## Title

## Growth Hormone Dosing in Obese Children

## Abstract (max 500 words)

## Background

Obesity has direct effects on dosing any drug by increasing the proportion of the total body weight (TBW) composed of lipid. Validated algorithms exist to convert a child’s actual weight to either an ideal (IBW) or lean body weight (LBW), but these are not widely used within paediatric practice. Pharmacokinetic data in obese patients do not exist for the majority of drugs and there is little direct evidence as to how obesity affects the overall risk-benefit of medications. Recombinant human growth hormone (rhGH) offers a unique opportunity to examine this, as the population receiving it routinely has height and weight measured, and the positive outcome (height gain) and adverse effect (increase in IGF-1) are both routinely measured. rhGH dosing derived by TBW may result in inappropriately high doses in obese children.

**Methods**

Retrospective audit of all paediatric patients treated with rhGH at a tertiary paediatric hospital in the UK with a catchment population of 2.7million**.** Change in height SDS and IGF-I SDS during the first year of treatment was stratified by initial BMI SDS in a mixed cohort, and a subgroup of GH deficient (GHD) patients. Alternative doses for those BMI SDS ≥2.0 (obese) were calculated using body surface area (BSA), IBW and LBW.

All patients who commenced treatment with rhGH between 2010 and 2014 were identified. The following data were extracted from the appointment prior to starting rhGH treatment: clinical indication, gender, BMI-SDS, height-SDS, and IGF-1 SDS. IGF-1 SDS 1 year (+/-3 months) and height SDS 1 year (+/-2 months) following the start of treatment was also recorded. Patients were studied in two cohorts: (1) an unselected cohort of patients with multiple diagnoses, and (2) only those with GHD. IGF-1 was measured using a validated solid-phase, enzyme-labeled chemiluminescent immunometric assay.

## Results

354 patients (133 female) received rhGH, including 213 (60.2%) with GHD. Obesity was present in 40 patients (11.3%) of the unselected cohort, and 32 (15.0%) of the GHD cohort. For GHD patients, gain in height SDS was directly related to BMI SDS, except in obese patients (p<0.05). For both the entire cohort, and GHD patients only, IGF-1 SDS was significantly higher in obese patients (p<0.0001 for both groups). Cross sectional data identified 265 children receiving rhGH, 81 (30.5%) with a BMI-SDS ≥1.75. For patients whose BMI-SDS ≥2.0, as expected the median daily dose of rhGH is reduced when the dose is calculated using IBW or LBW instead of TBW for both males and females. The dose reduction is largest when the dose is calculated using IBW. Alternate prescribing strategies for rhGH prescribing in obese patients suggest a saving of 27% - 38% annually.

## Conclusions

Gain in IGF-I SDS is greater in obese children, and is likely to be related to relatively higher doses of rhGH. Additional gain in height was not achieved at the higher doses administered to obese children. Alternative dosing strategies in the obese patient population should be examined in rigorous clinical trials.

## References