retrospectively. **Results:** Among 55 subjects, 39 had 15q11-13 deletion and 16 had uniparental disomy (UPD). Twenty (36.3%) were born SGA. All patients received GH treatment, and 11 (20%) discontinued GH treatemnt. Mean age at GH treatment initiation was 2.5 (range 0.3-12.4) years, and mean duration of treatment was 6.3 (range 1.0-11.3) years. Current height-SDS (-0.36 vs -0.16) and BMI-SDS (1.44 vs 1.33) did not differ between AGA and SGA group. Two patients in SGA group, but none in AGA group had diabetes mellitus. Mean glucose level was also higher in SGA group (100.1 vs 114.4 mg/dL) Conclusions: Our report gives an overview of growth profile and metabolic dysfunctions recorded in GH treated PWS patients. Growth profile did not differ between AGA and SGA group. Glucose level was higher in SGA group, so more careful monitoring and prevention for DM will be required in SGA group.

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Impact of BMI on Growth Hormone Stimulation Tests in Children and Adolescents: A Systematic Review and Meta-Analysis

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Background: Peak stimulated growth hormone (GH) levels are known to decrease with increasing BMI, possibly leading to overdiagnosis of GH deficiency (GHD) in children with overweight and obesity. However, current guidelines do not provide guidance how to interpret peak GH values of these children, nor has this been assessed systematically. The aim of this systematic review and meta-analysis was to study the effect of BMI on stimulated peak GH values in children, and to quantify to which extent peak GH values in children with obesity are decreased. **Methods:** We searched the Medline, Embase, Cochrane, Web of Science, and Google Scholar databases (13 July 2020) for studies reporting impact of BMI on peak GH in children. Where possible, individual participant data was extracted and/or obtained from the authors. Primary outcome was the association between peak GH values and BMI standard deviation score (SDS). Pooled correlation coefficients were calculated under a random effects model, and exploratory moderator analyses and meta-regression were performed. Study heterogeneity was assessed using the I^2 statistic. For studies with available individual participant data, linear mixed-models regression analysis was performed with BMI SDS as predictor and ln(peak GH) as outcome, accounting for used GH stimulation agent (fixed effect) and study (random effect). This systematic review was performed in accordance to the PRISMA guidelines. **Results:** In total, 56 studies were included, providing data on n=5100 children (1346 with individual participant data). Across all studies, a pooled *r* of -0.37 (95% CI -0.44 to -0.31, n=2785) was found. Study heterogeneity was large (I^2=58%). Pubertal status, sex, presence of syndromic obesity, and mean age and BMI SDS of the population did not significantly moderate the pooled *r* (all p>0.05). Individual participant data analysis revealed a beta of -0.11 (95% CI -0.08 to -0.15, p<0.001), *i.e.,* per 1 point increase in BMI SDS, peak GH decreases by 11% (95% CI 7 to 14%). In the 8 studies performed in children referred for short stature, obesity was present in 27/893 (3.02%) children without GHD and in 36/615 (5.85%) children with GHD (p=0.0069). This corresponds to a RR of 1.43 (95% CI 1.14 to 1.78, p=0.002) for a diagnosis of GHD in children with short stature with obesity compared to children without obesity. **Discussion:** To our knowledge, this is the first systematic review and meta-analysis to investigate the impact of BMI on peak GH values in children, showing a significant negative correlation and risk of overdiagnosis of GHD in children with obesity. All in all, with ever-rising prevalence of pediatric obesity, our study highlights the urgent need for BMI (SDS)-specific cut-off values for GH stimulation tests in children.

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Impact of IGF-1 Normative Datasets on Indication and Outcome of Growth Hormone Stimulation Testing

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In the Netherlands, the diagnosis of growth hormone deficiency in children follows the Dutch national guidelines for Triage and Diagnosis of Growth Disorders in Children. Initial biochemical evaluation includes an IGF-1 measurement as screening parameter for growth hormone deficiency. Based on the clinical probability of growth hormone deficiency and the IGF-1 Z-score, a growth hormone stimulation test is performed if serum IGF-1 Z-score is < 0 SD in case of a high probability and if serum IGF-1 Z-score is < -1 SD in case of low probability. An IGF-1 Z-score > 0 SD virtually excludes a growth hormone deficiency disorder. The interpretation of growth hormone stimulation testing is dependent on both the peak growth hormone concentration, but also on the baseline IGF-1 Z-score, particularly in cases of partial deficiency. Although, nation wide, Dutch laboratories have harmonized their measurement for IGF-1 (as was previously done for growth hormone), a Dutch harmonized normative data set has not been widely adopted. Moreover a clinical evaluation of the implementation of this dataset based on dynamic testing has not been published. To assess the impact of choice of a particular normative dataset on the diagnosis of growth hormone deficiency we recalculated Z-scores of IGF-1 measurements between 2016 and 2019, using our home reference values based on de normative dataset by Elmlinger (E)[1], and using the normative datasets defined by Bidlingmaier (B)[2] and by the Dutch IGF-1 harmonization program (NL). Based on these three Z-scores, the outcomes of growth hormone stimulation tests performed in this period (n=86) were reassessed according to the interpretation described in the Dutch guideline. Using all three normative datasets the same 4 patients were identified as likely to have a growth hormone deficiency, whereas 10(E), 10(B), or 8(NL) patients were identified as possible partial growth hormone deficiency. In 70(E), 66(B) or 72(NL) patients the growth

