division of Endocrinology, The Hospital for Sick Children, Toronto, Ontario, Canada, ²The University of Toronto, Toronto, Ontario, Canada, ³ Division of Respiratory Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada



< 2 yrs n=23

≥ 2 yrs n=21

*severe
CSA in 9/23
< 2 yrs

Resolved
with O2
treatment