hormone stimulation test was unaffected. Using normative dataset B, 6 patients displayed a pattern associated with a possible growth hormone resistance, or of bio-inactive growth hormone syndromes, which based on its incidence would be unlikely for a secondary care setting. A striking observation was however, that of all patients with a normal stimulation test 9 (E)/16 (B) or 30 (NL) had a IGF-1 Z-score of > 0 SD. This implies that, for the diagnosis of growth hormone deficiency, it is safe to implement the Dutch harmonized dataset, which in addition could result in a reduction in the number of growth hormone stimulation tests that have to be performed.

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Long-Term Effect of Aromatase Inhibition in Aromatase Excess Syndrome

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Aromatase excess syndrome (AEXS) is a very rare disorder characterized by prepubertal gynecomastia, bone age acceleration and early growth arrest. Heterozygote submicroscopic rearrangements within the promotor of *CYP19A1* result in overexpression of aromatase and enhanced aromatization of androgens. Long-term treatment effects of aromatase inhibitors are unknown. Retrospectively we collected data from file records of 7 boys (three sibling pairs and one sporadic case) with AEXS. Genetic analysis revealed upstream of *CYP19A1* a 165,901 bp deletion in 4 German cousins, a 198,662 bp deletion in 2 Japanese brothers and a 387,622 bp tandem duplication in a Japanese boy. All boys developed prepubertal gynecomastia, at 9.0 yr of age (median; range: 7.0 - 11.0). Height was +1.20 SDS (-0.24 - +1.98); predicted adult height was -1.29 (-3.29 - +1.09 SDS). Four boys were treated with anastrozole 1.0 mg daily, while three reached adult height untreated. Treatment with anastrozole was stopped after 5.6 yr (4.0 - 6.8). Three treated boys exceeded height prognosis by 2.4, 6.9 and 8.1 cm; while one untreated fell below prognosis by 8.6 cm. One treated with a low dose and two untreated reached their prognosis. Adult heights were -0.91 SDS with anastrozole (-2.86 - -0.29) and -0.15 SDS without (-2.31 - -0.03). Distance to target height was -0.22 SDS with anastrozole (-1.72 - +0.52) and +0.54 SDS without treatment (+0.23 - +1.30). Spontaneous growth in AEXS varied, even in the same family. Our data suggest that early started, long-term inhibition by aromatase inhibitor anastrozole (1 mg daily) promotes adult height in boys with AEXS.

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Long-Term Growth Hormone Therapy Does Not Advance Skeletal Maturation in Children and Adolescents

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Context: There is no consensus on the effect of recombinant human growth hormone (rhGH) therapy on skeletal maturation in children despite the current practice of annual monitoring of skeletal maturation with bone age in children on rhGH therapy. **Aims:** To investigate the effects of long-term rhGH therapy on skeletal age in children and explore the accuracy of bone age predicted adult height (BAPAH) at different ages based on 13 years of longitudinal data. **Methods:** A retrospective longitudinal study of 71 subjects aged 2-18 years, mean 9.9 ± 3.8y, treated with rhGH for non-syndromic short stature for a duration of 2-14y, mean, 5.5 ± 2.6y. Subjects with syndromic short stature and systemic illnesses such as renal failure were excluded. **Results:** Bone age minus chronological age (BA-CA) did not differ significantly between baseline and the end of rhGH therapy (-1.05 ± 1.42 vs -0.69 ± 1.63, p=0.09). Piece-wise regression however showed a quantifiable catch-up phenomenon in BA of 1.6 months per year of rhGH therapy in the first 6.5y, 95%CI 0.023 - 0.229, p=0.017, that plateaued thereafter, β=0.015, 95% CI -0.191-0.221, p=0.88. There was no relationship between BAPAH z score – height z score and the duration of rhGH therapy, p=0.68. BAPAH overestimated final adult height in younger subjects but became more precise in older subjects (p<0.0001). **Conclusion:** Long-term rhGH therapy demonstrated an initial catch-up phenomenon in skeletal maturation in the first 6.5y that plateaued thereafter with no overall significant advancement in bone age. These findings are reassuring and do not support the practice of yearly monitoring of skeletal maturation with bone age in children on rhGH therapy, especially in younger subjects where BAPAH is imprecise.

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LUM-201 Elicits Greater GH Response than Standard GH Secretagogues in Pediatric Growth Hormone Deficiency

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Presentation Type: OralScience Type and Topic: Clinical Trial **Introduction:** LUM-201 (ibutamoren, formerly MK-0677) is an orally administered GH-secretagogue that stimulates the GH secretagogue receptor (GHSR1a) in the hypothalamus and pituitary. LUM-201 is in development for long-term use in a subset of PGHD patients with moderate growth deficiencies. A diagnosis of PGHD is confirmed by low GH responses to standard GH secretagogues (clonidine, arginine, L-dopa, glucagon, insulin) so it is